
IBEC
Institute for Bioengineering of Catalonia
EXCELENCIA
SEVERO
OCHOA
IBEC
Annual Report 2015

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EXCELENCIA SEVERO OCHOA

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Annual Report 2015

Introduction

For me, the year 2015 will always be memorable as the one in which IBEC received the Severo Ochoa Excellence Award, becoming the nineteenth Spanish centre to do so. The award is a huge milestone in the evolution and consolidation of IBEC, and is the confirmation of a success story that started only a few years ago. This recognition validates our new IBEC Strategy for 2014-2017, with the panel of evaluators giving the go-ahead for our plans.

In fact, the Severo Ochoa was one of many awards in 2015. We received the 'Human Resources Excellence in Research' stamp from the European Commission, in recognition of our commitment to continuously improving our HR policies in line with The European Charter of Researchers and The Code of Conduct for the Recruitment of Researchers (Charter and Code). We are one of just ten CERCA institutes to have received the award; in the Spain as a whole, only 21 institutions have been recognized.

On an individual level, several of our researchers also received recognition for their efforts. ICREA research professor Xavier Trepat, leader of the Integrative Cell and Tissue Dynamics group (page 132), was named winner of this year's Banc Sabadell Award for Biomedical Research for his work on understanding the fundamental biophysical mechanisms underlying cell interaction and communication. Gabriel Gomila, who heads IBEC's Nanoscale Bioelectrical Characterization group (page 68), received an ICREA Academia Prize for excellence in research and capacity for leadership.

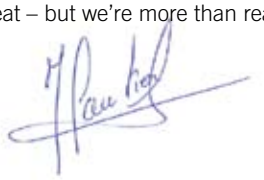
One of our newest recruits, Smart Nano-bio-devices group leader Samuel Sánchez (page 122), was the winner of the Premio Fundación Princesa de Girona Investigación Científica for his advances in the field of nanotechnology, as well as receiving a Proof of Concept grant from the European Research Council (ERC). Samuel started at IBEC in January 2015 alongside Nuria Montserrat, now Junior Group Leader of the Pluripotent Stem Cells and Activation of Endogenous Tissue Programs for Organ Regeneration group (page 98) and one of just eight young researchers in Catalonia to have received a prestigious ERC Starting Grant at the end of 2014. Our ERC success this year was further increased by the awarding of a consolidated grant to Elena Martínez (page 94) to engineer models of the intestinal epithelium. Joining us later in the year was Junior Group Leader Lorenzo Albertazzi (page 44), who aims to create a molecular 'toolbox' of supramolecular biomimetic structures – self-assembled synthetic materials able to mimic the complexity of biological machinery – for applications in nanomedicine and biotechnology, such as transporting drugs into the body or attacking viruses. His work is supported in part by the AXA Research Fund.

These young researchers, as well as the existing talent, have contributed to make IBEC's scientific output in 2015 among the best yet. During the year we celebrated 5 *Nature* group papers; 107 indexed journal papers in total, 77% of them in the first quartile; a new patent; and 13 PhD theses. Research highlights during the year included the discovery that hydraulic fracturing, or 'fracking', plays an important role in the epithelial tissues that lining the internal and external surfaces of our bodies; the participation of IBEC researchers in a study that used molecular "scissors" to remove mitochondrial mutations in mouse eggs; and the first ever fully biocompatible self-propelling particles that are powered by enzymes that consume biological fuels, such as glucose. 2015 also saw our collection of cutting-edge equipment receive the welcome additions of a BioAFM microscope and a 3D bioprinter for tissue engineering and regeneration.

On an institutional level, IBEC's collaboration with the Obra Social "La Caixa" has been going from strength to strength, with the launch of a joint programme on Healthy Living and Active Ageing and two projects funded under the first CaixaImpulse call, as well as those funded under the established RecerCaixa one. 2015 also saw IBEC continue to coordinate two Spanish Networks of Excellence: Nanomed Spain, the Spanish Platform for Nanotechnology; and the Spanish node of the European Institute of Innovation and Technology's Knowledge and Innovation Community (KIC) for healthy living and active ageing, EIT Health. IBEC also now collaborates on a project, coordinated by clinicians from Sant Joan de Déu/Hospital Clínic, with the Cellex Foundation; and the institute also became the home of the Associació Catalana d'Entitats de Recerca (ACER) as I took over the reins as president.

At the end of the year we were delighted to open our first call for applicants under IBEC's International PhD Programme. In the 2015 call, fellowships are being offered by the "la Caixa" foundation for the academic year 2016-2017 and by MINECO, through the 'Ayudas para contratos predoctorales para la formación de doctores' 2016 call. With our societal responsibilities in mind, we also made a big effort regarding transparency and the abundant information included in our webpage to satisfy the growing demand.

With all this, as well as hosting major events such as B·Debate, the TAU/IBEC symposium, and CellMech2015, and welcoming visitors that included Carmen Vela, Spain's secretary of state for research, development and innovation, Catalan political party Convergència i Unió (CIU) and a delegation from Kobe in Japan, 2015 was certainly a year to remember. As we move into 2016, it's going to be hard to beat – but we're more than ready to try!



Josep Samitier
Director of IBEC

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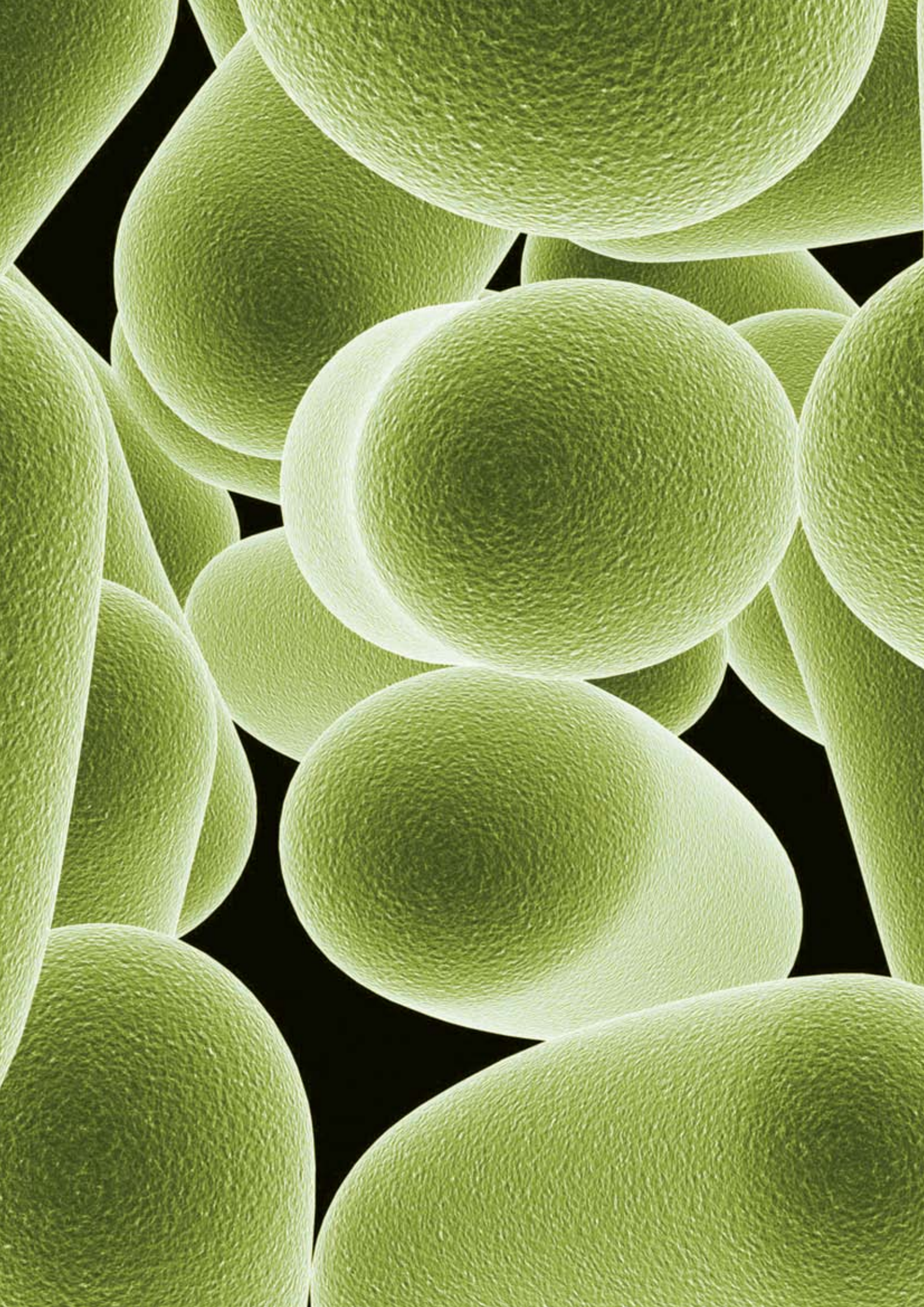
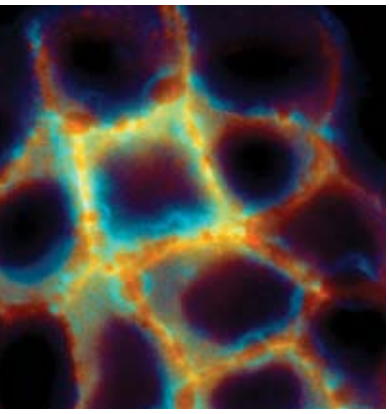
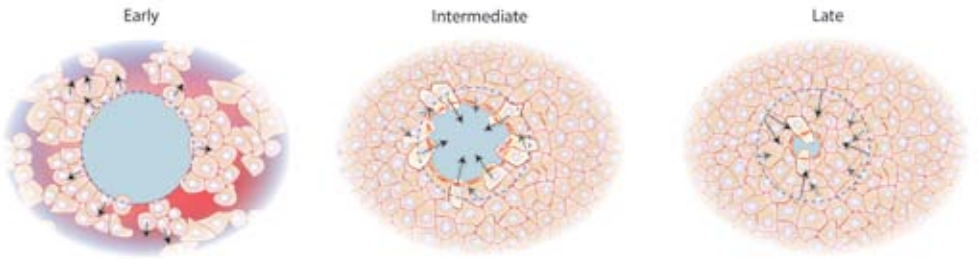


2015 in review

Scientific Highlights





Above: Wounds heal using a cellular 'tug-of-war': forces exerted by the cells surrounding the gap (dotted blue line) extend away at first, then direct towards the gap during contraction of the purse-string cable (red).

Left: 'Fracking' found in living tissues: the small fractures between cells, in blue, close within minutes.

January 2015

Key player identified in bacterial infections

In their paper published in *Infection and Immunity*, IBEC's Bacterial Infections: Antimicrobial Therapies group (page 128) found that ribonucleotide reductases (RNRs) – enzymes that provide the building blocks for DNA replication in all living cells – play an important role in *Escherichia coli* virulence and infection. Using intestinal cells and an *in vivo* model of infection, the group found that inactivating – or 'knocking out' – the protein nrdD and the transcriptional regulator nrdR decreased the ability of Crohn's disease-associated adherent-invasive *E. coli* strain AIEC LF82 to colonize the mucus of the gut. "This shows that RNRs, and particularly the NrdR protein, govern the virulence of Crohn's disease-associated *E. coli* by regulating the bacteria's movement and spread," explains Eduard Torrents, junior group leader at IBEC.

Dreux, N. et al (2015). Ribonucleotide reductase NrdR as a novel regulator for motility and chemotaxis during adherent-invasive Escherichia coli *infection.* Infection and Immunity *834, 1305-1317*

A further step towards light-controlled drugs

In 2014, scientists at IBEC, IRB Barcelona and the UB announced that they had achieved photo-switchable, or light-regulated, molecules to control protein-protein interactions, a major step towards the development of targeted, light-controlled drugs whose effects would be limited to a specific area and time, reducing side effects. In 2015, the same researchers made a discovery that greatly expands the field of potential inhibitors, as it questions the need for one of the previously supposed design requisites of these molecules.

"As many protein-protein interactions are mediated by short, often helical, linear peptides (small proteins), we thought our photoswitchable molecules had to be designed to mimic these rigid peptides in order to be able to inhibit them," explains Pau Gorostiza of IBEC's Nanoprobes and Nanoswitches group (page 72). "In fact, we found that they don't need to have the same rigid structure, and that flexible structures actually show a greater inhibitory capacity, as well as better photoswitching ability." This means that when developing further potential inhibitors, researchers can look to the wide group of more flexible peptides for their candidates.

Martín-Quirós, A. et al (2015). Absence of a stable secondary structure is not a limitation for photoswitchable inhibitors of β-Arrestin/β-Adaptin 2 Protein-Protein Interaction. Chemistry & Biology *221, 31-37*

Wounds heal using a cellular 'tug-of-war'

In a collaboration with colleagues at the Mechanobiology Institute in Singapore, IBEC researchers revealed in a *Nature Communications* paper that a 'tug-of-war' takes place

after our skin or other epithelial layer is damaged, particularly in deep injuries.

"We saw that the cells at the edge of the non-adherent gap spread themselves out as far as possible towards the centre – but measuring the direction of force revealed that they are actually pushing away from it," explains Xavier Trepat (page 132). This actually stabilises the cells like a cantilever bridge, where support at either end anchors the extension of the bridge into space until the two sides meet in the middle. Once the cells have spread as far as possible into the gap, a contractile 'purse-string' cable forms across the cells, encircling the gap, and the force exerted by these cells is reversed and the cells begin to pull each other towards the centre of the gap, continually speeding up the contraction of the protein cable. "As the cells move inwards to close the empty space, more contractile cables can reach out over the gap and connect to the other side," says Xavier. "These cables can contract rapidly, leading to the formation of a suspended cell sheet over the gap and complete closure."

This new knowledge of the mechanical properties of skin and internal epithelial cells may lead to advances in wound repair, especially in cases where the ECM is compromised.

Vedula, S.R. et al (2015). Mechanics of epithelial closure over non-adherent environments. Nat Commun., *6:6111*

February 2015

'Fracking' found in living tissues

In an article published in *Nature Materials*, researchers described their discovery that hydraulic fracturing, or 'fracking', plays an important role in the epithelial tissues that lining the internal and external surfaces of our bodies. "We wanted to understand how living tissues behave in response to the types of distortions experienced as a result of the heart beating, or breathing, for example," says Xavier Trepat (page 132), ICREA researcher and group leader at IBEC. "We expected that, faced with very large distortions, the tissues would respond by snapping as if under excessive tension. Surprisingly, we found that the behavior of the fibrous material that surrounds cells – the extracellular matrix – is a lot like a sponge; when squeezed, it releases water. The same happens when we compress the tissues of our body; they release water which, when it hits the cells, creates an hydraulic fracture."

Fracking has different consequences in living tissue than in the earth's subsoil; ruptures underground are irreversible, whereas the body is able to repair hydraulic breaks. The discovery of fracking in living tissues open avenues to new biotechnological applications. "Fracking could be used to cause small, reversible fractures in difficult to access tissues, and these could be used to deliver drugs in a controlled manner," says Xavier.

Casares, L. et al (2015). Hydraulic fracture during epithelial stretching. Nature Materials, *143, 343-351*

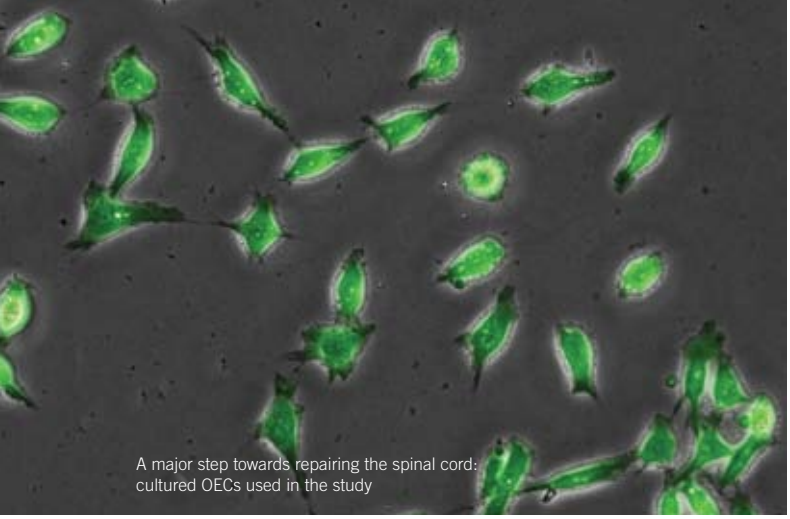
March 2015

A major step towards repairing the spinal cord

The olfactory system is an area of the body that can renew itself, and it does this by using olfactory ensheathing cells (OECs) to guide newly formed axons – long projections of nerve cells – towards the body's central nervous system. Naturally, researchers have already tried transplanting OECs to the spine, to see if this ability also works to promote axonal regeneration in spinal cord injuries and neural diseases. But in this environment, the good work of the OECs is curtailed by the persistent presence of inhibitory molecules that impede not only their guiding abilities, but also the regrowth of axons.

In a paper published in *Cell Mol Life Sci*, three research groups at IBEC revealed that a particular molecule, chondroitin sulphate proteoglycans or CSPG for short, causes this impediment by adversely affecting the migratory abilities of the OECs. The researchers already knew that OEC migration is also inhibited by the insulating material myelin, but this could be overcome by engineering a batch of OECs that over-produce the Nogo receptor protein, which abolishes the inhibitory properties of myelin. These OECs, when introduced into damaged spinal cords, are able to migrate longer distances in this inhibitory post-lesion environment. "We already knew how to deal with myelin and stop it inhibiting OEC migration," says José Antonio del Rio (page 113). "Now we know we have to try to do the same thing with CSPG, so that we can move closer to having OECs with their full migratory capabilities intact."

Reginensi, D. et al (2015). Increased migration of olfactory ensheathing cells secreting the Nogo receptor ectodomain over inhibitory substrates and lesioned spinal cord. Cell Mol Life Sci, *7214, 2719-2737*



A major step towards repairing the spinal cord: cultured OECs used in the study

New hope against antibiotic resistance

The increasing prevalence of bacteria that are resistant to current antibiotics pose an escalating threat to human health. In 2015, researchers at IBEC identified a molecule with huge potential as a new type of antibacterial agent.

"During the course of infection, bacteria need to multiply inside the body, and they require active DNA synthesis to multiply," says Eduard Torrents of the Bacterial Infections: Antimicrobial Therapies group (page 128). "By targeting the key enzyme that allows this to happen, we can inhibit the growth of undesirable and disease-causing bacteria."

The molecule, known as M-HA, works as a 'radical scavenger' compound to inhibit ribonucleotide reductase, an essential enzyme in DNA replication and repair. It also demonstrates low toxicity in eukaryotic cells, which heralds a great improvement on existing RNR-inhibiting drugs, which are mostly used against cancer or viruses and are too toxic to be used as antibacterials.

"It's crucial that we find new antibacterials that function in a new way in order to replace the existing antibiotics that are being rendered useless by bacterical resistance," says Eduard. "These new drug candidates should also work in a way which will not allow such a level of resistance to build up all over again."

Julián, E. et al (2015). Methyl-hydroxylamine as an efficacious antibacterial agent that targets the ribonucleotide reductase enzyme. PLoS ONE *103*

April 2015

A new mechanism in cell communication that promotes metastasis

The Integrative Cell and Tissue Dynamics group (page 132) led by Xavier Trepat, ICREA researcher at IBEC, showed in *Nature Cell Biology* that the physics of communication between cells is as important as the chemistry behind it. The researchers – together with colleagues at the Technical University of Catalonia (UPC) and the Rovira i Virgili University (URV) – combined molecular biology, nanotechnology and mathematical models to not only identify the molecules involved in the physical communication between cells, but also to show that some of these molecules are altered in various cancers. "We expected to find a single protein responsible for the transmission of forces between cells, and we found a dozen," says Xavier.

The mechanisms they discovered open new possibilities for the control of metastasis, but what has surprised researchers has been discovering how these proteins work together. "Our analysis suggests that proteins control cell force in a very similar way to the way modern electronic systems control appliances – that is, using what engineers call proportional-integral-derivative controller (PID controller) systems," explains Xavier. "This shows that cells developed advanced control systems million of years before we did!"

Bazellières, E. et al (2015). Control of cell-cell forces and collective cell dynamics by the intercellular adhesome. Nature Cell Biology *174, 409-420*

Genetic "editing" to fight inherited disease

Researchers at IBEC participated in a study that used molecular "scissors" to remove mitochondrial mutations in mouse eggs.

This group of diseases affecting the mitochondria – small 'power plants' that generate energy in the body's cells – are transmitted exclusively from mother to child. The only option today for parents who want to make sure their children don't inherit mitochondrial diseases is to use pre-implantation genetic diagnosis to select embryos, although this still doesn't guarantee a healthy baby.

In the study, published in *Cell*, researchers developed a simple technique to eliminate mitochondrial mutations in eggs or embryos at an early stage of development. The researchers focused on two types of molecules – nucleases – that can be designed to cut specific DNA strands and function like a sort of "molecular scissors". A team at the Salk Institute, which led the research, designed nucleases that only cut the mitochondrial DNA in eggs or embryos containing muta-

tions that cause disease, leaving healthy mitochondria intact. Nuria Montserrat (page 98), group leader at IBEC, contributed the characterization and design of cellular systems used.

Reddy, P. et al (2015). Selective elimination of mitochondrial mutations in the germline by genome editing. Cell *1613, 459-469*

IBEC groups join forces to combat chronic bacterial infections

A study published in the *Journal of Controlled Release* described a new nanoparticle strategy able to target hard-to tackle infections caused by biofilm-forming bacteria.

In the study, which involved IBEC's Biomaterials for Regenerative Therapies (page 58) and Bacterial Infections: Antimicrobial Therapies (page 128) groups, PLGA nanoparticles loaded with the antibiotic ciprofloxacin which had been functionalized with DNase I, a nuclease that digests DNA, were fabricated. They were then tested for antibiofilm activity against biofilms of *P. aeruginosa*, a bacterium that's often the cause of lung problems in cystic fibrosis patients, and their results compared favorably with those of free-soluble ciprofloxacin, and ciprofloxacin encapsulated in untreated and poly(lysine)-coated nanoparticles.

The results open new avenues towards eradicating established bacterial biofilms by modifying the surface of the nanoparticles and thus tailoring them to target specific bacterial infections.

Baelo, A. et al (2015). Disassembling bacterial extracellular matrix with DNase-coated nanoparticles to enhance antibiotic delivery in biofilm infections. Journal of Controlled Release *209, 150-158*

June 2015

Malaria strategy uses unaffected red blood cells as drug carriers

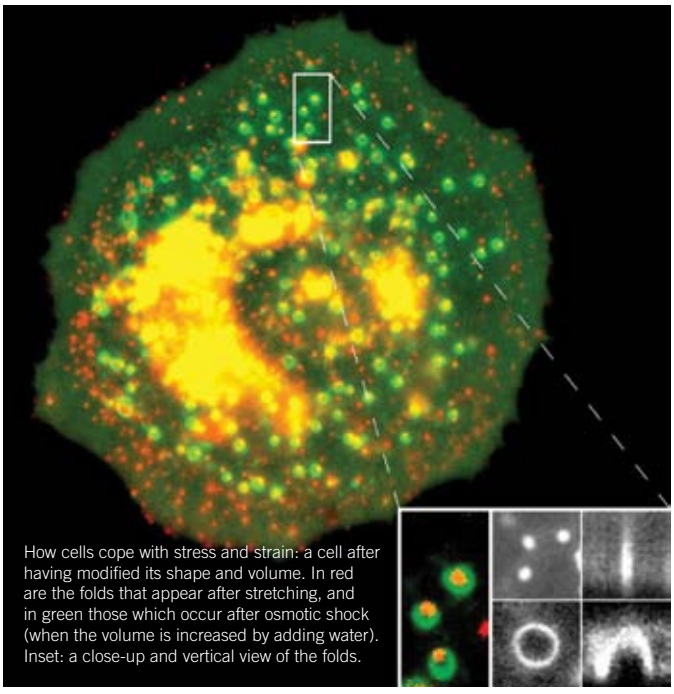
IBEC and ISGlobal's joint unit, Nanomalaria (page 64), published a new therapeutic strategy against malaria which tackles a major hurdle in current treatments, which is that most antimalarial drugs start working on the infected cell quite late in *Plasmodium*'s life cycle, when their effect is often too short to be lethal to the parasite. The new strategy proposes using unaffected red blood cells (RBCs) as drug carriers, thereby ensuring that the parasite doesn't even get the chance to start its development cycle, which it normally does during a 'recovery period' after a quick and stealthy entry into an RBC.

The work was done in collaboration with GlaxoSmithKline, as one of the few cases of partnerships involving industry in the research and development of innovative antimalarial nanomedicines.

Moles, E. et al (2015). Immunoliposome-mediated drug delivery to Plasmodium*-infected and non-infected red blood cells as a dual therapeutic/prophylactic antimalarial strategy.* Journal of Controlled Release *210, 217-229*

How cells cope with stress and strain

During critical biological processes such as embryonic development, breathing, the pumping of the heart, wound healing and tumor growth, the body's cells are stretched and distorted to adapt to their environment. The cell's membrane, though, is rigid and inflexible. So how does it withstand all these constant deformations without breaking?



How cells cope with stress and strain: a cell after having modified its shape and volume. In red are the folds that appear after stretching, and in green those which occur after osmotic shock (when the volume is increased by adding water). Inset: a close-up and vertical view of the folds.

Researchers at IBEC demonstrated that every time a cell is compressed or stretched, it forms and then quickly eliminates small folds in its membrane to allow for changes and prevent tearing. The study also reveals that the area of the cell membrane is able to increase or decrease to accommodate the cell shape almost immediately, which is essential for vital processes such as breathing.

"Given that continuous cellular shape changes also occur in cancer or during wound healing, the implications of this finding are very important," says Pere Roca-Cusachs (page 102), who led the study. "The challenge now is to find out to what extent this new knowledge can help us to intercept during tumor progression, improve tissue regeneration, or to solve problems that occur in respiratory and cardiovascular diseases."

Kosmalska, A. J. et al (2015). Physical principles of membrane remodelling during cell mechanoadaptation. Nature Communications *6, 7292*

July 2015

New avenues to understanding epilepsy in rapid progressive dementia

In *Scientific Reports*, the Molecular and Cellular Neurobiotechnology group (page 113) outlined findings that could lead to a better understanding of rapid neurodegenerative diseases that involve epileptic fits, such as Creutzfeldt-Jacob disease (CJD).

The cellular prion protein PrP^C – found naturally in healthy brain and decreased in several diseases such as bovine spongiform encephalopathy and human rapid progressive dementia (RPD) CJD – has long been thought to be neuroprotective, so the IBEC researchers hypothesized that an explanation for seizure symptoms in these neurodegenerative diseases could be associated with the loss of function of PrP^C. "We demonstrated that mice lacking PrP^C showed an increased susceptibility to epileptic episodes leading to cell death in the hippocampal region, supporting the notion that the protein is involved in neuroprotection against seizures, and that it actively participates in the increased epileptic response observed in mice, independently of the genetic background, that lack it," says José Antonio del Río.

Their study, which also involved researchers at the UB, IDIBELL, CIBERNED, CISA-INIA, DZNE in Germany, and SISSA in Italy, also revealed that other factors in parallel with PrP^C deletion, such as the genetic background of some of the mice used for PrP^C analysis, or the presence of so-called 'Prnp-flanking genes' in the mixed genetic background of PrP^C knockout mice, might contribute to susceptibility to epileptic fits in its absence.

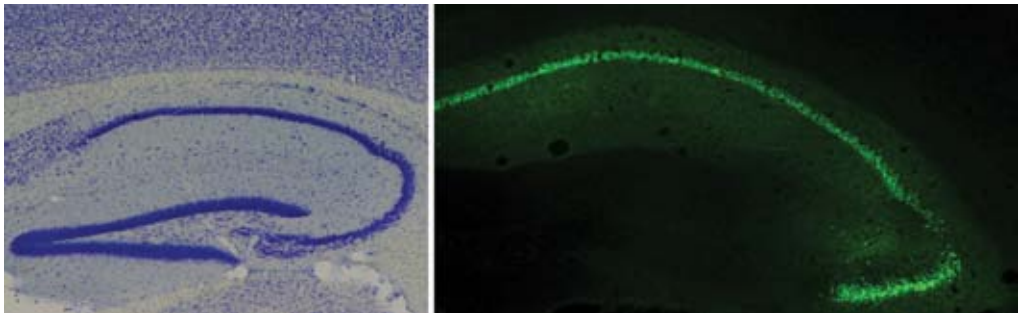
Carulla, P. et al (2015). Involvement of PrP^C in kainate-induced excitotoxicity in several mouse strains. Scientific Reports *5, 11971*

September 2015

Fourth generation biomaterial mimics bone

IBEC researchers elucidated in *Nanoscale* a brand new biomaterial that paves the way towards a fourth generation of effective struc-

New avenues to understanding epilepsy in rapid progressive dementia: hippocampal section of two prion protein knock-out mice that over-express a truncated form of the prion protein DF35. On the left, a Nissl staining of a non-treated mice showing the typical structure of the CA1-CA3 pyramidal layers. On the right, FluoroJade B staining 24h after the KA-treatment. The stain specifically marks neuronal degeneration, so the neurodegenerative pattern shown is related only to KA-treatment, demonstrating the essential neuroprotective role of the prion protein.



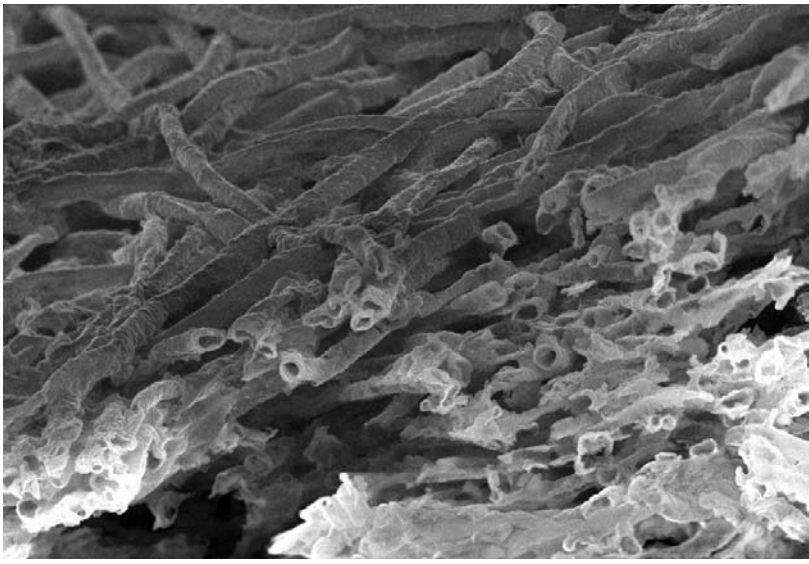
tures for tissue regeneration.

The Biomaterials for Regenerative Therapies group (page 58) and their collaborators in The Netherlands and Poland described a hybrid material which faithfully mimics the structure of bone's extracellular matrix. By doing so, it offers the correct interactions between constituents to encourage cells to behave in the way required to successfully regenerate tissue.

To make their hybrid material, the group took polylactic acid electrospun fibers and coated them with a bioactive, organically modified glass known as ormoglass. In comparison to fibers without the glass, the material showed improved hydrophilicity and mechanical properties, better bioactive ion release to aid angiogenesis, and exhibited a surface roughness that enabled good cell adhesion and spreading after just one day of culture.

"With this new material we're closer to the next generation, which would mimic natural tissues, recreating the molecular architecture and biochemical environment to surround cells with the proper stimuli to spread and grow," says Nadège Sachot, first author on the paper. There is also the possibility to expand the material's application to additional tissue types depending on architecture and composition, such as an angiogenic coating for regeneration of muscles, or a tube coating for arterial replacement.

Sachot, N.et al (2015). Towards 4th generation biomaterials: A covalent hybrid polymer-ormoglass architecture. Nanoscale *737, 15349-15361*



4th generation biomaterial mimics bone: morphology of the inorganic shell remaining after thermal treatment of the fibers. Only the inorganic bioactive coating skeleton remains, reproducing their previous shape.

October 2015

Safe nanomotors propelled by sugar

Researchers developed the first ever fully biocompatible self-propelling particles that are powered by enzymes that consume biological fuels, such as glucose.

In *Nanoletters*, IBEC group leader and ICREA research professor Samuel Sánchez (page 122) and his collaborators at Max Planck Institute for Intelligent Systems (MPI-IS), the University of Tübingen and the MPI for Solid State Research, described their fabrication of enzyme-powered synthetic nanomotors that overcome the disadvantages of current systems by being both biocompatible and powered by biologically benign fuels.

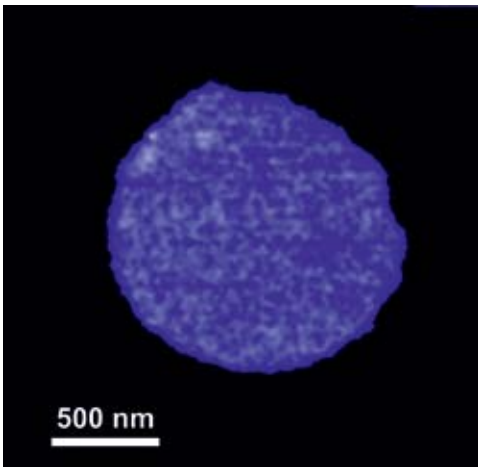
"To be safe for use in applications in medicine in the body, nanoparticles need to be made out of biocompatible and biodegradable materials, as well as being capable of both autonomous motion using biologically benign fuels and cargo delivery – such as drug delivery – at small scales," says Samuel. "We've tackled all these issues with our new particles. They're made from hollow mesoporous silica proven to be harmless to cells and tissues, and their self-propulsion is powered by the biocatalytic reactions of three different naturally occurring enzymes: catalase, urease, and glucose oxidase."

The next steps for the researchers will be to explore how to increase the effective driving force and guide their bio-friendly nanomotors by external manipulation methods, such as chemotaxis, magnetic control or ultrasound, leading to directional movement for active drug delivery to specific locations.

Ma, X. et al (2015). Enzyme-Powered Hollow Mesoporous Janus Nanomotors. Nano Lett.*, 15 (10), pp 7043–7050*

Possible new treatment for bladder cancer using a mycobacterium

Collaborators at IBEC and the Universitat Autònoma de Barcelona found a mycobacterium that is more effective in treating superficial bladder cancer and does not cause infections, unlike those used up to now.



Another big step towards understanding the electric properties of the cell: nanoscale dielectric image of a bacteriorhodopsin monolayer patch

The administration of the bacterium *Mycobacterium bovis* (BCG) is the current treatment for superficial bladder cancer, and is inserted directly into the bladder through a catheter. BCG prevents new tumours from appearing, but despite its efficacy it has many adverse side effects, the most serious being BCG infections that need to be treated with antituberculous drugs.

The researchers discovered that another type, *Mycobacterium brumae*, is able to reduce the growth of tumour cells in the bladder and activate an immune response. *M. brumae* is a rapid-growth, non-pathogenic mycobacterium, making it easier and quicker to produce on a large scale than BCG, which is significant given that in the last few years BCG production problems have led to supply issues for certain bladder cancer patients.

The study, published in the journal *European Urology Focus*, was led by Dr. Esther Julián of the UAB's Department of Genetics and Microbiology and conducted in collaboration with the Bacterial Infections and Antimicrobial Therapies group (page 128) led by Eduard Torrents at IBEC.

Noguera-Ortega. E., et al (2015). The non-pathogenic Mycobacterium brumae inhibits bladder cancer growth in vitro, ex vivo, *and* in vivo. European Urology Focus, *DOI: 10.1016/j.euf.2015.03.003.*

Another step towards understanding cells' electric properties

Having measured the electric polarizability – a fundamental property that directly influences its biological functions – of DNA for the first time ever last year, IBEC´s Nanoscale Bioelectrical Characterization group (page 68) made a further breakthrough in the understanding of the dielectric properties of cell constituents by measuring the electric polarizability of the main components of the cell membrane – namely lipids, sterols and proteins – with a spatial resolution down to 50nm.

To achieve their aim, the researchers increased the sensitivity and accuracy of a methodology they developed over the years at IBEC, which is based on electrostatic force microscopy (EFM), to enable its use with insulating substrates such as mica or glass, common in biomembrane research. This technique enables them not only to explore the morphology of small scale biological complexes, but also to measure their electric polarizability for the first time ever. By revealing this inherent electrical property that makes each biomembrane unique, researchers can now realistically predict the electrical functionality of these cell constituents and gain a new understanding of the essential role they play in our bodies.

In addition, this achievement could open the door to the development of a new label-free nanoscale biomembrane characterization method based on the local dielectric response, similar to one the researchers developed already for single nanoparticles and viruses, which may answer fundamental questions on how cell membranes are organized at the smallest scales.

Dols-Perez, A. et al (2015). Nanoscale electric polarizability of ultrathin biolayers on insulator substrates by electrostatic force microscopy. Nanoscale

November 2015

How we learn in chunks

In some research conducted with colleagues at the University of California San Diego, IBEC senior researcher Jordi Fonollosa (page 89) shed some light on the mechanisms behind how we memorize sequences – as well as how failures in these mechanisms can provide insight into neurological disorders.

Previous behavioral experiments suggest that humans and some animals learn and recall sequences in smaller segments. By segmenting a sequence of elements into blocks, or chunks, information becomes easier to retain

and recall in the correct order. In the paper published in *PLoS Computational Biology*, Jordi and his collaborators used computational models to demonstrate both learning and recall of a chunking representation of sequences. "We hypothesized that sequences can be learned and stored in a manner that could be compared to a ball rolling down a pinball machine," explains Jordi. "Learning can be identified with the gradual placement of the pins. After learning, the pins are placed in a way that, at each run, the ball follows the same trajectory (recall of the same sequence) that encodes the perceptual sequence. Simulations show that the dynamics share several features observed in behavioral experiments, such as increased delays before new chunks are loaded."

Because chunking is a hallmark of the brain's organization, efforts to understand its dynamics can provide valuable insights into the brain and its disorders. Failures in learning chunking sequences provide new insights into the dynamical causes of neurological disorders such as Parkinson's disease and schizophrenia.

Fonollosa, J., Neftci, E.& Rabinovich, M. (2015). "Learning of Chunking Sequences in Cognition and Behavior." Plos Computational Biology, *epub ahead of print*

December 2015

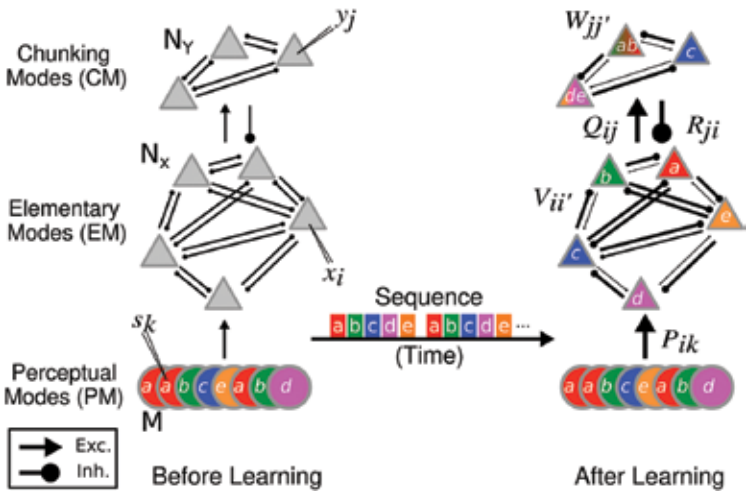
Key protein has potential as cancer repressor

In a paper published in *Nature Cell Biology*, IBEC junior group leader Pere Roca Cusachs (page 102) and his collaborators at Columbia University and Singapore's Mechanobiology Institute revealed the potential of a protein found in cell cytoskeletons as a repressor of cancer.

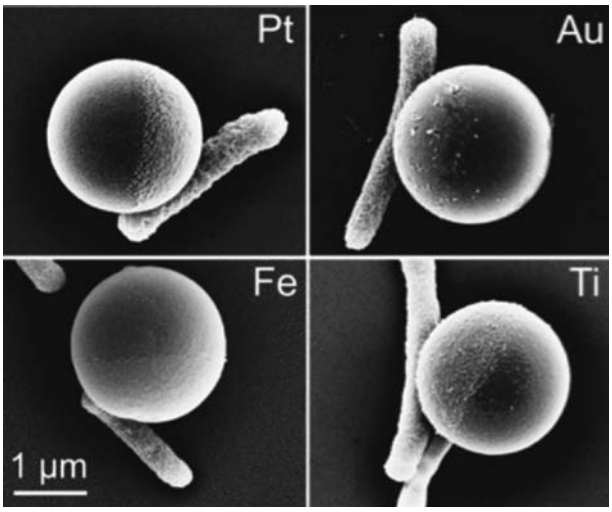
The ability of cells to sense the rigidity of the extracellular matrix affects the regulation of their activity in development, wound healing and other essential processes. Correspondingly, abnormal rigidity sensing by cells is involved in many medical disorders; for example, the anchorage-independent growth of cancer cells indicates that their rigidity sensing machinery is malfunctioning.

After forming adhesions to the matrix, cells test its rigidity by applying forces to it; these forces are applied via local micrometre-scale contractions, like steps, but how the force of these contractions is regulated by rigidity is unknown. We do know that on soft matrices, cells produce low forces, leaving the adhesions small, so the signals that promote cell growth and proliferation are absent; on stiffer substrates, stronger adhesions are built, thereby allowing them to exert higher forces and proliferate. Cancer cells, however, can override the requirement for stable adhesions in order to proliferate, so they are able to grow on soft matrices too.

The researchers analyzed rigidity sensing with a new high-resolution technology by tracking cells' displacement of flexible submicron pillars by contractile forces. They found that actomyosin-based contractile units (CUs) – which are like muscle fibres, but on a cellular level – simultaneously moved opposing pillars in regular-sized small steps, independent of rigidity. What correlated with rigidity was the number of steps taken to reach a force level that activated recruitment of α-actinin (an actin-binding protein with multiple roles in different cell types) to the CUs. "When we removed a protein, tropomyosin 2.1, that normally restricts actomyosin, we observed much larger steps



How we learn in chunks: the two-layer network for learning chunking dynamics. In this example, the input sequence (a, b, c, d, e) is presented repeatedly. Initially, all the synaptic connections within a matrix are similar with small random variations. After several sequence presentations, the input patterns and their order are learned according to a hierarchical order: at a lower layer composed of elementary modes and at a higher level composed of chunking modes. In the elementary layer, the weights *Vii'* in the directions a to b, b to c, and d to e are weakened (arrow thickness denotes coupling strength), while the weights in the opposite direction are strengthened. Similarly, the weights *Wjj'* learn the trajectories along three chunks: ab, c and de.



Harnessing *E. coli* to power micromotors for drug delivery: SEM images of *E. coli* attached to Janus particles

– special types of particles whose surfaces have two or more distinct physical properties. The *E. coli* preferred platinum of all the four types of metals tested, and adhered only to the metal side, allowing the particle's polystyrene surface to be used to attach the drug. "Our bio-hybrid was capable of carrying a load of up to 2 µm in diameter, and demonstrated the ability to transport DOX, an anti-cancer drug," says Samuel.

Future challenges of bacteria-powered swimmers will be to operate in *in vivo* systems with a more complex 3D swimming environment, but a better understanding of the bacteria-surface interface will be essential for their success.

Stanton, M.M. et al. (2015). Bio-hybrid Janus Motors Driven by Escherichia coli. Adv Mat Interfaces*, epub head of print*

and higher forces – like those found in stiffer substrates – that resulted in a malfunction in rigidity sensing," says Pere. "As a result, we can conclude that tropomyosin 2.1 acts as a suppressor of cell growth on soft matrices by cells usually able to do so, such as cancer cells, by controlling force production and supporting proper rigidity sensing."

Wolfenson, H. et al. (2015). "Tropomyosin Controls Sarcomere-like Contractions for Rigidity Sensing and Suppressing Growth on Soft Matrices". Nature Cell Biology*, epub ahead of print*

Harnessing *E. coli* to power micromotors for drug delivery

Samuel Sánchez (page 122) worked with the part of his group at the MPI for Intelligent Systems on a finding, highlighted on the inside cover of *Advanced Materials Interfaces*, which elaborated a promising micromotor for medical drug and cargo delivery that is powered by *Escherichia coli*.

Bacteria can be harnessed to power such micromotors within a living organism by converting the surrounding chemical energy into mechanical work. They therefore count as bio-friendly fuels, whereas up until now micromotors have relied on toxic fuel sources and materials in their design, making them irrelevant for biomedical applications.

To achieve the bacteria-powered micromotors, the researchers integrated *E. coli* onto metal-capped, polystyrene Janus particles

Cells are liquids – but behave like solids

Living cells have long been thought to behave like fluids, but scientists at IBEC revealed that they behave like solids rather than the liquids they are made of. Traditional material science could never predict this behaviour, but cells are not traditional materials; they are 'active materials' able to consume energy and transform it into a force, a movement, or a deformation. Thanks to their active nature, cells can circumvent established dogmas of materials science.

The discovery stems from the researchers' development of a new technique called "self-rheology" that allowed them to study the very slow behaviour of a material. This is usually very hard to do, as it requires applying a controlled force or deformation for a very long time; but using the technique, the colleagues found out that cells are constantly applying forces on each other. "Thanks to the ability of cells to naturally pull on and squeeze each other, we realized we didn't need to apply any force on the cells. We just let them do their thing, and then visualized the resulting forces and deformations," explains Romaric Vincent (page 132), first author on the paper.

The finding changes the way we think about processes such as embryo development or wound healing. "When an embryo develops, or when a wound heals, cells undergo very large deformations to enable new shapes," says group leader and ICREA research professor Xavier Trepat, who believes the discovery will prompt the scientific community to develop the laws of active matter.

Vincent, R. et al. (2015). Active tensile modulus of an epithelial monolayer. Physics Review Letters*, pub ahead of print*

Microwave electromagnetic properties of single bacterial cells measured

Researchers at IBEC and their collaborators from the Johannes Kepler University of Linz, The University of Manchester and the company Keysight Technologies measured the electromagnetic properties of biological materials at the level of a single bacterial cell and at very high frequencies (gigahertz).

The Nanoscale Bioelectrical Characterization group (page 68) achieved this novel breakthrough by using a technique referred to as scanning microwave microscopy. With this technique a single cell or microorganism, in this case a bacterial cell, can be imaged by using microwaves similar to those used in microwave ovens, from where the microwave electromagnetic properties can be quantified at the nanoscale.

"New advances in non-invasive medical imaging techniques for cancer diagnostics, therapeutic ablation techniques for cancer treatment and novel electrosurgical techniques are under development based on the use of microwaves and on the knowledge of the high frequency electromagnetic properties – the complex permittivity – of biological tissues," explains Gabriel Gomila. "Now, we have demonstrated the possibility to measure this key physical property also at the level of a single cell, providing unique information about their internal structure and biochemical composition, and of their state and phase." It can also be used to design and implement label-free electrical techniques for counting, sizing, separating and identifying cells, thus opening even more avenues towards new and improved biological and medical applications.

Biagi, M.C. et al, (2015). "Nanoscale electric permittivity of single bacterial cells at GHz frequencies by scanning microwave microscopy". ACS Nano*, epub ahead of print*

Shrinking technologies to dig deeper into the body's secrets

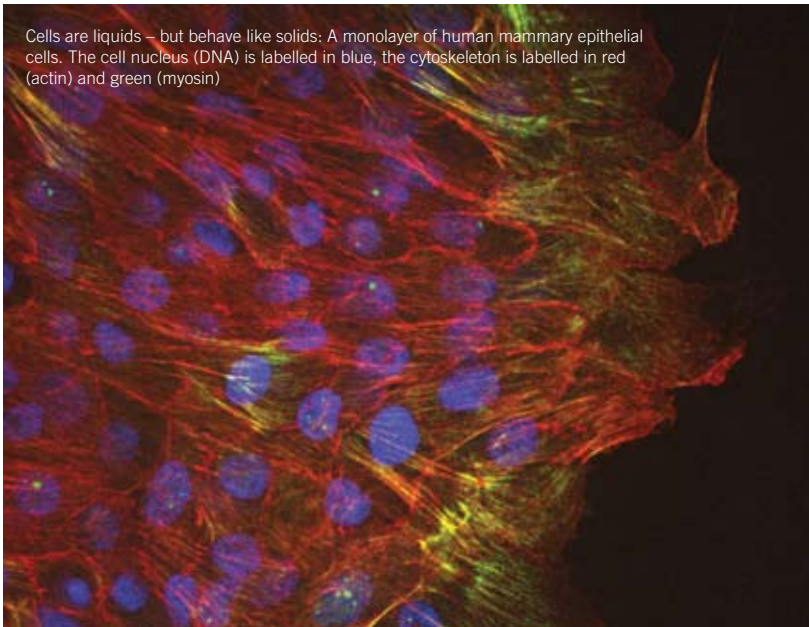
A team of scientists developed a brand new technique that miniaturizes the way we study biomolecular interactions, allowing multiple analyses inside living cells for the first time. The work, led by CSIC, involved former IBEC PhD student Juan Pablo Agusil, who's now at CSIC's Barcelona Microelectronics Institute (IMB-CNM).

Published in *Advanced Materials*, the study described a new technology, Suspended Planar-Array chips, whose extraordinary degree of miniaturization permits their use at the microscale. Two previous methods, planar array chips and suspension arrays of particles have long been used to study biomolecular interactions and carry out complex molecular analyses; but while planar array chips are good for molecular multiplexing, they are too large for exceptionally small volumes, and while suspension arrays allow the analysis of small volumes, they don't allow multiple detections in a single device. The researchers combined the advantageous aspects of the two techniques to come up with Suspended Planar-Array chips; essentially, they miniaturized a typical planar array by a factor of 1010, a reduction so dramatic that it even permits analysis inside living cells.

"Using just one Suspended Planar-Array device, we can enter the cell and make multiple detections of biological parameters," Juan Pablo says. "This is the first time a multiplexed planar array has gone inside a living cell."

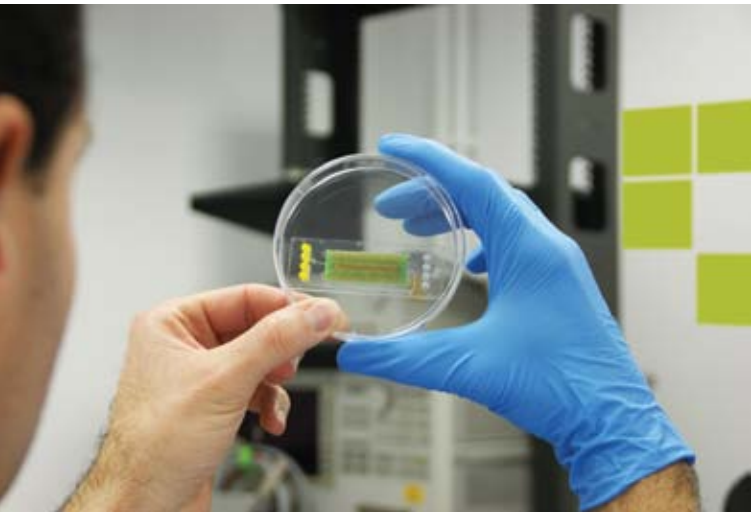
The interdisciplinary nature, versatility and potential of the technique could be of major interest to scientists working in many different disciplines, such as advanced materials, engineering, chip technology, printing of self-assembled nanolayers, biomaterials, cell biology and nanotechnology.

Torras, N. et al (2015). Suspended Planar-Array Chips for Molecular Multiplexing at the Microscale. Advanced Materials*, epub ahead of print*



Cells are liquids – but behave like solids: A monolayer of human mammary epithelial cells. The cell nucleus (DNA) is labelled in blue, the cytoskeleton is labelled in red (actin) and green (myosin)

News Highlights



IBEC and Genomica create joint unit for research and development of diagnostic devices

February 2015

Josep Samitier elected new president of ACER

IBEC Director Josep Samitier was named new president of the Associació Catalana d'Entitats de Recerca (ACER). Josep took the reins from IFCO director Lluís Torner, who has held the position since 2009. The association's first President was the Hon. Mr. Andreu Mas-Colell. The other members of the Director's Board are ICAC's Joan Gómez Pallarès (Secretary), Ramon Gomis (IDIBAPS), Jordi Galí (CREI) and Josep M. Monfort (IRTA) as members.

ICREA Academia Award for IBEC group leader

Gabriel Gomila (page 68), IBEC group leader and Associate Professor at the UB, received an ICREA Academia Prize 2014 for excellence in research and capacity for leadership. Bestowed annually by the Catalan Institution for Research and Advanced Studies (ICREA) to encourage university professionals with an outstanding research career to stay in the Catalan university system, this year's list of 30 winners was made up of 10 researchers from the UB, 8 from the UAB, 6 from the UPC, 3 from the UPF, 2 from Universitat de Girona and one from the Universitat Rovira i Virgili.

IBEC and Genomica create joint unit for research and development of diagnostic devices

IBEC and Genomica S.A.U. (Grupo Zeltia), the leading Spanish company in molecular diagnostics, announced the creation of a Joint Research Unit that will provide an operational framework for close interaction on various R&D activities related to healthcare. The unit, which will be located at IBEC's headquarters in Barcelona, will see researchers and industry technicians sharing a host of know-how and in-house capabilities to develop and bring to market point-of-care diagnostic products and other medical devices and technologies.

March 2015

Presentation of EIT Health Spain at the PCB

In March the official presentation of EIT-Health Spain took place at the PCB. This local node of EIT-Health, the European Institute of Innovation and Technology's "Knowledge and Innovation Community (KIC)" for healthy living and active ageing, is led by the University of Barcelona coordinated by IBEC Director Josep Samitier, Dr. Jordi Alberch, Vice President for Research, Innovation and Transfer at the UB, and Dr. Montserrat Vendrell, Director General of the PCB and BIOCAT.

The event was attended by Secretary of State Carmen Vela, as well as other institutional representatives of the ministries involved: the Generalitat de Catalunya, Comunidad de Madrid and the Generalitat Valenciana.

IBEC researcher wins ERC Consolidator Grant for research into intestinal diseases

Elena Martínez, head of IBEC's Biomimetic Systems for Cell Engineering group (page 94), was awarded a prestigious European Research Council (ERC) Consolidator Grant to engineer models of the intestinal epithelium, an essential tool for understanding disease and tissue regeneration.

The highly sought-after ERC Consolidator grants are awarded to EU-based Principal Investigators with talent and proven potential who are still consolidating their own independent research team or programme. In this call, nearly 2528 proposals were submitted, of which 372 were selected for funding.

Public event on IBEC research into light-controlled drugs

As Spain's expert in optogenetics and optopharmacology, IBEC group leader Pau Gorostiza (page 72) was the star of the next "Diálogos por la Ciencia" event in Madrid.

An initiative of the Fundación "la Caixa", "Diálogos por la Ciencia" are a new way of communicating science to the public, in which prestigious scientists with international recognition are interviewed live in front of a audience of the public by a renowned journalist.

ICREA research professor Pau, who heads IBEC's Nanoprobes and Nanoswitches group, talked about his work developing light-controlled drugs at the event on 25th March.

April 2015

Samuel Sánchez wins FPdGi award for scientific research

IBEC group leader Samuel Sánchez (page 122) was this year's winner of the Premio Fundación Princesa de Girona Investigación Científica for his advances in in the field of nanotechnology.

Samuel's work was recognised in particular for his pioneering design of self-propelled nanorobots that could improve the accuracy of drug delivery, as well as having potential environmental applications.

This year was the sixth edition of the national FPdGi Awards, which are given by the Fundación Princesa de Girona and which recognise the innovative and exemplary careers of young people between the ages of 16 and 35.

Convergència representatives visit IBEC

In April, representatives of Catalan political party Convergència i Unió (CIU) visited IBEC as part of a tour of the PCB.

Congresswoman Imma Riera and organiza-

Samuel Sánchez receiving the Premio Fundación Princesa de Girona Investigación Científica prize from the king and queen

L-r: Jordi Camí, PRBB director; Miquel Molins, president of the Fundacío Banc Sabadell; IBEC's Xavier Trepat; and Isabel Illa, Chief of Neuromuscular Diseases at Hospital Santa Creu i Sant Pau, at the Banc Sabadell Award for Biomedical Research press lunch in May

tional secretary Josep Rull met IBEC Director Josep Samitier, who gave them an overview of IBEC, before visiting the Nanotechnology Platform (page 138), guided by coordinator Mateu Pla.

IBEC group leader a fem.talent award winner

IBEC group leader Alicia Casals (page 52) received a 2015 fem.talent Award at the fem. talent Fòrum in Barcelona in April.

Alicia won the prize for "Career trajectory", recognising such milestones as the creation in 2011 of IBEC/UPC spin-off Rob Surgical Systems. Other award categories were "Emerging Talent", "Innovation" and "Communication".

The forum is a yearly conference of fem. talent, an initiative of the Network of Science and Technology Parks of Catalonia (XPCAT) that aims to promote equality of opportunity between men and women. This year the theme was "Smart Time: intelligent management of time," with the objective of discussing innovative ideas and different practices in the field of time management.

IBEC receives 'HR Excellence in Research' award from the European Commission

IBEC was awarded the 'Human Resources Excellence in Research' from the European Commission, in recognition of its commitment to continuously improving its HR policies in line with The European Charter of Researchers and The Code of Conduct for the Recruitment of Researchers (Charter and Code).

IBEC can now use the official HR Excellence in Research logo to help promote itself as a provider of a stimulating and favourable work environment according to the Charter and Code, which describe the rights and responsibilities of researchers and their employers and contribute to the creation of a labour market that is transparent, attractive and open at an international level.

IBEC receives Severo Ochoa Excellence Award

The Institute for Bioengineering of Catalonia was one of the two centres in Spain to be awarded accreditation in the 2015 round of the Severo Ochoa Excellence programme.

The Ministry for Economy and Competitiveness announced the winners of the coveted distinction, selected by an international panel of more than 70 judges, in April. Severo Ochoa Excellence Awards identify and promote research centres and units in Spain that stand out as international references in their specialized fields.

The award was presented at a ceremony at MINECO in Madrid in July.

May 2015

Israel's former Chief Scientist among visitors for TAU/IBEC symposium

Top scientists from Tel Aviv University (TAU), including Israel's former Chief Scientist of the Ministry of Science and Technology, visited Barcelona to take part in a joint symposium

with IBEC in May.

With many similarities between Catalonia and Israel – which are almost neck-and-neck when it comes to research output in *Science* and *Nature*, with over 30 publications per million inhabitants and similar levels of funding under FP7 – the event built on the fact-finding mission of Artur Mas and Barcelona-based scientists to Israel last year and is supported by AGAUR.

Xavier Trepat winner of the 10th Banc Sabadell Award for Biomedical Research

IBEC group leader and ICREA research professor Xavier Trepat (page 132) was this year's winner of the Banc Sabadell Award for Biomedical Research for his work on understanding the fundamental biophysical mechanisms underlying cell interaction and communication.

The news was made public at a press lunch (left) attended by the President and Vice President of the Fundació Banc Sabadell, Miquel Molins and Sònia Mulero, as well as jury members Jordi Camí (UPF), Isabel Illa (UAB) and Eduard Batlle (ICREA/IRB).

June 2015

IBEC group leader in new CIBER-BBN steering committee

Biomedical Signal Processing and Interpretation group leader and UPC professor Raimon Jané (page 78) was appointed as a member of the new CIBER-BBN Steering Committee. CIBER-BBN's Permanent Commission announced the names of the 10-strong committee, which will stand for the next four years, in June.

Raimon, who will take part in the committee as Training Coordinator, will carry out his duties alongside other researchers including Ramón Martínez-Máñez (Universitat Politècnica de València) as director and José Becerra (Universidad de Málaga) as subdirector.

July 2015

Launch of BIB

IBEC is a key player in a new network of organizations working together to exploit Big Data from life and food sciences

July saw the launch of the Associació Bioinformatics Barcelona (BIB), a network of 25 members including universities, research centres, hospitals, major scientific facilities, and pharmaceutical, technology and and bioinformatics companies, which aims to respond to the challenges posed by the growth of big data and position Barcelona as a world leader in bioinformatics.

September 2015

CaixaImpulse selects two IBEC initiatives to promote tech transfer in science

The 15 research projects that have been selected for funding under in the first CaixaImpulse call, including two IBEC projects, were presented at the Palau Macaya in September.

Xavier Puñet, a PhD student in the Bioma-

The winners of the first CaixaImpulse competition at the presentation at the Palau Macaya in September. Xavier Puñet is second from left, and Eduard Torrents third from right.

Carmen Vela and Josep Samitier during the secretary of state's visit to IBEC

terials for Regenerative Therapies group (page 58), presented Dermoglass, a dressing that stimulates revascularization in chronic wounds such as skin ulcers and promotes the formation of healthy skin. The other IBEC project selected for funding is RNRbiotics led by Eduard Torrents, group leader of the Bacterial infections: antibiotic therapy group (page 128), which aims to develop new antimicrobial agents effective against resistant bacterial infections, currently considered as one of the main threats to human health (World Health Organization).

Visit of HT Cluster partners to IBEC

IBEC welcomed some of its partners from HT Cluster, a new alliance of industry, research centres and other bodies working in the health technologies sector in Catalonia, through its doors in September. IBEC Director Josep Samitier and researchers Elisabeth Engel, Xavier Puñet, Lucas Pedraz, Agustín Gutiérrez and Mateu Pla gave talks to the visitors, who represented some of the businesses and other organizations that form the cluster. Afterwards, Mateu led a tour of IBEC's facilities.

Reaching out to the public at the Nit Europea de la Recerca

IBEC group leader and ICREA Research Professor Pau Gorostiza (page 72) took part in the Barcelona version of European Researcher's Night on Friday 25th September.

Held at the CCCB, the Nit Europea de la Recerca Barcelona was in celebration of the Year of Light. Pau took part in a round table moderated by BIOCAT on the subject of "Humans amb més llum: re-evolució humana gràcies a les noves tecnologies basades en la llum".

October 2015

Secretary of State visits IBEC

IBEC had the chance to show off its research facilities and investigators to Carmen Vela, Spain's secretary of state for research, development and innovation.

After inaugurating the IBEC-organized B·Debate on "Future Tools for Biomedical Research" at CosmoCaixa at the beginning of the day, Ms. Vela was taken on a tour of IBEC's laboratories, where she chatted with heads of research groups – including Nuria Monserrat, Samuel Sánchez, Elena Martínez, Eli Engel, Lorenzo Albertazzi and Pau Gorostiza – about their work. Afterwards, Ms. Vela enjoyed morning coffee with IBEC's directorate and several more group leaders.

Learning from the experts

IBEC group leader Samuel Sánchez (page 122) was one of the experts and professionals invited to take part in CEDE's "Talento en Crecimiento" event at the Palacio de Exposiciones y Congresos in A Coruña at the beginning of October.

He took to the stage with some of the most influential business leaders, entrepreneurs and experts in the country, including Francisco Reynes, CEO of Abertis, Juan Urdiales, co-founder of Jobandtalent, and Maria Salamero, Director of Innovation and Knowledge at Agbar, all of which were there to give the 500 young attendees advice on career advancement, personal branding, mobility and employability.

IBEC success in Human Brain Project funding call

A research project involving IBEC group leader and ICREA research professor Pau Gorostiza was chosen for funding under a

Call for Expressions of Interest (CEoI) on Systems and Cognitive Neuroscience by the Human Brain Project (HBP) FET Flagship.

The four selected projects from the total of 57 proposals submitted address ambitious cognitive and systems neuroscience questions and rely on the collaboration of researchers from different European countries. The project involving Pau, Wave Scaling Experiments and Simulations (WaveScalES), is coordinated by Pier Stanislao Paolucci at the Instituto Nazionale di Fisica in Rome and will study the neuronal networks underling sleep and wakefulness under normal conditions and in disease.

IBEC researcher in "Innovators Under 35" European Summit

IBEC group leader Samuel Sánchez (page 122) was one of the experts invited to attend the Innovators Under 35 European Summit in Brussels, a gathering of the European winners of MIT Technology Review's "Innovators under 35" list. Samuel gave a talk, "The Evolution of Nanorobots", at the event, which brought together the winners of the prestigious recognition from Germany, Belgium, France, Italy and Poland as well as Spain. The summit aimed to create a strong community of those innovators recognized annually by the prestigious publication to share their knowledge and experience in fields ranging from nanotechnology and energy to software or transportation.

November 2015

IBEC ERC grantee meets business angels

IBEC group leader and ICREA research professor Pau Gorostiza (page 72) was one of nine ERC Proof of Concept holders to take part in the European Business Angel Network (EBAN) Winter University in Copenhagen.

Pau pitched his project, THERALIGHT: Therapeutic Applications of Light-Regulated Drugs, to the investors from all over the world at the event, which he attended alongside eight other awardees specially selected by the ERC. Together they made up nearly half of the 20 European start-ups hoping to catch the eye of an investor interested in exploring the innovation potential of their findings.

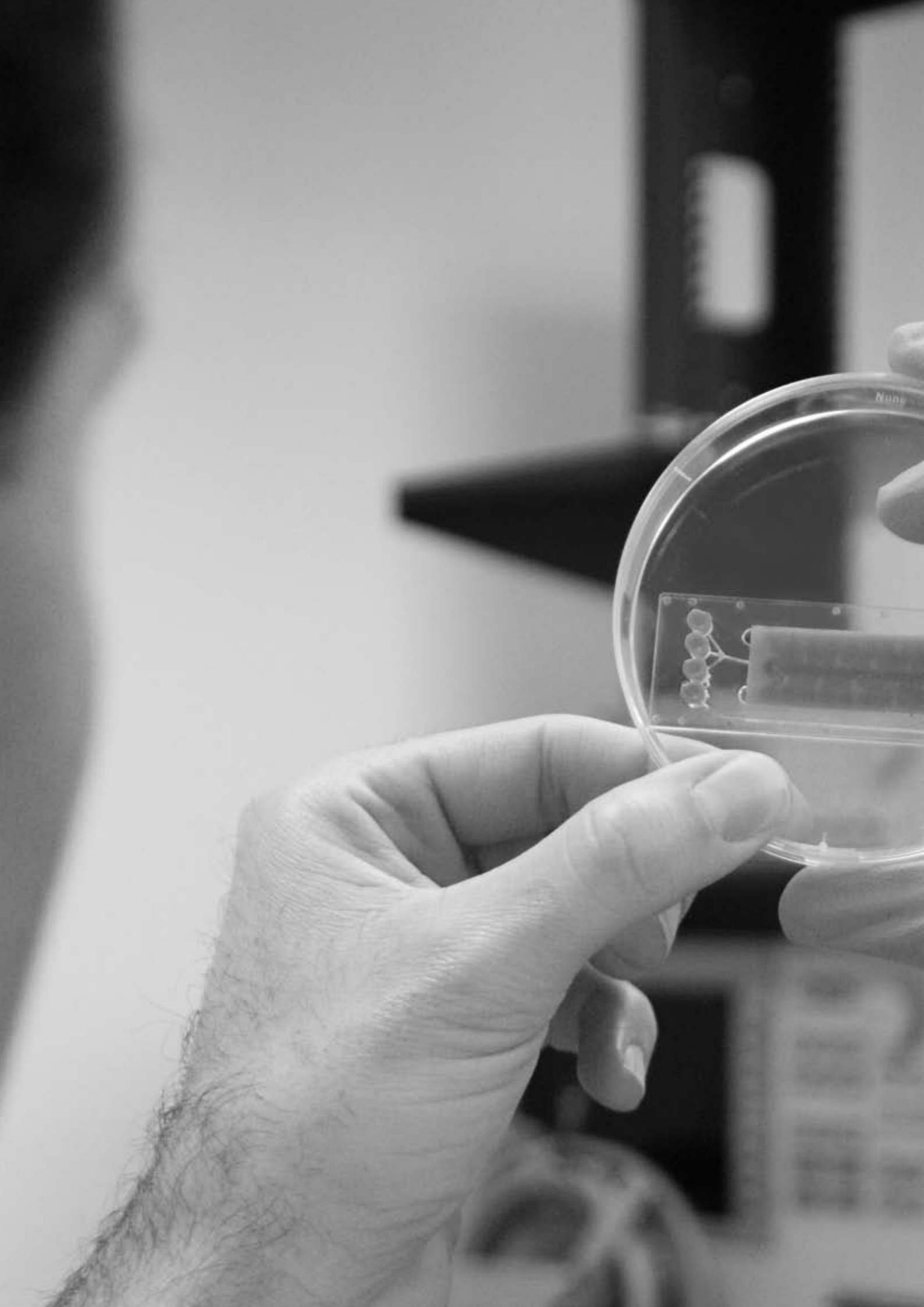
Pau Gorostiza and fellow round table members, including former IBEC group leader Maria García Parajo, at the Nit Europea de la Recerca

The EBAN Winter University is the global summit on venture finance and innovation in science, space, technology and the creative industries, and provides an opportunity for researchers to interact with industry and attract investments into their start-ups and innovative frontier research.

A history of biomedicine in Spain in 28 chapters

The life and career of IBEC Director Josep Samitier was one of the "28 Historias de Ciencia e Innovación Biomédica en España/28 Stories of Science and Biomedical Innovation in Spain" in a book launched in November by the Fundación Botin in Madrid.

The book celebrates the foundation's ten years of close collaboration with some of the top scientists in Spain in the field of biomedicine under its Technology Transfer programme, working together to develop products or services that improve quality of life and provide business and investment opportunities. IBEC's partnership with the foundation has been in regard to the technology transfer of results obtained by the Nanobioengineering group within the project 'Desarrollo de Tecnologías en Bionanomedicina para diagnóstico y terapia'.



About IBEC

IBEC Strategy 2014-2017

IBEC's Strategic Plan for the period 2014-2017 identifies the following four areas in which to concentrate efforts:

- To expand the centre both in size and in results by recruiting new professionals and scientists, as well as renewing groups that perform at the highest standard in terms of both scientific quality, and transfer and innovation.
- To focus its scientific work on the areas where it can stand out most distinctively and compete internationally, with an orientation towards scientific and technological challenges with a high impact on people's health and quality of life.
- To forge alliances with organisations of recognised international standing to consolidate the institute's path of specialisation, differentiation and internationalisation.
- To improve the way the institute is managed by implementing tools such as an integrated management system and management by results, in order to make the best use of resources and align management with its strategy.

In this way, IBEC's Strategic Plan for 2014-2017 is structured in terms of four strategic goals:

- **SG1.** To consolidate top-class science which enables IBEC to strengthen its international position, by focusing its core activity on three areas of application: "Bioengineering for Regenerative Therapies", "Bioengineering for Future Medicine" and "Bioengineering for Active Ageing".
- **SG2.** To develop technology and applications thereof that help to improve business competitiveness and the quality of hospital services.
- **SG3.** To run a distinctive specialist training programme to attract international talent.
- **SG4.** To develop a culture of excellence in management, self-sustainability and management by objectives.

Each of these strategic goals is pursued in the following areas of action: Research, Technology transfer and translation, Training development, Human resources (see opposite), Management, Alliances, and Communication.

July's workshop on work-life balance in research

HRS4R: Gender and Diversity Committee

Part of IBEC's Strategic Plan 2014-2017 has been the design and implementation of a new Human Resources Strategy for Researchers (HRS4R) according to the principles of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers.

One of the first measures of the HRS4R's Action Plan was to set up a Gender and Diversity Committee, which includes researchers at different career stages and support services staff. The committee has been meeting on a trimestral basis since its creation in June 2014 to work on the design, preparation and implementation of the 'IBEC Equal Opportunities and Diversity Management Plan' which includes 17 actions to be implemented in 2014-2016.

2015 was a very busy year for IBEC's Gender and Diversity Committee, resulting in the fulfilment of several of those actions.

- To increase and improve dissemination of gender and diversity issues, the committee **published two articles** in IBEC's newsletter "*Inside*IBEC", and the IBEC community was regularly informed about relevant activities occurring outside the institute.
- To progress towards respect and equality at work, a specific commission was created to work on the improvement and dissemination of IBEC's **anti-harassment protocol**. Informative leaflets were made available to the entire IBEC community, and all members of the commission attended training to be better prepared in case of a harassment situation.
- Another important aspect of the Equal Opportunities and Diversity Management plan is to guarantee the opportunity for anyone to submit their ideas and proposals for improvements in the institute. For this purpose, the Gender and Diversity Committee, together with the Human Resources Unit, developed **I-Box (Ideas-Box)**, an online platform accessible via IBEC's Intranet and open to all IBEC members. The first call for proposals was on December 1st, when people were invited to send ideas and suggestions related to IBEC's performance, including its scientific results and status; its internal procedures and processes; its financial, health and safety protocols; or motivational ideas, to give a few examples. The suggestions implemented will be entered into a yearly competition to determine the best ideas of the year.

Gender and Diversity events held at IBEC in 2015:

- 25 May

Workshop in gender and diversity

Open to the entire IBEC community, and especially aimed at the members of the aforementioned committee, this workshop provided the basic concepts and tools in the field, focusing on the understanding of the values, beliefs and expressions of people with different age, gender, race, religion, etc.

- 15 July

Workshop on work-life balance in research

In this session, four IBEC group leaders were invited to participate as guest speakers in a round table session where they shared with the audience their experiences as successful role models who have managed to reach a leading position in research while, at the same time, raising their children or taking care of their family. In addition, concepts such as vertical segregation or the 'glass ceiling' effect were discussed.

Transparency

In compliance with Law 19/2014 (Transparency, public access to information and good governance), a new section of the IBEC website provides all the information we are obliged to provide in order to adhere to the principles of this law.

The section (**www.ibecbarcelona.eu/about-us/transparency**) contains the following information and/or documents (in Catalan):

Organització

Estructura organitzativa i de funcionament

- Organs de govern i organigrames
- Acords de creació i funcionament d'entitats del sector públic
- Cartes i catàlegs de serveis
- Catàleg de procediments

Alts càrrecs i directius

- Relació d'alts càrrecs i directius
- Incompatibilitats
- Activitats, béns i interessos
- Retribucions, indemnitzacions i dietes
- Codi de bones pràctiques per als alts càrrecs de la Generalitat de Catalunya

Empleats públics

- Relació de llocs de treball del sector públic
- Personal adscrit per adjudicataris de contractes signats amb l'Administració
- Retribucions, indemnitzacions i dietes

Convocatòries: accés i resolució

- Convocatòries personal laboral, col·lectius específics i formació per promoció.

Representació sindical

- Nombre i cost d'alliberats sindicals.

Econòmica i finances

Pressupostos

- Pressupostos aprovats
- Pressupostos executats
- Pressupostos liquidats
- Comptes anuals

Informes d'auditoria de comptes i fiscalització

- Informes d'auditoria de comptes i fiscalització

Patrimoni de la Generalitat de Catalunya

- Inventari de béns immobles
- Béns mobles de valor especial
- Gestió de patrimoni
- Contractació patrimonial

Subvencions i ajuts

- Subvencions i ajuts públics previstos
- Subvencions i ajuts públics atorgats
- Control financer de les subvencions i els ajuts

Contractació

Contractes

- Contractes

Convenis

- Registre de convenis de col·laboració
- Altres convenis

Territori

Plans territorials sectorials

- Plans territorials sectorials

Informació cartogràfica

- Informació cartogràfica

Procediments i actuacions jurídiques

Normativa

- Normativa sectorial
- Directives, instruccions i circulars
- Normativa en tràmit

Règim d'intervenció administrativa

- Actes amb incidència sobre el domini públic i sobre la gestió dels serveis públics

Revisió d'actes administratius

- Revisió d'actes administratius

Resolucions administratives i judicials amb rellevància pública

- Resolucions administratives i judicials amb rellevància pública

Dictàmens

- Respostes a consultes sobre interpretació i aplicació de la normativa

Línies d'actuació

Plans i programes generals i sectorials, auditories i informació estadística

- Plans i programes generals i sectorials, auditories i informació estadística

The IBEC foundation

IBEC is a non-profit foundation established at the end of 2005 by the Generalitat de Catalunya (Autonomous Government of Catalonia), the University of Barcelona (UB) and the Technical University of Catalonia (UPC).

The main governing body of IBEC is its Board of Trustees with representatives from the Catalan ministries of Health and Research, the UB and UPC. The Board of Trustees meets twice a year to approve IBEC's annual budget and monitor its activity to ensure that it pursues scientific excellence with societal impact. For executive purposes, a Management Committee (chosen from the Board) monitors IBEC's activities through *ad hoc* meetings with the Director and Managing Director.

The Board's decisions are guided by an independent International Scientific Committee (ISC). This committee ensures practices and criteria are implemented in accordance with international standards of excellence in research.

IBEC's relationship with the universities

IBEC's forerunner, the Centre of Research for Bioengineering (CREB) of the Technical University of Catalonia (UPC), was founded in 1992 by six research groups from five different departments with the aim of collaborating in research and industrial projects in the broader area of bioengineering. IBEC's first director, Prof. Josep A. Planell, was director of CREB from 1997 and led the process that resulted in the creation in 2003 of the Catalan Reference Centre for Bioengineering (CREBEC), composed of different divisions from the above-mentioned CREB and the Research Centre on Bioelectronics and Nanobioscience (CBEN) of the University of Barcelona (UB). CREBEC, which aimed to coordinate the multidisciplinary research activities in biomedical engineering carried out in Catalonia, was transformed at the end of December 2005 into the Institute for Bioengineering of Catalonia (IBEC).

Today, two thirds of IBEC group leaders are faculty members at either UB or UPC. IBEC's PhD students are able to follow their doctoral courses at the universities, which offer degrees in physics, chemistry, biology, materials science and engineering, among others, and masters courses related to bioengineering and nanomedicine, attracting students from all over the world. Several others of IBEC's research staff are also involved in the doctoral programmes, particularly in the joint Biomedical Engineering Programme. Moreover, being located on the same campus, the relationship with both universities and the access to their facilities – library, scientific services, etc – is very fruitful.

IBEC's current director, Josep Samitier, was Vicerector of Research and Innovation and Acting Rector of the University of Barcelona (UB) from 2005 to 2008. He remains Full Professor of Electronics in the university's Physics Faculty.

The research groups affiliated with the two universities which are seconded at IBEC are listed on page 146.

Board of Trustees

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Hble. Sr. Andreu Mas-Colell Minister of Economy and Knowledge Generalitat de Catalunya

FIRST VICE-PRESIDENT

Hble. Sr. Boi Ruiz i Garcia Minister of Health Generalitat de Catalunya

SECOND VICE-PRESIDENT

Excm. i Mgfc. Sr. Dídac Ramírez i Sarrió Rector University of Barcelona (UB)

Excm. i Mgfc. Sr. Enric Fossas Colet Rector Technical University of Catalonia (UPC)

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Dr. Xavier Gil Mur Full Professor Technical University of Catalonia (UPC)

Dr. Fernando Orejas Valdes Vice-President for Research Policies Technical University of Catalonia (UPC)

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Dr. Xavier Gil Mur
Full Professor Technical University of Catalonia (UPC)

SECRETARY

Sr. Josep Maria Alcoberro Pericay
CERCA, Ministry of Economy and Knowledge, Generalitat de Catalunya

International Scientific Committee

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Professor in Biomedical Signal and Data Processing Department of Biomedical Engineering, Politecnico di Milano, Italy

Prof. Charles J. Dorman
Chair of Microbiology Trinity College Dublin, Ireland

Prof. Günter R. Fuhr
Director Fraunhofer Institute for Biomedical Engineering, Germany

Prof. Roger Kamm
Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering Massachusetts Institute of Technology, Boston, MA, USA

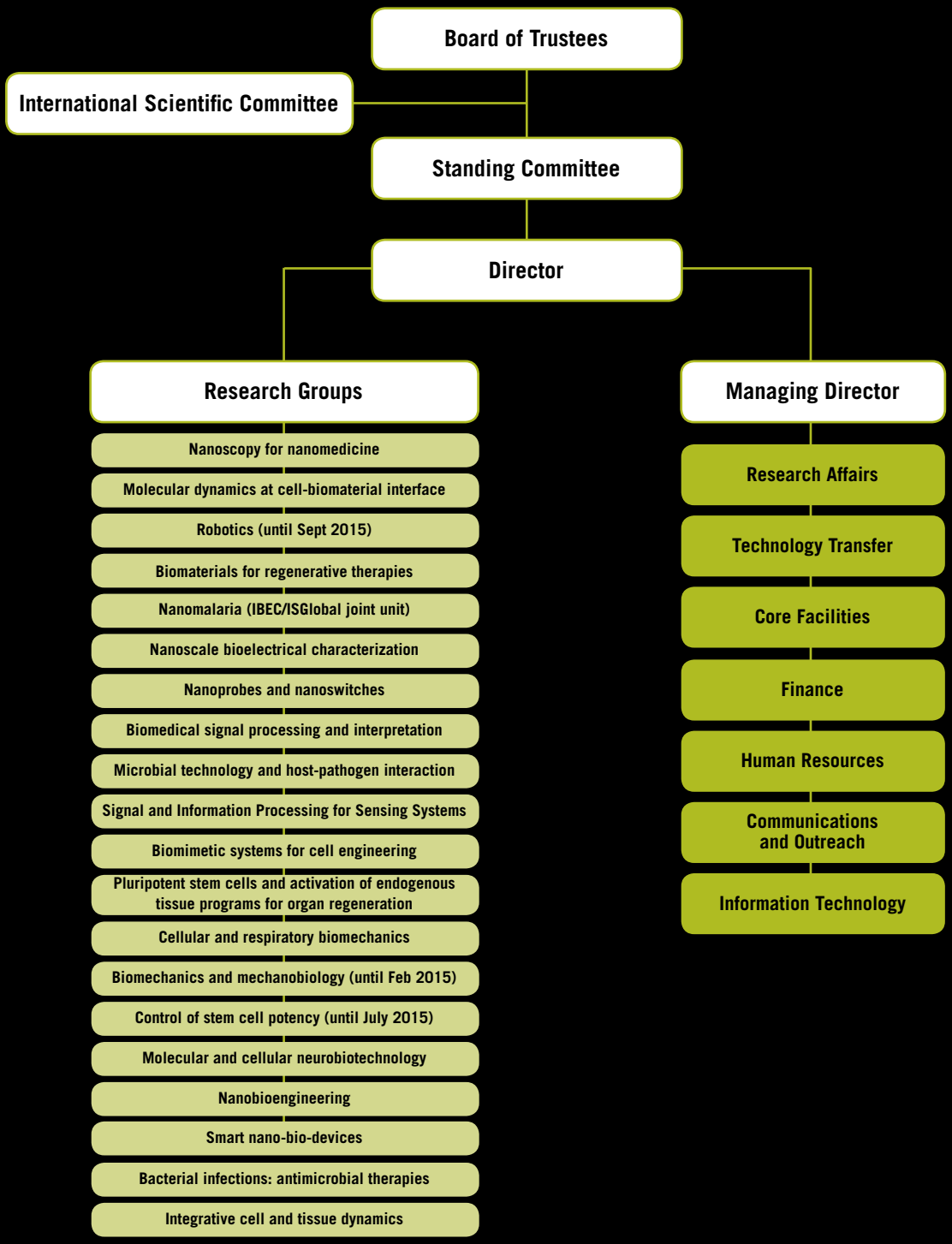
Prof. Chwee Teck Lim
Professor / Deputy Head Department of Biomedical Engineering and Department of Mechanical Engineering, National University of Singapore, Singapore

Prof. Krishna Persaud
Professor of Chemoreception School of Chemical Engineering and Analytical Science, University of Manchester, UK

Prof. Bernat Soria
Director Departamento de Células Troncales, Centro Andaluz de Biología Molecular (CABIMER), Seville, Spain

Prof. Molly Stevens **Professor of Biomedical Materials and Regenerative Medicine / Research Director for Biomedical Material Sciences, Institute of Biomedical Engineering** Imperial College, London, UK

Jocelyne Troccaz, PhD
Director de Recherche, CNRS Equipe Gestes Médico-Chirurgicaux Assistés par Ordinateur (GMCAO), Laboratoire TIMC-IMAG, Université Joseph Fourier-CNRS, France



Organisational chart

Support services

IT Technician
Francisco Contreras

IT Manager
Juli Bafaluy

Funding Manager
Esther Gallardo

Project Manager
Javier Selva

Coordinator of Project Management Office
Javier Adrián

INFORMATION TECHNOLOGY

HR Junior Technician
Ciara Boter

HR Technician
Ricard Rius

Head of Human Resources
Carol Marí

Occupational Hazards Prevention Technician
Raquel Guillén

HR Technician
Núria Jané

Head of Communications and Outreach
Vienna Leigh

HUMAN RESOURCES

Director
Josep Samitier

Managing Director
David Badia

Assistant to the Director
Ester Sánchez

IMS Developer
Carles Ortega

DIRECTORATE

For the staff list for Core Facilities, see pages 140-141

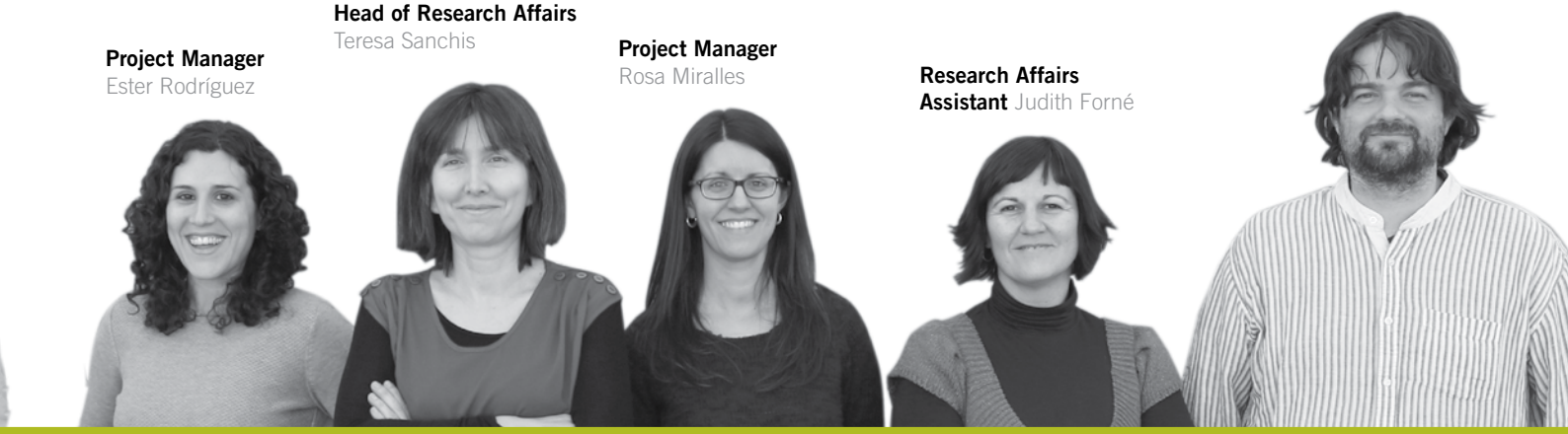
Project Manager
Ester Rodríguez

Head of Research Affairs
Teresa Sanchis

Project Manager
Rosa Miralles

Research Affairs Assistant Judith Forné

Project Manager
Guillermo Talavera



RESEARCH AFFAIRS

Coordinator of Media Relations and Branding
Àngels López

Communications and Outreach Assistant
Carolina Llorente

Coordinator of Events Pilar Jiménez

COMMUNICATIONS AND OUTREACH

Head of Technology Transfer Xavier Rubies
(since November 2015)

TT Project Manager
Marta Soler

TECHNOLOGY TRANSFER

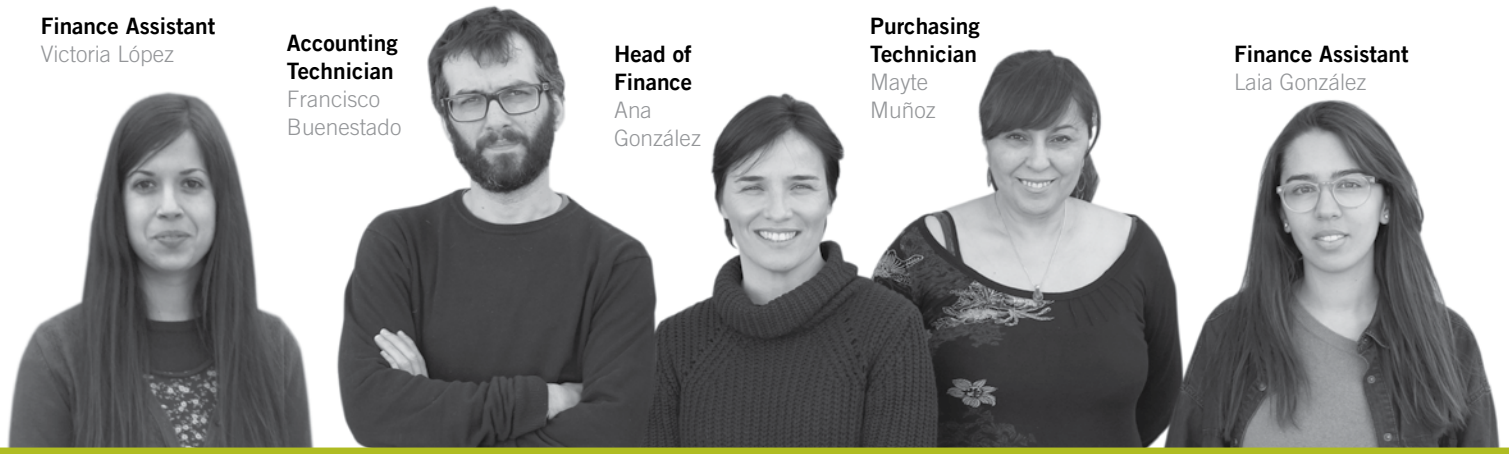
Finance Assistant
Victoria López

Accounting Technician
Francisco Buenestado

Head of Finance
Ana González

Purchasing Technician
Mayte Muñoz

Finance Assistant
Laia González



FINANCE

Not pictured:

KNOWLEDGE EXCHANGE: Arantxa Sanz, Head of Knowledge Exchange, until August 2015; Miroslava Ogorelkova, Project Manager, until September 2015

RESEARCH AFFAIRS: Rosa Bonet, Funding Manager, until January 2015

Statistics

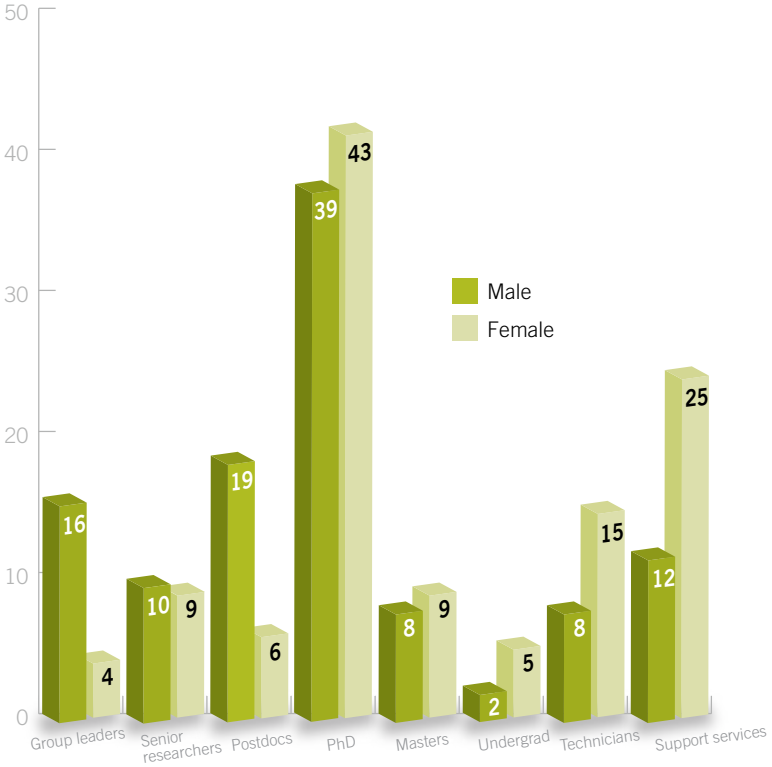
In 2015 IBEC's total staff, including administration staff as well as researchers, students and technicians, numbered 230. Of the researchers, some work on an in-house basis, some come from the University of Barcelona or the Technical University of Catalonia, and some are funded through programmes that support the recruitment of research staff such as the Bosch i Gimpera Foundation, ICREA and the Ramón y Cajal programme (MEC).

The following statistics reflect the state of affairs on 31st December 2015.

1. Age of all IBEC staff (researchers, technicians and administration)

2. Gender of all staff

3. All staff by gender and job category



4. IBEC staff by nationality (map)

The 230 personnel at IBEC in 2015 (including administration staff) represented

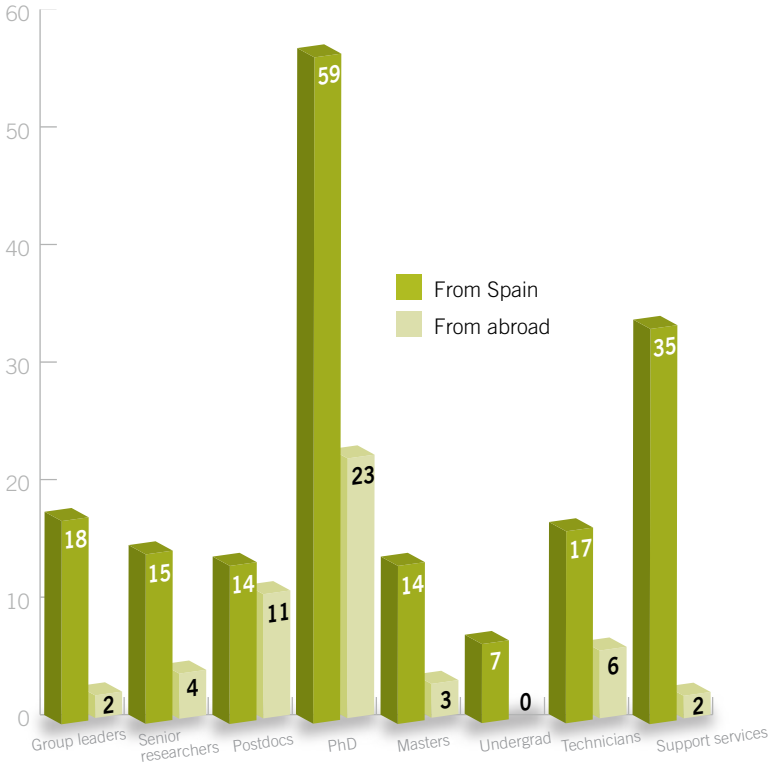
28 countries

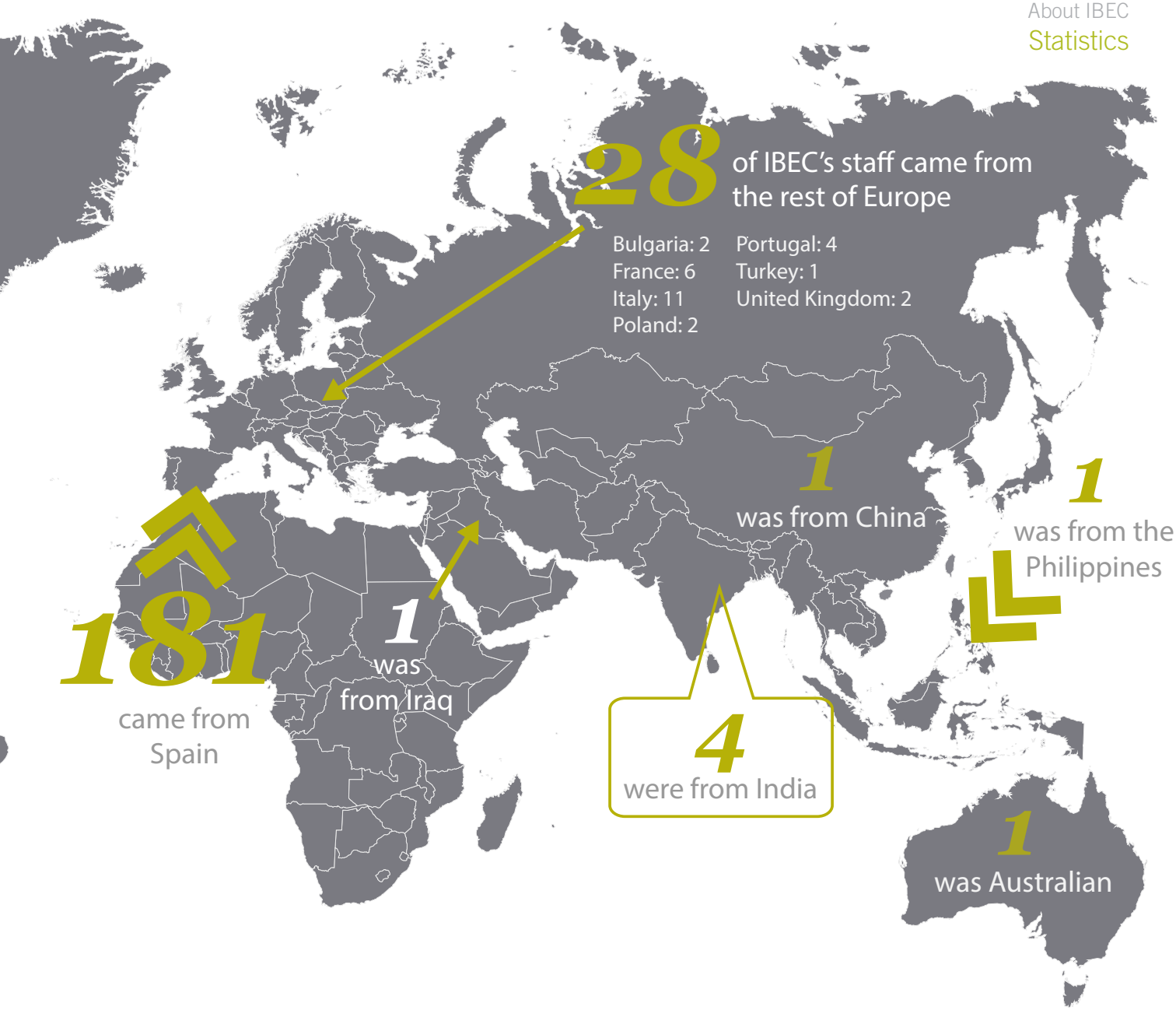
1 came from the United States

Argentina: 2
Brazil: 1
Colombia: 3
Cuba: 3
Mexico: 1
Panama: 1
Uruguay: 1

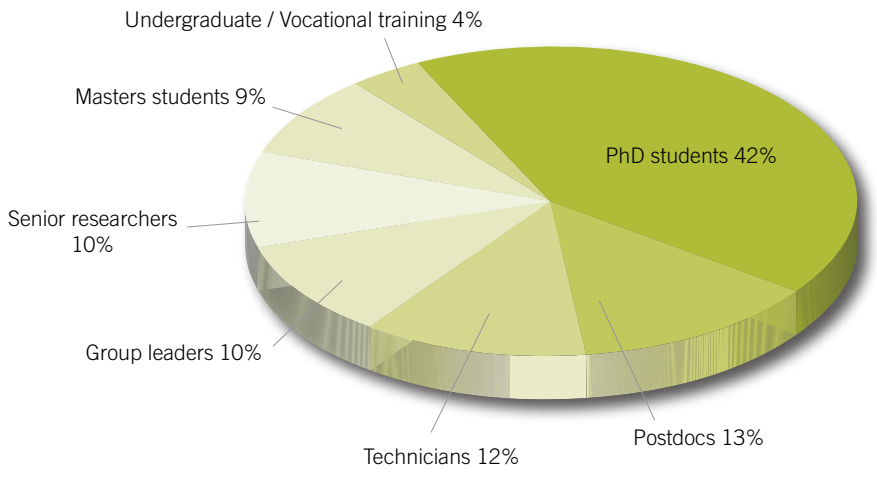
12 were from Latin America

5. IBEC researchers by nationality (Spain/other) and job category





6. IBEC researchers and technicians by job category

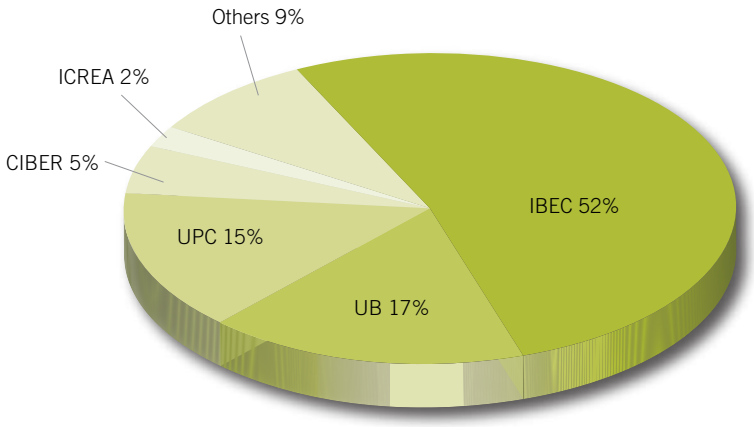


7. Mobility during 2015

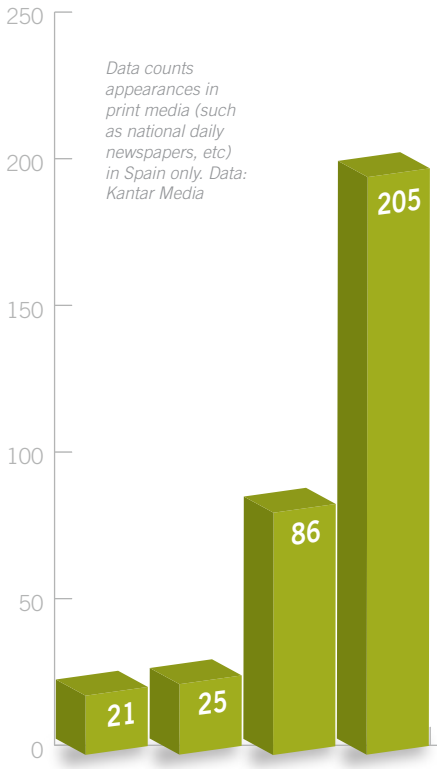
Data refers to researchers only.
Average length of stay in host institutions: 3-6 months.

Number of researchers who spent time in labs elsewhere	**21 (11%)**
In Spain	**4**
In the rest of Europe	**15**
In the rest of the world	**2**

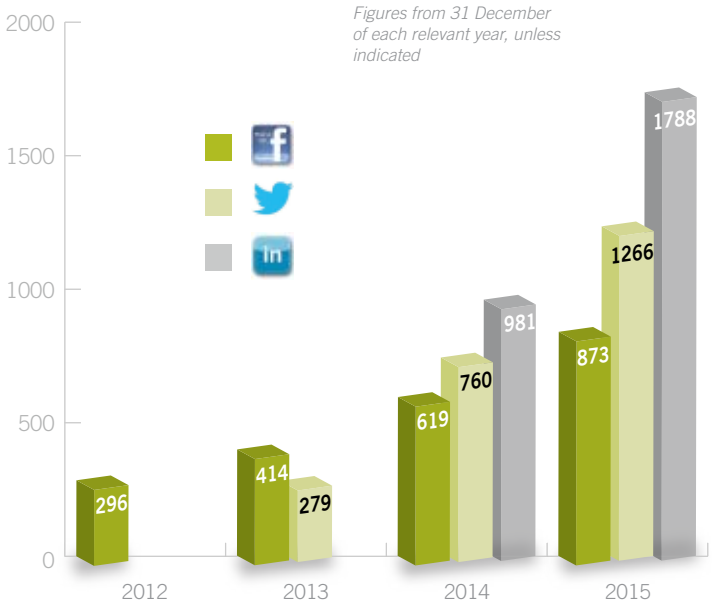
8. IBEC staff by contracting institution



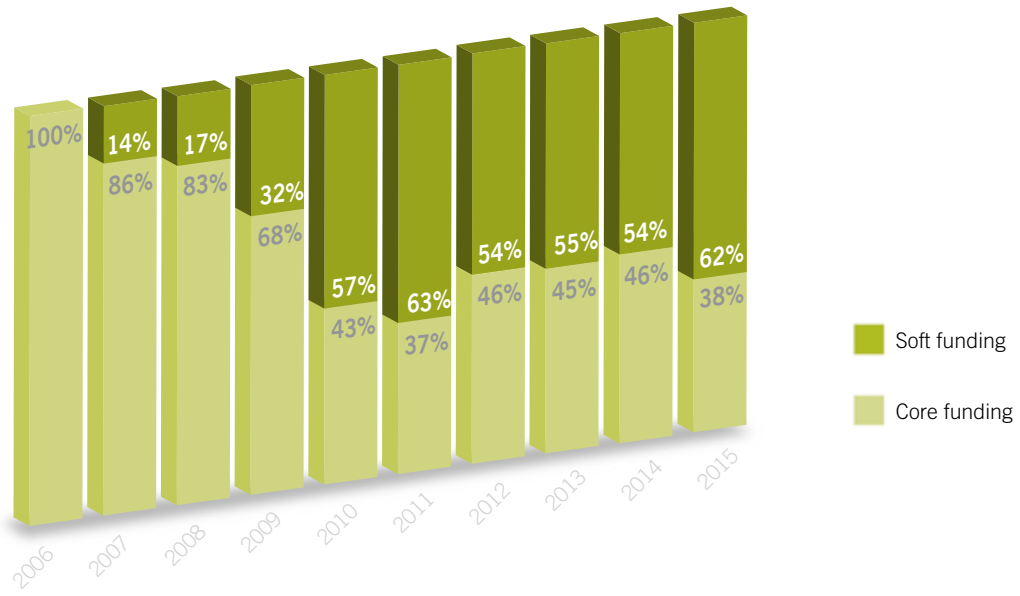
9. Media appearances 2012-2015



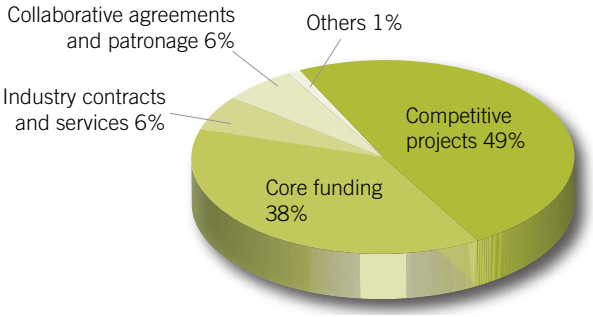
10. Number of followers on social media 2012-2015



11. Funding sources in 2015*



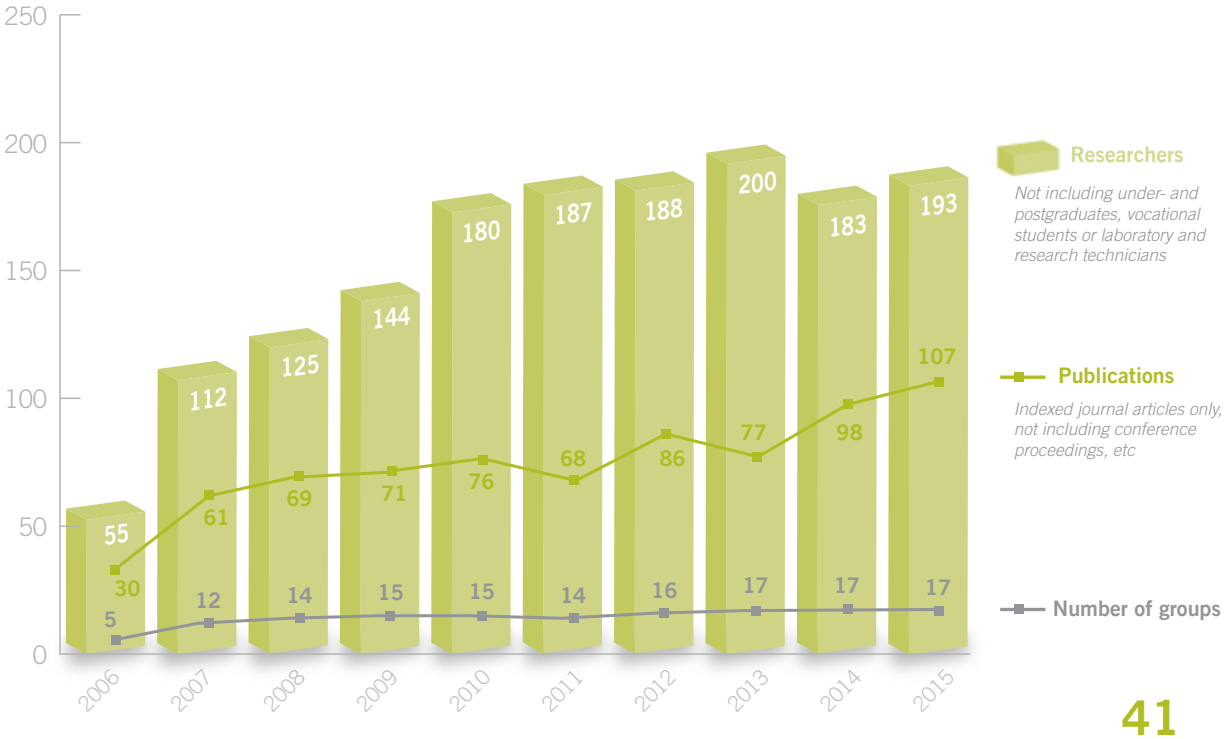
Graph: Percentage of funding from core v. competitive sources. Core funding is funding from trustees. Soft funding includes competitive projects (funded by sources such as the EU's H2020 programme, the Spanish Ministry of Science or the Catalan Ministry of Research), Industry contracts, funding from private institutions.



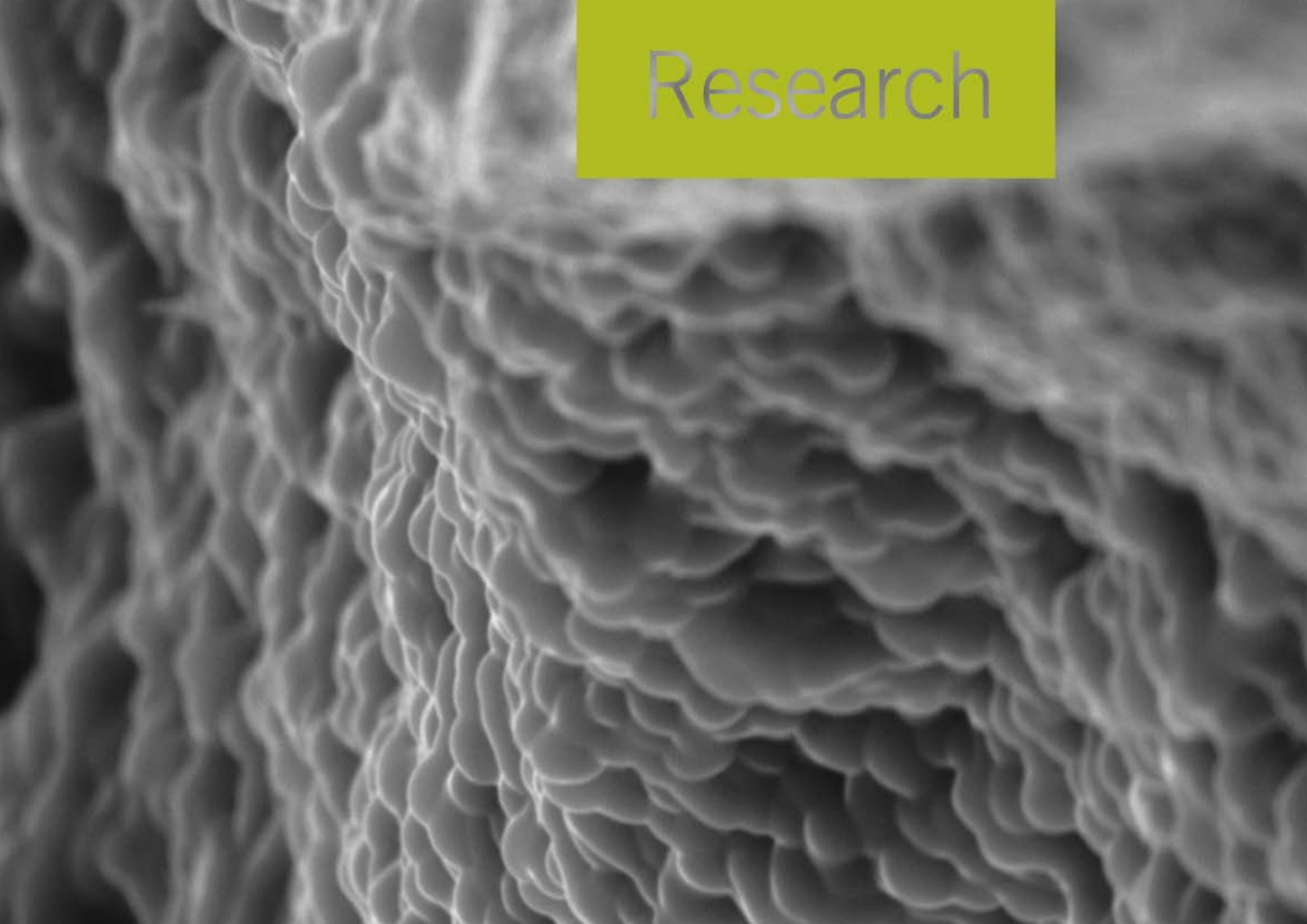
Pie chart: Different sources of funding in 2015, broken down into types.

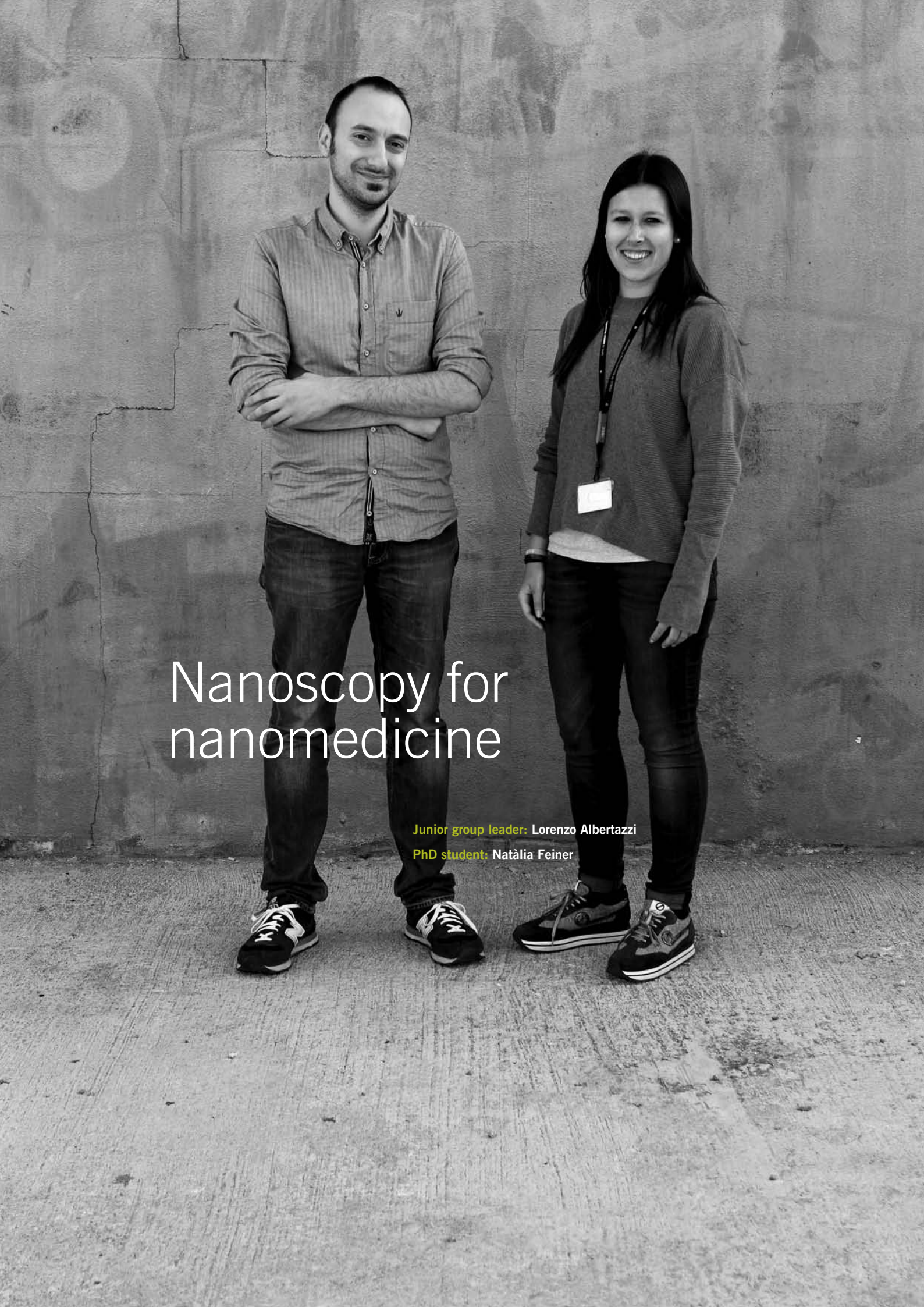
** Figures for 2015 are provisional, pending audit*

12. 2006-2015: Evolution of IBEC (researchers, publications, groups)



Nanoscopy for nanomedicine 44
Molecular dynamics at cell-biomaterial interface 47
Robotics (until September 2015) 52
Biomaterials for regenerative therapies 58
Nanomalaria (IBEC/ISGlobal joint unit) 64
Nanoscale bioelectrical characterization 68
Nanoprobes and nanoswitches 72
Biomedical signal processing and interpretation 78
Microbial technology and host-pathogen interaction 84
Signal and Information Processing for Sensing Systems 89
Biomimetic systems for cell engineering 94
iPSCs & activation of endogenous tissue programs for organ regeneration 98
Cellular and respiratory biomechanics 102
Control of stem cell potency (until July 2015) 108
Molecular and cellular neurobiotechnology 113
Nanobioengineering 117
Smart nano-bio-devices 122
Bacterial infections: antimicrobial therapies 128
Integrative cell and tissue dynamics 132


Research



Nanoscopy for nanomedicine

Junior group leader: Lorenzo Albertazzi

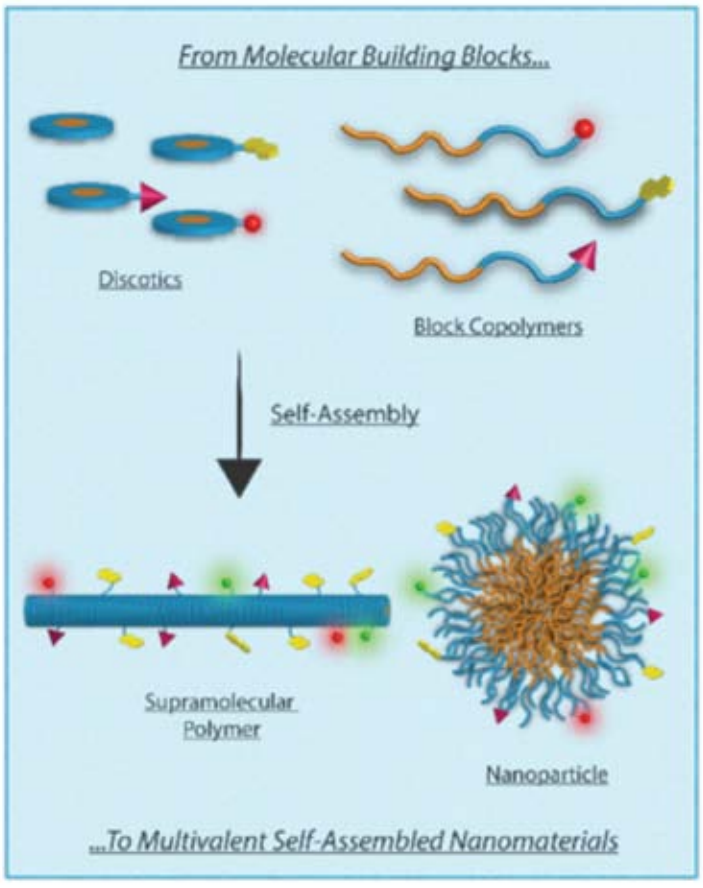
PhD student: Natàlia Feiner

The main goal of our group is to use Super Resolution Microscopy (Nanoscopy) to visualize and track in living cells and tissues self-assembled nanomaterials with therapeutic potential (Nanomedicine). The understanding of materials-cell interactions is the key towards the development of novel nanotechnology-based therapies for treatment of cancer and infectious diseases.

Our group aims to use a multidisciplinary approach, at the interface of chemistry, physics and biology, to develop novel nanomaterials for the treatment of cancer and infectious diseases.

Many biological structures are made of multiple components that self-organize into complex architectures. Here we want to mimic this phenomenon to develop novel bioactive materials such as nanoparticles or nanofibers able to build themselves. We showed how this powerful approach can be used to design materials for intracellular delivery of therapeutic moieties such as drugs or siRNA.

To study the behavior of such complex nanomaterials in action we make use of a variety of optical microscopy techniques, in particular of Super Resolution Microscopy (nanoscopy). Nanoscopy can achieve a resolution down to 20 nm, 10 times better than classical optical imaging and represents an ideal tool to visualize nanosized objects in the biological environment. In particular we demonstrated how STORM (Stochastic Optical Reconstruction Microscopy) can be used to image nanomaterials interactions with cellular structures.



Collaborations with other research centres

Roey Amir, Tel Aviv University, Israel

Ilja Voets, Eindhoven University of Technology, The Netherlands

Giovanni Pavan, SUPSI, Switzerland

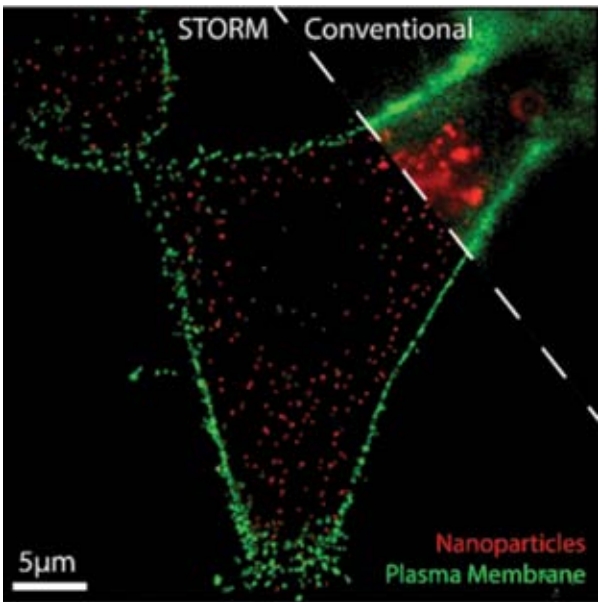
Bruno De Geest, University of Ghent, Belgium

Salvador Borros, IQS Barcelona

Scientific equipment and techniques

- Nikon NSTORM Super Resolution Microscope
- Super Resolution microscopy
- Single particles tracking
- TIRF fluorescence imaging
- Fluorescence spectroscopy
- Dynamic light scattering

Widefield (upper right corner) and STORM super resolution image of HeLa cell internalizing polymer nanoparticles



Molecular Dynamics at Cell-Biomaterial Interface

Group leader/ICREA research professor: George Altankov

Senior researcher: Firas Awaja

PhD student: Dencho Gugutkov

Masters students: Maria Valeska Bianchi, Laura Pacheco

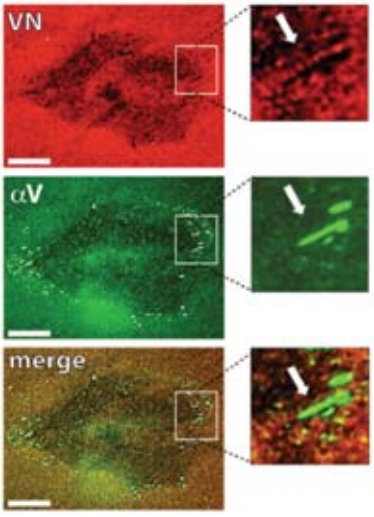
Undergraduate students: Andrea Costa, Núria Canal

We are interested in cell–biomaterials interaction, and more specifically, on the dynamic formation of the provisional extracellular matrix (ECM) – the thin protein layer that cells recognize, produce, and remodel at the materials interface.

We aim to learn how this process affects the biocompatibility of materials, and if it can be controlled by engineering the surface properties of materials. For this purpose, we perform systematic studies in the following directions:

Remodelling of ECM proteins at cell-biomaterials interface

ECM remodelling is a dynamic process that occurs in various physiological and pathological conditions, such as normal development, wound healing and angiogenesis, but also in atherosclerosis, fibrosis, ischemic injury and cancer. It consists of two fundamental processes: assembly and degradation. The organization of ECM is fundamental for biology and medicine, and its proteolytic degradation is a physiological mechanism for the removal of excess ECM. Although matrix remodelling is a subject of extensive biomedical research, the way it is related to the biocompatibility of materials is poorly understood and is therefore a hot topic of our research.



Left: This figure demonstrates the pericellular proteolytic activity of endothelial cells (dark zones) adhering to vitronectin co-localizing with the αv integrin clusters in focal adhesions. Scale bars represent 20 µm.

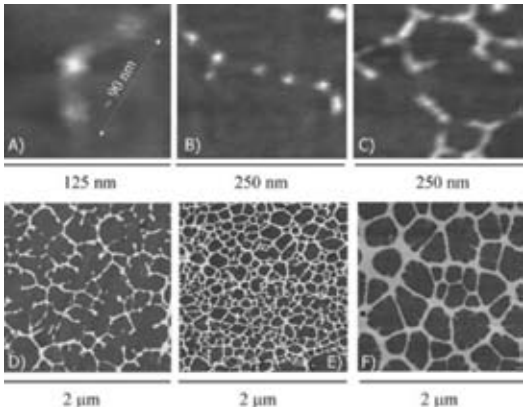
ECM organization at the biomaterial interface depends on the allowance of cells to rearrange adsorbed matrix proteins – a process strongly dependent on proper functioning of integrin receptors. We anticipate that materials that bind proteins loosely will support the arrangement of a provisional ECM, while stronger binding provokes its degradation.

Biomaterials surface-driven assembly of ECM proteins at the nanoscale

Upon adsorption at material interfaces, proteins may assemble spontaneously and this interaction has significant consequences for their biological response. Recently we have employed distinct silane-inspired chemistries and polymer compositions to create model substrates with tailored densities of -OH, -COOH, $-NH_2$ and $-CH_3$ groups, thus varying the chemistry, charge and hydrophilic/ hydrophobic balance. In a series of communications combining AFM and other nanoindentation techniques, we have described a novel phenomenon of substratum-driven protein assembly depicting the fate of various matrix proteins such as fibronectin, collagen IV, vitronectin and fibrinogen at the above model biomaterials interfaces.

Specifically, we show that by varying the density of chemical functions one can tailor both the assembly and degradation of proteins. Following those findings we aim to control ECM remodelling by engineering specific material properties. Understanding the behavior of ECM proteins on flat biomaterials interface further boosts an important bioengineering target – the biohybrid organ

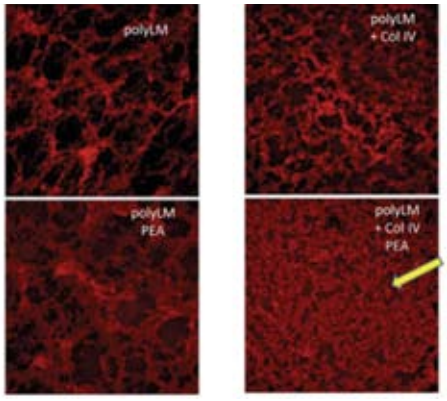
Below: Material driven fibronectin fibrilogenesis at nanoscale as observed with AFM (Gugutkov *et al,* 2009)



technologies based on two-dimensional protein layers that mimic the arrangement of the natural basement membrane.

Development of artificial basement membrane

This project aims to develop a synthetic basement membrane (BM) to be used as a supportive lining for cellularized implants, with specific focus on the design of a bioengineered blood vessel. Taking advantage of the self-assembly properties of the two principal components of the BM, laminin and collagen IV, composite matrices of these molecules are produced by mixing them before or during the polymerization of laminin under acidic conditions.

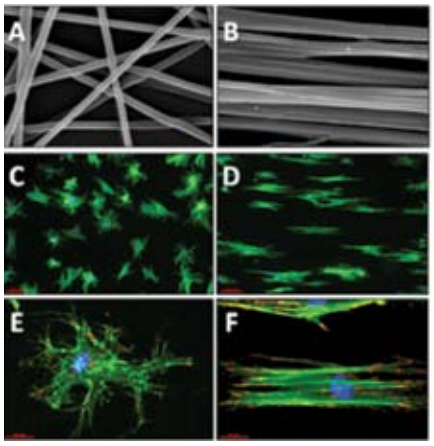


Above: Fluorescent confocal images of poly-laminin and poly-laminin/Col IV composite matrices showing the "condensation" effect of PEA surface resembling the physiological basement membrane

Selected composites will be deposited on scaffolds produced using electronspun nanofibers preferentially made of polyethyl acrilate (PEA), which additionally favour networking of laminin and collagen IV. The resemblance to natural BM will be evaluated in terms of their morphological features and ability to properly induce the formation of biomimetic monolayers of endothelial cells. This project is driven involving joint efforts of Dr Coelho-Sampaio's Lab from the Federal University of Rio de Janeiro, Brazil.

Electrospinning of nanofibers from natural and synthetic polymers for guiding cellular behaviour

In solution, proteins can form structures of various shapes, including fibers with a diameter of only a few nanometers and with lengths up to centimeters. A fascinating possibility to mimic similar ECM structures is to engineer protein-like or matrix protein-containing nanofibers via electrospinning technology. For this purpose we are developing electrospun nanofibers from natural (e.g., fibrinogen) and synthetic polymers (e.g. PLA, PEA) in order to direct the desired cellular response via spatially organized cues (e.g. fiber size and geometrical organization) as well as by tailoring their chemical and mechanical properties.



Left: Hybrid PLA/fibrinogen nanofibers deposited in random (A) and aligned (B) configurations. Human mesenchymal stem cells adhere to the fibers and acquire a stellate-like (C & E) or elongated (D & F) morphology, depending on the fiber orientations (staining: vinculin in red and actin in green).

Nanofibers-based 3D constructs to provide cells with spatially organized stimuli

Examining hierarchical biology in only two dimensions (i.e., cells confined to a monolayer) is in most cases insufficient as cells typically exhibit unnatural behavior if excised from native three-dimensional (3D) tissues. Therefore, within the European FIBROGELNET project (under our coordination) we are developing 3D biohybrid constructs that combine the structural and biological properties of electrospun nanofibers with the optimized mechanical properties of specific

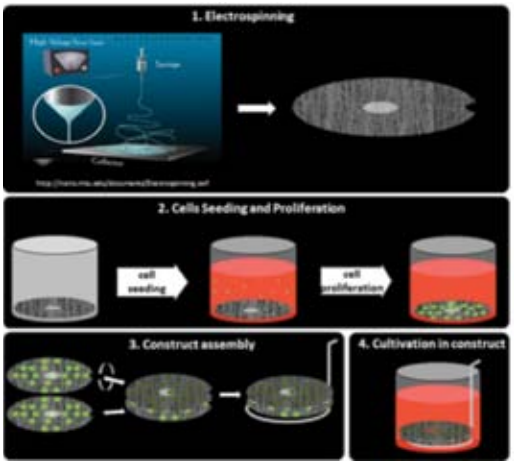
Publications

- Keremidarska, M., Gugutkov, D., Altankov, G. and Krasteva, N. (2015). Impact of electrospun nanofibres orientation on mesenchymal stem cell adhesion and morphology. *Comptes Rendus de L'Academie Bulgare des Sciences*, 68 (10): 1271-1276
- Toromanov, G., Gugutkov, D., Gustavsson, J., Planell, J., Salmerón-Sánchez, M. and Altankov, G. (2015). Dynamic behavior of vitronectin at the cell-material interface. *ACS Biomaterials Science & Engineering*, 1 (10): 927-934

Book Sections

- Rico, P., Cantini, M., Altankov, G. and Sanchez, M. (2015). Matrix-protein interactions with synthetic surfaces. In: "Polymers in Regenerative Medicine: Biomedical Applications from Nano- to Macro-Structures" (ed. Monleon Pradas, M. and Vicent, M. J.). John Wiley & Sons Inc, Hoboken, USA. p91-146

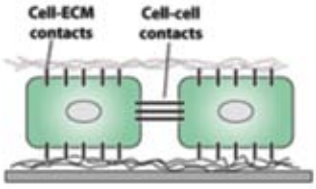
hydrogels in order to provide stem cells with relevant spatial orientation in three dimensions.



Schematic illustration of the STRUCTGEL concept.

Creating dynamic stem cell niches using stimuli-responsive biomaterials

In addition to engineering the spatial configuration of cellular microenvironments, we are also interested in addressing the dynamic (i.e., temporal) aspects of the stem cell niche. To do that we take advantage of stimuli-responsive polymers to obtain control over an artificial cell-adhesive environment via dynamically altering either cell-cell (using cadherin-like ligands) or cell-matrix (using ECM proteins) interactions. By modulating the strength of adhesive protein-to-substratum interactions we aim to control the stem cell adhesive machinery, and which allows us to mimic the dynamic conditions of the stem cell niche.



Stimuli-responsive polymers are used to spatio-temporally control cell-cell and cell-ECM interactions in the microenvironment.

Research projects

- **STRUCTGEL** Nanostructured gel for cellular therapy of degenerative skeletal disorders (2012-2015)
PI: **George Altankov** (coordinator)
EU - EuroNanoMed

- **FIBROGELNET** Network for development of soft nanofibrous construct for cellular therapy of degenerative skeletal disorders (2013-2017)
PI: **George Altankov** (coordinator)
EU - FP7-PEOPLE-2012-IAPP

- **HEALINSYNERGY** Material-driven Fibronectin Fibrillogenesis to Engineer Synergistic Growth Factor Microenvironments (2013-2015)
PI: **George Altankov**
MINECO, MAT359-2012-P4-L02-AC

Collaborations with other research centres

Center for Biomaterials, Technical University of Valencia, Spain

Institute of Pharmacy, Martin Luther University, Halle, Germany

Institute of Biomedical Science, Federal University of Rio de Janeiro, Brazil

Institute for Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, Bulgaria

Institute of Solid State Physics, Bulgarian Academy of Sciences, Sofia, Bulgaria

Institute of Cytology of the Russian Academy of Science and Institute of Neurology named after Prof. A.L.Polenov, St. Petersburg, Russia

Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, United Kingdom

Industrial collaborations:

Bio-Elpida, France

BulGen, Bulgaria

Scientific equipment and techniques

- Universal fluorescent microscope for performing dynamic studies with living cells
- Full facilities for cell culturing
- Electrospinning device designed for the production of nanofibers from natural and synthetic polymers
- Laboratory freeze-dryer (Telstar Cryodos)
- Spectrofluorometer Fluormax 4 (Horiba, Jobin Yvon)
- Complete chromatographic and electrophoretic equipment
- Flow chamber setup for measuring the strength of cell adhesion
- Equipment for photo-polymerization processes
- Programmable compact spin coater

Robotics

Group leader: Alícia Casals

Senior researchers: Joan Aranda, Manel Frigola

PhD students: Eduard Bergés, Xavier Giralt, Albert Hernansanz, Vijaykumar Rajasekaran

Masters student: Esteban Mora

Research Technician: Manuel Vinagre

The growing potential of robotics in the medical field leads to face challenging problems, but at the same time creates great expectancies to the society, as new devices and equipment are envisioned as killing solutions with respect to current technology.

The IBEC's Robotics group research aims to contribute to the slow but continuous advances in the medical field, in the areas of assistance to disabled, in rehabilitation and assistance in surgery. A common factor in these three areas is the need of adaptation to the user's needs, what implies perceiving not only the user's will and status, but also the environment conditions and the evolution of the ongoing activity.

Our current research within the HYPER project (Hybrid Neuroprosthetic and Neurorobotic Devices for Functional Compensation and Rehabilitation of Motor Disorders) is to search for new adaptive control algorithms focusing on specific actions, as the transition from sit to stand or keeping the walking pattern under internal or external perturbations. This control has to deal with disturbances caused by muscle synergies, taking into account unpredictable effects of artificial stimulation in muscles during rehabilitation therapies or other effects as fatigue or the own user's attention to the therapy. In this field, the work carried out has been focused on developing a control system with variable hierarchy and a status evaluator that allows adapting the control variables, mainly the variable stiffness at each joint, to reach the desired response and stability.

Being human-robot interaction a key factor in medical robotics, our research in assistive robotics is devoted to interpret human activity and the operation context so as to be able to program robots to cooperate proactively in assisting disabled in their daily tasks. This implies the extraction of relevant image features to recognize human posture and actions and relate them to the context environment and the evolution of tasks and activities, using recognition and learning techniques. The challenge is finding adequate algorithms that are reliable enough and can reduce the amount of data to process so as to be able to operate in real time. Figure 1 shows the original data, the human joints, and the reduction of triangles, trisarea feature, that define each posture in a sequence of poses corresponding to the human movement. For the adequate robot control this information has to be compatible with the environment status, thus perception and context interpretation is necessary. Further work has been done on the integration of multiple robot arms to deal with tasks that need cooperative actuation.

The research in surgical robots has progressed going deeper in the development of robot aids, as the analysis of tissues deformation aiming to solve problems as physiological movement detection for robot motion compensation or for estimation of the force applied on the tissues due to the lack of sensors to be integrated on the surgical tools. Figure 2 shows a sequence of images of the heart and the changes produced on the heart surface by the forces applied. The image processing operates from the minimization of an energy functional using the l_1–regularized optimization class in which cubic b-splines are used to represent the changes produced on the heart surface.

In technology transfer, much progress has been done in the spin-off, Rob Surgical Systems S.L, having already started the experimentation with models in an experimental operating room and advancing in the regulatory process. We have also advanced in the Surgitrainer project, a training simulator for minimally invasive surgery and a new specific robotic trainer has been designed, built and evaluated in Hospital de Sant Pau and in the Leuven premises of our partner, as part of the European Society for Gynaecological Endoscopy. We are now in the process of creating a company with the aim of progressively advancing in new robot surgical techniques that assist surgeons from the training phase to their assistance in clinical interventions.

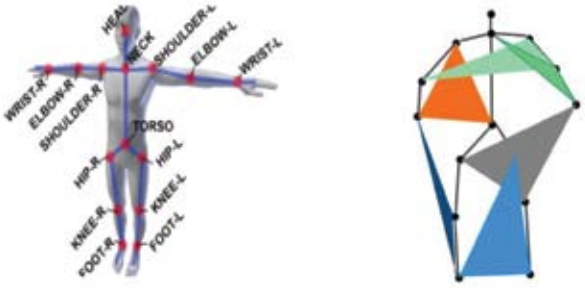


Figure 1: Pose descriptor and trisarea as new geometric pose-based feature for human motion recognition

Filed patents

■ **Dispositivo para simular una operación endoscópica vía orificio natural**
(submitted on 11th December 2015)
Inventors: Casals, A., Hernansanz, A., Rovira, A., Basombra, J. and Comas, R. Fundació Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau; Universitat Politècnica de Catalunya; Fundació Institut de Bioenginyeria de Catalunya.
Patent number: P201531796

Research projects

■ **IPRES** Interacción persona robot en entornos semiestructurados bajo criterios de permitividad (2012-2015)
PI: **Alícia Casals** (project coordinator)
MINECO

■ **HYPER** Hybrid NeuroProsthetic and NeuroRobotic Devices for Functional Compensation and Rehabilitation of Motor Disorders (2010-2015)
PI: **Alícia Casals**
MINECO, Actividad Investigadora CONSOLIDER – INGENIO 2010

■ **InHANDS** Interactive robotics for Human Assistance iN Domestic Scenarios (2013-2015)
PI: **Joan Aranda**
RecerCaixa

■ Desenvolupament d'un sistema robòtic de baix cost d'ajut de la marxaper a nens amb transtorns motors greus (2014-2016)
PI: **Alícia Casals**
RecerCaixa

■ Grup de recerca consolidat (2014-2016)
PI: **Alícia Casals**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (SGR 2014)

■ Validación clínica robot quirúrgico (2015-2018)
PI: **Alícia Casals**
MINECO

■ **HYSTRAINER** Entrenador quirúrgic per cirurgia histeroscòpica (2015)
PI: **Alícia Casals**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Ajuts per a projectes innovadors amb potencial d'incorporació al sector productiu - LLAVOR

Publications

■ Hernansanz, A., Casals, A. and Amat, J. (2015). A multi-robot cooperation strategy for dexterous task oriented teleoperation. *Robotics and Autonomous Systems*, 68 156-172

■ Rajasekaran, V., Aranda, J., Casals, A. and Pons, J. L. (2015). An adaptive control strategy for postural stability using a wearable robot. *Robotics and Autonomous Systems*, 73 16-23

■ Morales, R., Badesa, F. J., Garcia-Aracil, N., Aranda, J. and Casals, A. (2015). Autoadaptive neurorehabilitation robotic system assessment with a post-stroke patient. *Revista Iberoamericana de Automatica e Informatica Industrial*, 12 (1): 92-98

Conference Papers

■ Alsaleh, S. M., Aviles, A. I., Sobrevilla, P., Casals, A. and Hahn, J. K. (2015). Automatic and robust single-camera specular highlight removal in cardiac images. *37th Annual International Conference of the IEEE,* Milan, Italy. Published by IEEE (2015/08/25)

■ Aviles, A. I., Alsaleh, S. M., Sobrevilla, P. and Casals, A. (2015). Force-feedback sensory substitution using supervised recurrent learning for robotic-assisted surgery. *37th Annual International Conference of the IEEE,* Milan, Italy. Published by IEEE (2015/08/25)

■ Rajasekaran, V., Aranda, J. and Casals, A. (2015). Compliant gait assistance triggered by user intention. *37th Annual International Conference of the IEEE,* Milan, Italy. Published by IEEE (2015/08/25)

■ Urra, O., Casals, A. and Jané, R. (2015). The impact of visual feedback on the motor control of the upper-limb. *37th Annual International Conference of the IEEE,* Milan, Italy. Published by IEEE (2015/08/25)

- Mur, O., Frigola, M. and Casals, A. (2015). Modelling daily actions through hand-based spatio-temporal features. *International Conference on Advanced Robotics*, Istanbul, Turkey. Published by IEEE (2015/07/31).
- Aviles, A. I., Alsaleh, S., Sobrevilla, P. and Casals, A. (2015). Sensorless force estimation using a neuro-vision-based approach for robotic-assisted surgery. *7th International IEEE/ EMBS Conference on Neural Engineering*, Montpellier, France. Published by IEEE (2015/04/22).

Book Sections

- Rokbani, N., Casals, A. and Alimi, A. (2015). IK-FA, a New Heuristic Inverse Kinematics Solver Using Firefly Algorithm. In: "Computational Intelligence Applications in Modeling and Control" (ed. Azar, A. T. and Vaidyanathan, S.). Springer International Publishing, Lausanne, Switzerland, 575: 369-395
- Vinagre, M., Aranda, J., Casals, A., Aranda, J. and Casals, A. (2015). A new relational geometric feature for human action recognition. In: "Lecture Notes in Electrical Engineering" (ed. Ferrier, J. L., Gusikhin, O., Madani, K. and Sasiadek, J.). Springer, Lausanne, Switzerland, 325: 263-278

- System for teleguidance, planning and pre-robotic automatization for IntraOperative (2013-2015)
PI: **Alícia Casals**
Fundación Investigación Biomédica del Hosp. Gregorio Marañon

- **TAM** Desenvolupament d'un sistema intel·ligent de selecció i manipulació d'objectes en un entorn estèril (2014-2015)
PI: **Alícia Casals**
Industrial project with Technologies for Advanced Manufacturing and Robotics, S.L.

Collaborations with other research centres

Dr. Ramon Rovira and Gabriel Gili Hospital de Sant Pau, Barcelona, Spain

Dr. Enric Laporte Corporació Sanitària Parc Taulí, Sabadell, Spain

Dr. Oriol Puig Hospital de la Vall d'Hebrón, Barcelona, Spain

Dr. Carlos Torrens Hospital del Mar, Barcelona, Spain

Dr. Javier Magriñá Mayo Clinic, Scottsdale, Arizona, USA

Dr. Rudi Campo President of ESGE, European Society for Gynaecological Endoscopy

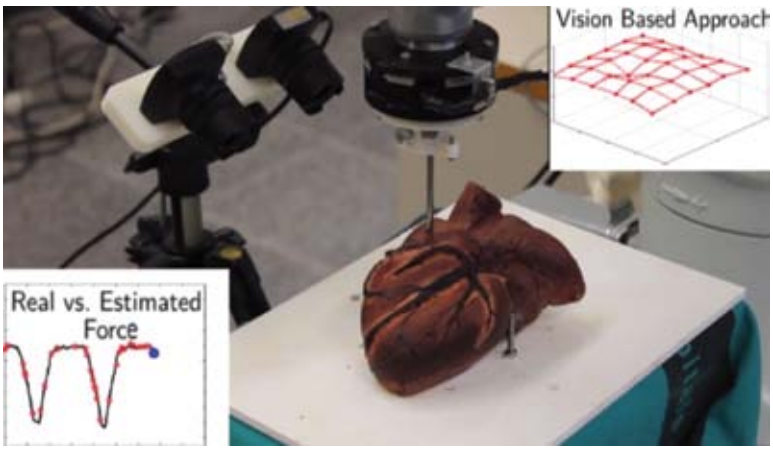
Prof Paolo Fiorini Università degli Studi di Verona, Verona, Italy

Prof Nicolás García Universidad Miguel Hernández de Elche, Alicante, Spain

Research Prof. José L. Pons Bioengineering group, CSIC, Madrid, Spain

Prof. Joerg Raczkowsky Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

Figure 2: Sequence of a sit-to-stand experiment with the assistance of the HYPER neuroprosthesis and reurorobot.



Scientific equipment and techniques

- Basic electronics laboratory equipment
- A 50' 3D monitor
- 6D magnetic positioning sensors (Polhemus)
- Ultrasound probe: B-Ultrasonic Diagnostic Equipment Model WED-2000
- 2 PC with multiprocessor architecture (Tesla C2050)
- A BCI working platform based on an Emotiv Epoc headset (EEG acquisition system)
- KUKA lightweight robot specially designed for mobility and interaction with humans and a priori unknown environments. It is equipped with a control environment developed by the team to program anatomic constraints to operate in virtual environments
- Computer controlled LED-based lighting system for the operating room
- Experimental robotized kitchen composed of a robot, several adapted cupboards, a kitchen counter and a PC for robot and environment control
- 2 robot operated 3 degrees of freedom surgical instruments
- Baxter: Robot Baxter research edition, with two sensorized arms and with integrated vision The robot operates under OROCOS and is provided with an anticollision application for a safe operation of its two arms.
- A Robotic arm with a two fingers gripper, Mico research edition, from Kinova.
- A 3-finger adaptive robot gripper, from Robotiq

Biomaterials for regenerative therapies

Junior group leader: Elisabeth Engel

Senior researchers: Oscar Castaño, Miguel Angel Mateos, Soledad Pérez

Postdoctoral researcher: Andy Luis Olivares

PhD students: Irene Cano, Joan Martí, Claudia Navarro, Jesús Ordoño, Xavier Puñet, Aitor Sánchez

Masters students: Pau Atienza, Camille Marc, Cristina Rodríguez, Gerard Rubí

Undergraduate students: Laia Gili, Marc Batista, Ester Cardet

Laboratory technician: Belén González

Biomaterials for regenerative therapies

Research in the Biomaterials for Regenerative Therapies group is devoted to the development and knowledge transfer to industry of innovative biomaterials and scaffolds for tissue regeneration.

We design, fabricate and characterise bioactive and biodegradable materials and investigate their interactions with biological entities, both in terms of their fundamental aspects and with specific applications for tissue engineering purposes in mind. The aim is the repair and functional restoration of tissues or organs by means of 3D scaffolds, cells and signals.

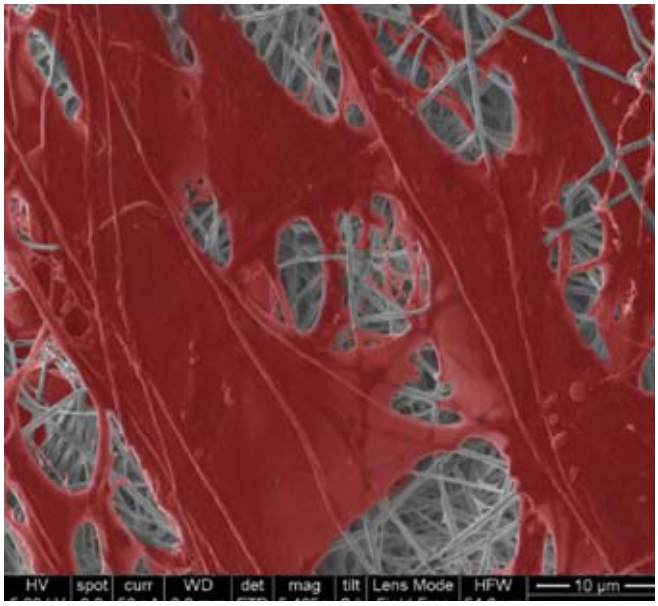
Two main research areas are being developed in the group:

Production of polymeric biomaterials using different fabrication techniques. By using a polymer nanoprecipitation technique, the group produced nanoparticles for antibiotic drug delivery (Baelo A. *et al.*, 2015, *Journal of Controlled Release*) that effectively treated persistent bacterial infections. The use of a jet break-up polymer precipitation technique together with protein/peptide functionalization allowed the group to produce micro particles for effective cell delivery (Levato R. *et al.*, 2015, *Acta Biomaterialia*).

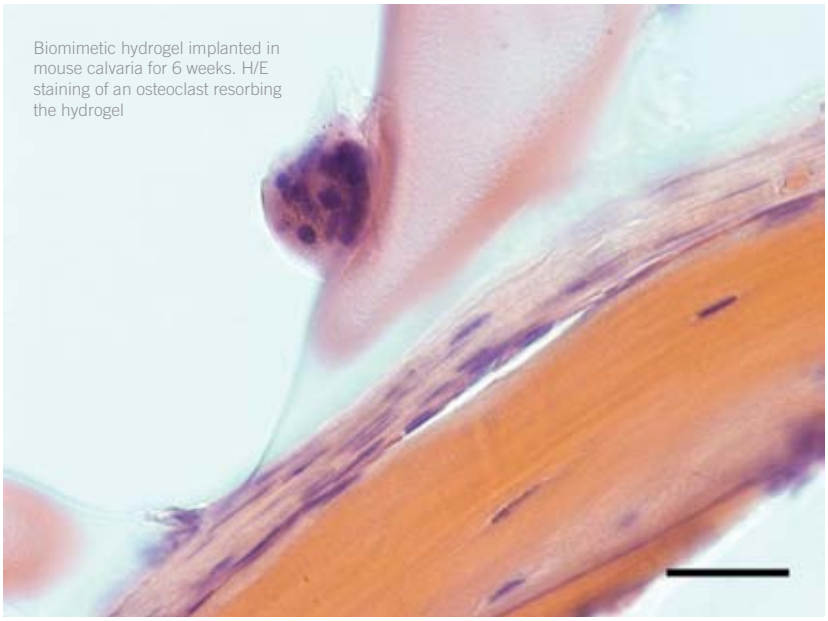
The production of structured bioactive nanocomposites that can enhance vascularization, bone and skin regeneration, either by electrospinning, rapid prototyping or microparticles production. Recent advances describe a novel hybrid material which faithfully mimics the structure of bone's extracellular matrix, recreating the molecular architecture and biochemical environment to surround cells with the proper stimuli to spread and grow (Sachot N *et al.*, 2015, *Nanoscale*). Other biomaterials developed in the group such as hybrid fibrous mats with different contents of calcium-releasing nanoparticles are able to induce angiogenesis in *in vivo* models (Oliveira H. *et al.*, 2016, *Acta Biomaterialia*).

In collaboration with the group of Rodriguez-Cabello from the University of Valladolid, the group developed microstructured biomimetic hydrogels using new crosslink methods that induce bone formation (Sánchez-Ferrero A. e*t al.*, 2015, *Biomaterials*).

In 2015, the Dermoglass project was selected for funding under the first CaixaImpulse call, a funding programme promoted by the Obra Social "la Caixa", that aims to promote technology transfer in science.



Endothelial precursor cells (red) seeded on ormoglass/ PLA blends



Biomimetic hydrogel implanted in mouse calvaria for 6 weeks. H/E staining of an osteoclast resorbing the hydrogel

Research projects

- **THE GRAIL** Tissue in Host Engineering Guided Regeneration of Arterial Intimal Layer (2012-2016)
PI: **Elisabeth Engel, Soledad Pérez** (scientific coordinator)
EU - Cooperation - HEALTH

- **nAngioFrac** Angiogenic nanostructured materials for non-consolidating bone fractures (2012-2015)
PI: **Elisabeth Engel, Oscar Castaño** (scientific coordinator)
EU - EURONANOMED - PI11/03030

- **INSBIOMAT** Biomateriales instructivos para regeneración cardíaca *in vivo* (2015-2016)
PI: **Elisabeth Engel**
MINECO Acciones Dinamización "Europa Excelencia"

- Andamios diseñados para promover una vascularización eficiente para fracturas óseas no consolidadas (2012-2015)
PI: **Oscar Castaño**
MINECO MAT2011-29778-C02-01

- Diseño y desarrollo de Biomateriales bioactivos para la regeneración de la piel basada en la señalización controlada de liberación de iones (2013-2016)
PI: **Elisabeth Engel**
MINECO MAT2012-38793

- **BIOTENDON** Tendon Tissue Engineering: A Helping Hand for Rotator Cuff Tears (2014-2015)
PI: **Elisabeth Engel, Miguel A. Mateos-Timoneda** (scientific coordinator)
RecerCaixa

Collaborations with other research centres

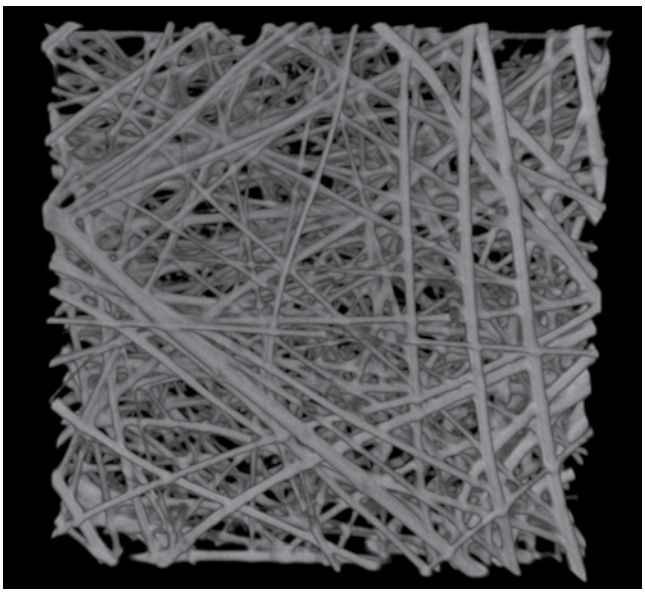
Dr. Ernest Mendoza Applied Nanomaterials Laboratory, Research Centre in Nanoengineering, Technical University of Catalonia (UPC, BarcelonaTech), Spain

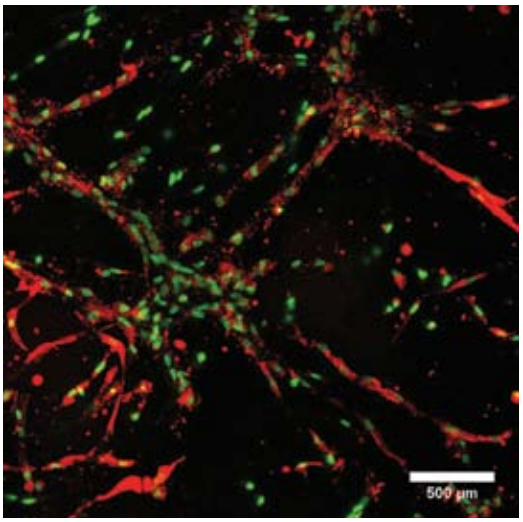
Publications

- Sánchez-Ferrero, A., Mata, Á., Mateos-Timoneda, M. A., Rodríguez-Cabello, J. C., Alonso, M., Planell, J. and Engel, E. (2015). Development of tailored and self-mineralizing citric acid-crosslinked hydrogels for *in situ* bone regeneration. *Biomaterials*, 68 42-53
- Baelo, A., Levato, R., Julián, E., Crespo, A., Astola, J., Gavaldà, J., Engel, E., Mateos-Timoneda, M. A. and Torrents, E. (2015). Disassembling bacterial extracellular matrix with DNase-coated nanoparticles to enhance antibiotic delivery in biofilm infections. *Journal of Controlled Release*, 209 150-158
- Sachot, N., Mateos-Timoneda, M. A., Planell, J. A., Velders, A. H., Lewandowska, M., Engel, E. and Castaño, O. (2015). Towards 4th generation biomaterials: A covalent hybrid polymer-ormoglass architecture. *Nanoscale*, 7 (37): 15349-15361
- Levato, R., Planell, J. A., Mateos-Timoneda, M. A. and Engel, E. (2015). Role of ECM/peptide coatings on SDF-1α triggered mesenchymal stromal cell migration from microcarriers for cell therapy. *Acta Biomaterialia*, 18 59-67
- Kovtun, A., Goeckelmann, M. J., Niclas, A. A., Montufar, E. B., Ginebra, M. P., Planell, J. A., Santin, M. and Ignatius, A. *In vivo* performance of novel soybean/gelatin-based bioactive and injectable hydroxyapatite foams. *Acta Biomaterialia*, 12 (1): 242-249
- Sachot, N., Castano, O., Planell, J. A. and Engel, E. (2015). Optimization of blend parameters for the fabrication of polycaprolactone-silicon based ormoglass nanofibers by electrospinning. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, 103 (6): 1287–1293

■ Won, J. E., Mateos-Timoneda, M. A., Castaño, O., Planell, J. A., Seo, S. J., Lee, E. J., Han, C. M. and Kim, H. W. (2015). Fibronectin immobilization on to robotic-dispensed nanobioactive glass/polycaprolactone scaffolds for bone tissue engineering. *Biotechnology Letters*, 37 (4): 935-342

3D reconstruction of PLA fibers. Confocal microscopy using a fluorescent marker





hMSC embeded in PEG hydrogels. Cytoplasms are stained in red, nuclei in green

Dr. Małgorzata Lewandowska Faculty of Materials Science & Engineering, WUT Warsaw University of Technology, Poland

Dr. Manuel Doblaré Group of Structural Mechanics and Materials Modelling, Institute of Engineering Research, (I3A), Universidad de Zaragoza, Spain

Dr. Margarita Calonge Institute of Ophthalmobiology (IOBA), Universidad de Valladolid, Spain

Dr. María Vallet Regí Facultad de Farmacia, Universidad Complutense de Madrid, Spain

Dr. Mário Barbosa New Therapies group, Institute for Biomedical Engineering (INEB), University of Porto, Portugal

Prof. Mateo Santin Brighton Studies in Tissue Mimicry and Aided Regeneration (BrightSTAR) Research Group, University of Brighton, UK

Prof. Wouter J.A. Dhert & Dr. Jos Malda Department of Orthopaedics, University Medical Center Utrecht, The Netherlands

Scientific equipment and techniques

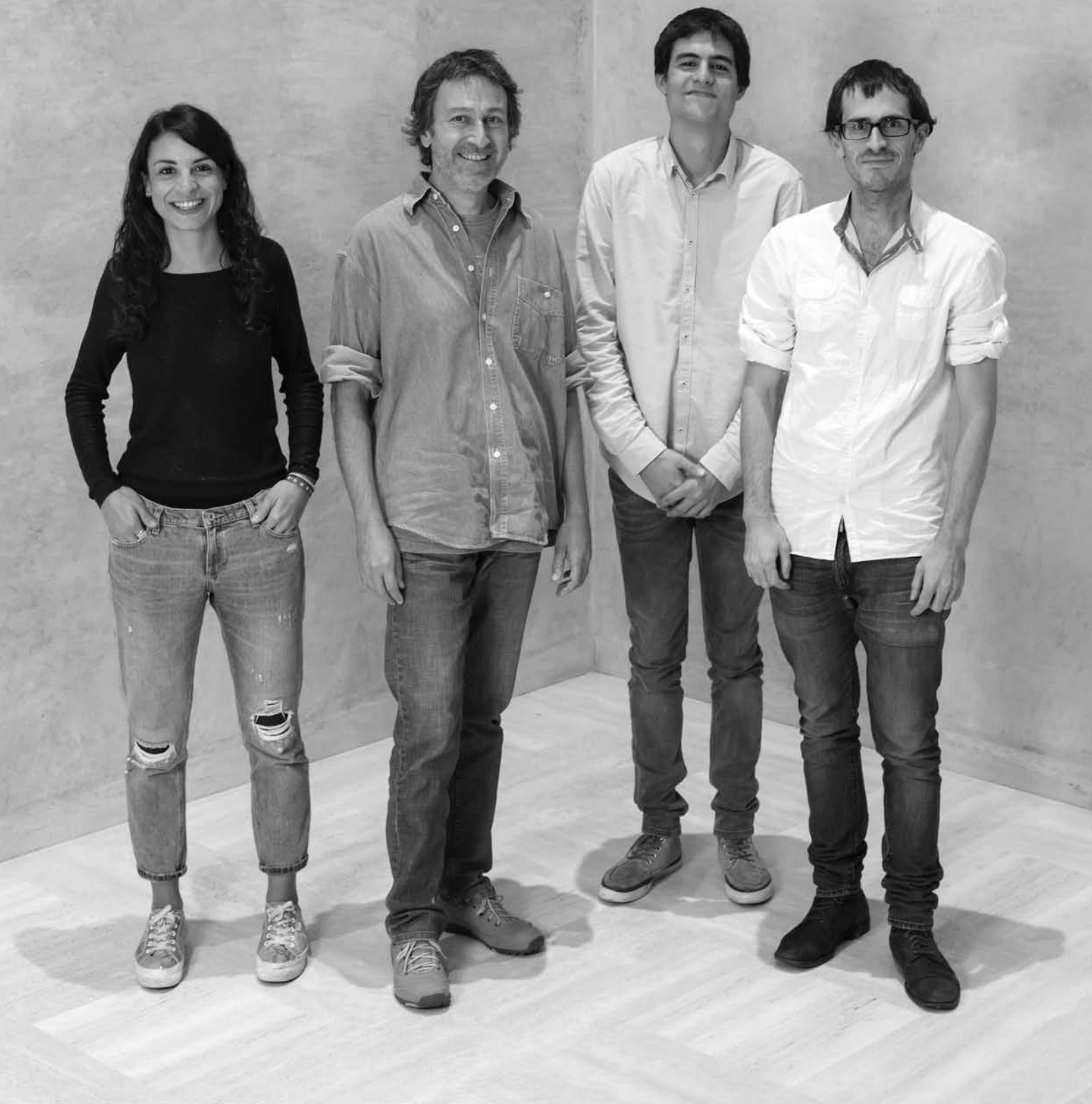
- Surface characterization equipment (contact angle, Z potential, nanoindenter)
- Cell culture facilities
- Molecular Biology equipment: protein and DNA electrophoresis
- Thermocycler (PCR)
- Rapid prototyping tool
- Peptide synthetiser
- Combustion furnace
- Electrospinning device
- Spin-coater
- Vibrational viscosimeter
- ElectroForce® BioDynamic® test instrument

Nanomalaria
(joint unit IBEC/ISGlobal)

Head of Joint Unit: Xavier Fernàndez-Busquets

PhD students: Joana Azevedo, Arnau Biosca, Elena Lantero, Elisabet Martí, Ernest Moles

Undergraduate student: Aida Montserrat



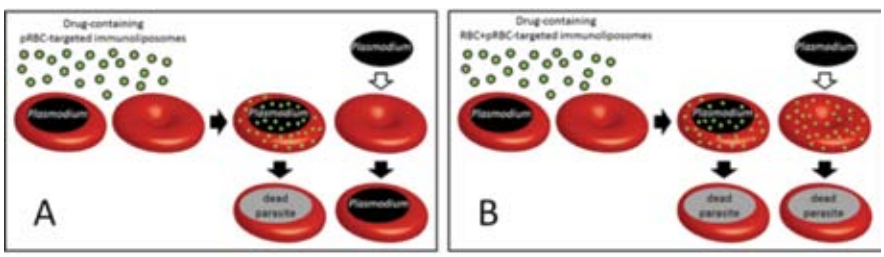
The current activity of the Nanomalaria group is focused on the development of nanomedicine-based systems to be applied to malaria prophylaxis, diagnosis and therapy.

Malaria is arguably one of the main medical concerns worldwide because of the numbers of people affected, the severity of the disease and the complexity of the life cycle of its causative agent, the protist *Plasmodium spp*.

The clinical, social and economic burden of malaria has led for the last 100 years to several waves of serious efforts to reach its control and eventual eradication, without success to this day. With the advent of nanoscience, renewed hopes have appeared of finally obtaining the long sought-after magic bullet against malaria in the form of a nanovector for the targeted delivery of antimalarial drugs exclusively to *Plasmodium*-infected cells. Nanotechnology can also be applied to the discovery of new antimalarials through single-molecule manipulation approaches for the identification of novel drugs targeting essential molecular components of the parasite. Finally, methods for the diagnosis of malaria can benefit from nanotools applied to the design of microfluidic-based devices for the accurate identification of the parasite's strain, its precise infective load, and the relative content of the different stages of its life cycle, whose knowledge is essential for the administration of adequate therapies. The benefits and drawbacks of these nanosystems have to be considered in different possible scenarios, including economy-related issues that are hampering the development of nanotechnology-based medicines against malaria with the dubious argument that they are too expensive to be used in developing areas. Unfortunately, it is true that the application of nanoscience to infectious disease has been traditionally neglected, with most research resources overwhelmingly biased towards other pathologies more prominent in the developed world. Thus, extra ingenuity is demanded from us: malaria-oriented nanomedicines not only need to work spotless; they have to do so in a cost-efficient way because they will be deployed in low-income regions.

The driving force of the Nanomalaria group is our personal commitment to applying nanomedicine to infectious diseases of poverty though our current research lines: (i) Exploration of different types of encapsulating structure (liposomes, synthetic and natural polymers), targeting molecule (protein, polysaccharide, nucleic acid), and antimalarial compound (e.g. new structures derived from marine organisms and antimicrobial peptides) for the assembly of nanovectors capable of delivering their drug cargo with complete specificity to diseased cells. (ii) Study of metabolic pathways present in *Plasmodium* but absent in humans, with the aim of identifying specific enzymes as therapeutic targets. (iii) Use of single-molecule force spectroscopy strategies for the biodiscovery of new antimalarial and antibiotic agents. (iv) Design of new methods for the targeted drug delivery to *Plasmodium* stages in the mosquito vector. (v) Investigation of novel drugs against insect-borne diseases working through radically new mechanisms. (vi) Extension of our activities to new pathologies including leishmaniasis, Chagas' disease, and tuberculosis. Our current efforts are centered on the engineering of innovative therapeutic strategies requiring minimal clinical assays and therefore amenable to being applied in the field in years instead of decades.

Different outcomes expected when antimalarial drugs are targeted (A) only to *Plasmodium*-infected erythrocytes, or (B) to all erythrocytes. In the latter case the parasite will encounter the drug upon invasion



Publications

- Manca, M. L., Castangia, I., Zaru, M., Nácher, A., Valenti, D., Fernàndez-Busquets, X., Fadda, A. M. and Manconi, M. (2015). Development of curcumin loaded sodium hyaluronate immobilized vesicles (hyalurosomes) and their potential on skin inflammation and wound restoring. *Biomaterials*, 71 100-109
- Moles, E., Urbán, P., Jiménez-Díaz, M. B., Viera-Morilla, S., Angulo-Barturen, I., Busquets, M. A. and Fernàndez-Busquets, X. (2015). Immunoliposome-mediated drug delivery to Plasmodium-infected and non-infected red blood cells as a dual therapeutic/prophylactic antimalarial strategy. *Journal of Controlled Release*, 210 217-229
- Castangia, I., Nácher, A., Caddeo, C., Merino, V., Díez-Sales, O., Catalán-Latorre, A., Fernàndez-Busquets, X., Fadda, A. M. and Manconi, M. (2015). Therapeutic efficacy of quercetin enzyme-responsive nanovesicles for the treatment of experimental colitis in rats. *Acta Biomaterialia*, 13 216-227
- Urbán, P., Ranucci, E. and Fernàndez-Busquets, X. (2015). Polyamidoamine nanoparticles as nanocarriers for the drug delivery to malaria parasite stages in the mosquito vector. *Nanomedicine*, 10 (22): 3401-3414
- Moles, E. and Fernàndez-Busquets, X. (2015). Loading antimalarial drugs into noninfected red blood cells: An undesirable roommate for Plasmodium. *Future Medicinal Chemistry*, 7 (7): 837-840
- Castangia, I., Manca, M. L., Matricardi, P., Catalán-Latorre, A., Nácher, A., Diez-Sales, O., Fernàndez-Busquets, X., Fadda, A. M. and Manconi, M. (2015). Effects of ethanol and diclofenac on the organization of hydrogenated phosphatidylcholine bilayer vesicles and their ability as skin carriers. *Journal of Materials Science: Materials in Medicine*, 26 137

Cryo-transmission electron microscope image of liposomes being assayed for the encapsulation of drugs specifically targeted to red blood cells infected by the malaria parasite *Plasmodium falciparum.*
CryoTEM image artistic editing by Marc Cirera, www.marccirera.com

Research projects

- **NANOMISSION** Engineering of nanovectors for the delivery of antimalarial drugs to Plasmodium transmission forms (2015-2017)
PI: **Xavier Fernàndez-Busquets**
Biotechnology Programme, MINECO, Spain (BIO2014-52872-R)

- Amphoteric polyamidoamines as innovative tools to selectively direct antimalarial drugs towards Plasmodium-infected red blood cells (2014-2016)
PI: **Xavier Fernàndez-Busquets**
Fondazione CARIPLO (2013-0584)

- **NANOMALNET** Exploración de nuevas moléculas direccionadoras eficientes para la liberación de antimaláricos (2012-2015)
PI: **Xavier Fernàndez-Busquets**
MICINN, I+D-Investigación fundamental no orientada

- Group for the study of self-aggregating proteins (2014-2016).
PI: Salvador Ventura Zamora (UAB)
Consolidated Research Group certified by the Generalitat de Catalunya, Spain (2014-SGR-938)

Collaborations with other research centres

Prof. Dario Anselmetti Universität Bielefeld, Germany

Prof. Maria Antònia Busquets University of Barcelona, Spain

Prof. Elisabetta Ranucci Università degli Studi di Milano, Italy

Prof. José Manuel Bautista Universidad Complutense de Madrid, Spain

Dr. Matthias Rottmann Swiss Tropical and Public Health Institute, Basel, Switzerland

Prof. Robert Sinden Imperial College London, UK

Dr. Israel Molina Hospital Universitari Vall d'Hebron, Barcelona

Prof. José Luis Serrano Instituto de Nanociencia de Aragón, Zaragoza

Prof. Manuel Llinas Pennsylvania State University, USA

Dr. Santiago Imperial University of Barcelona, Spain

Dr. Eduardo Prata Vilanova Universidade Federal do Rio de Janeiro, Brazil

Dr. Maria Manconi Università de Cagliari, Sardinia, Italy

Dr. Krijn Paaijmans CRESIB, Barcelona, Spain

Dr. Ellen Faszewski Wheelock College, Boston, USA

Prof. Lyn-Marie Birkholtz University of Pretoria, South Africa

Prof. Bernard Degnan University of Brisbane, Australia

Dr. Francisco J. Muñoz Parc de Recerca Biomèdica de Barcelona, Spain

Prof. Salvador Ventura Universitat Autònoma de Barcelona, Bellaterra, Spain

Dr. Iñigo Angulo-Barturen GlaxoSmithKline, Tres Cantos, Madrid, Spain

Prof. Max Burger NOVARTIS AG, Basel, Switzerland

Dr. Juan José Valle-Delgado Aalto University, Helsinki, Finland

Prof. Mats Wahlgren Karolinska Institutet, Stockholm, Sweden

Dr. Fatima Nogueira Instituto de Higiene e Medicina Tropical, Lisboa, Portugal

Dr. Anne-Françoise Mingotaud Université Paul Sabatier, Toulouse, France

Dr. Christian Grandfils University of Liège, Belgium

Scientific equipment and techniques

- Zeiss Primostar microscope
- Shake 'N' Stack (Thermo Hybaid) hybridization oven
- Rotatory evaporator RS 3000-V (Selecta)
- *Plasmodium falciparum* cell cultures

- Moles, E., Valle-Delgado, J. J., Urbán, P., Azcárate, I. G., Bautista, J. M., Selva, J., Egea, G., Ventura, S. and Fernàndez-Busquets, X. (2015). Possible roles of amyloids in malaria pathophysiology. *Future Science OA*, 1 (2): FSO43

Book Sections

- Fernàndez-Busquets, X., de Groot, N. S. and Ventura, S. (2015). Structural and computational insights into conformational diseases: A review. In: "Frontiers in Medicinal Chemistry" (ed. Atta-ur-Rahman, Reitz, A. B., Choudhary, I. and Wang, J.). Bentham Science Publishers, Bussum, The Netherlands. 7: 134-182

Nanoscale bioelectrical characterization

Group leader: Gabriel Gomila

Postdoctoral researcher: Lázaro René Izquierdo

PhD students: Maria Chiara Biagi, Martí Checa, Marc Van der Hofstadt

Masters student: Jennifer Maria Cruzado

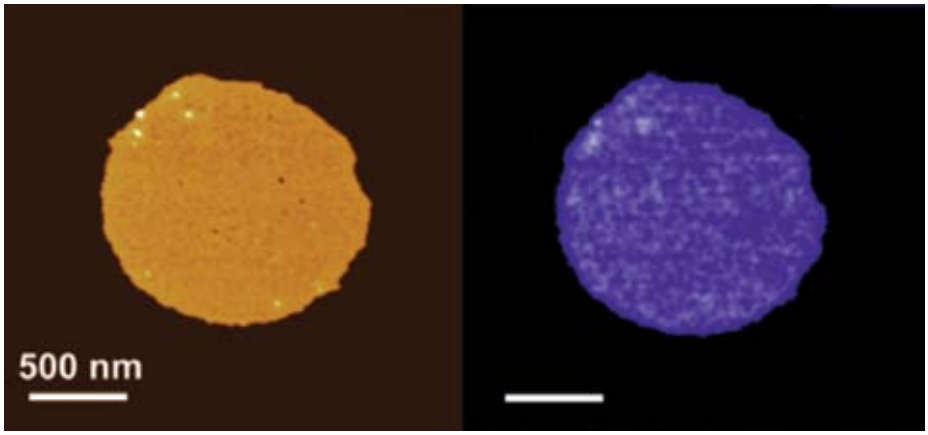
Laboratory technician: Rubén Millán

The main goal of the Nanoscale bioelectrical characterization group is to develop new experimental setups based on atomic force microscopy and theoretical frameworks enabling the measurement of the electrical properties of biological samples at the nanoscale (for example, biomembranes, single viruses or single bacteria).

Our main objective is to contribute to develop new label-free biological characterization methods and new electronic biosensors.

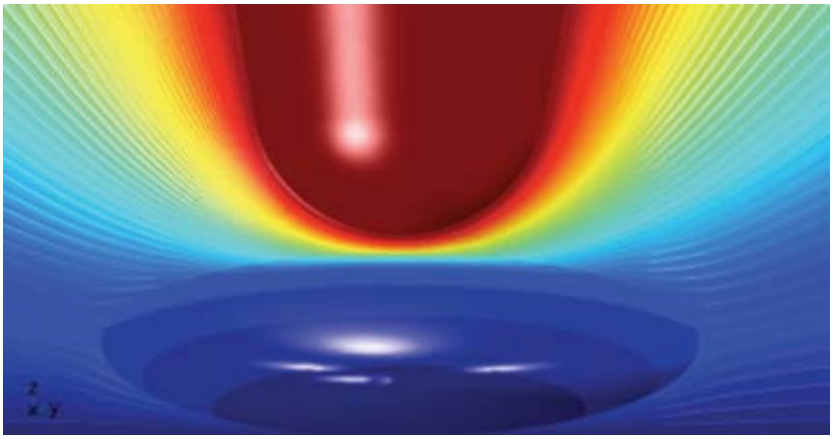
During 2015 we have measured the electric polarizability of the main components of the cell membrane – namely lipids, sterols and proteins – with a spatial resolution down to 50 nm. To achieve it we pushed forward the limits of a nanoscale dielectric microscopy technique based on Electrostatic Force Microscopy and developed over the years by our group. Quantifying the response of membrane's electrical dipoles to electric fields is essential in understanding fundamental bioelectric phenomena such the exchange of ions between the cell and the environment, the formation of electric potentials that can propagate over long distances or the cell response to externally applied electrical fields. We have also determined, for the first time, the electromagnetic properties of single bacteria cells in the high frequency range (> GHz) with the use of the Scanning Microwave Microscope and of specific 3D simulation models. We showed that with this approach one can detect the presence of small-scale nanostructures inside microorganisms, providing endless applications in the label-free imaging of single bacterial cells at high spatial resolution. Finally, the group continued its efforts towards revealing nanoscale phenomena in living cells. In particular, we optimized the use of a recently developed Atomic Force Microscope imaging mode (dynamic jumping mode) to image with nanoscale spatial resolution single bacterial cell growth and division on planar supports.

Topography and dielectric image (capacitance gradient) of a bacteriorhodopsin monolayer patch, 5.3 nm thick on a mica substrate. By combining information from the two images the dielectric constant of the protein layer can be determined with sub-50 nm lateral spatial resolution.



Publications

- Dols-Perez, A., Gramse, G., Calo, A., Gomila, G. and Fumagalli, L. (2015). Nanoscale electric polarizability of ultrathin biolayers on insulator substrates by electrostatic force microscopy. *Nanoscale*, 7 18327-18336
- Van Der Hofstadt, M., Hüttener, M., Juárez, A. and Gomila, G. (2015). Nanoscale imaging of the growth and division of bacterial cells on planar substrates with the atomic force microscope. *Ultramicroscopy*, 154 29-36
- Botaya, L., Otero, J., González, L., Coromina, X., Gomila, G. and Puig-Vidal, M. (2015). Quartz tuning fork-based conductive atomic force microscope with glue-free solid metallic tips. *Sensors and Actuators A: Physical*, 232 259-266



Electrical potential distribution corresponding to the electric interaction between a voltage biased sharp conducting tip of radius 250 nm and a single bacterial cell. The bacterial cell is represented as a 3D ellipsoid structure with uniform electric polarization. From the calculated electric potential distribution the tip-bacteria capacitance can be calculated and compared to experimental measurements obtained with the Scanning Microwave Microscope, in order to determine the electric permittivity of a single bacteria cell at GHz frequencies.

Research projects

- **NANOELECTOMOGRAPHY** Electrical nanotomography based on scanning probe microscopy for nanomaterials and biological samples (2014-2016)
  PI: **Gabriel Gomila**
  MINECO (TEC2013-48344-C2-1-P)

- **V-SMMART Nano** Volumetric Scanning Microwave Microscopy Analytical and Research Tool for Nanotechnology (2012-2015)
  PI: **Gabriel Gomila**
  European FP7-NMP-SME project

- **NANOMICROWAVE** Microwave Nanotechnologies for Semiconductor and Life Sciences. (2013-2016)
  PI: **Gabriel Gomila**
  European FP7-PEOPLE-ITN project

- ICREA Academia Award (2015-2019)
  PI: **Gabriel Gomila**
  Catalan Institution for Research and Advanced Studies (ICREA) / Generalitat de Catalunya

Collaborations with other research centres

Dra. Laura Fumagalli, University of Manchester, United Kingdom

Prof. Jose L. Carrascosa Department of Structure of Macromolecules, Centro Nacional de Biotecnología, Spain

Dr. Manel Puig Departament d'Electrònica, University of Barcelona, Spain

Dr. Ferry Kienberger Agilent Technologies Austria, Linz, Austria

Prof. Marco Sampietro Politecnico di Milano, Italy

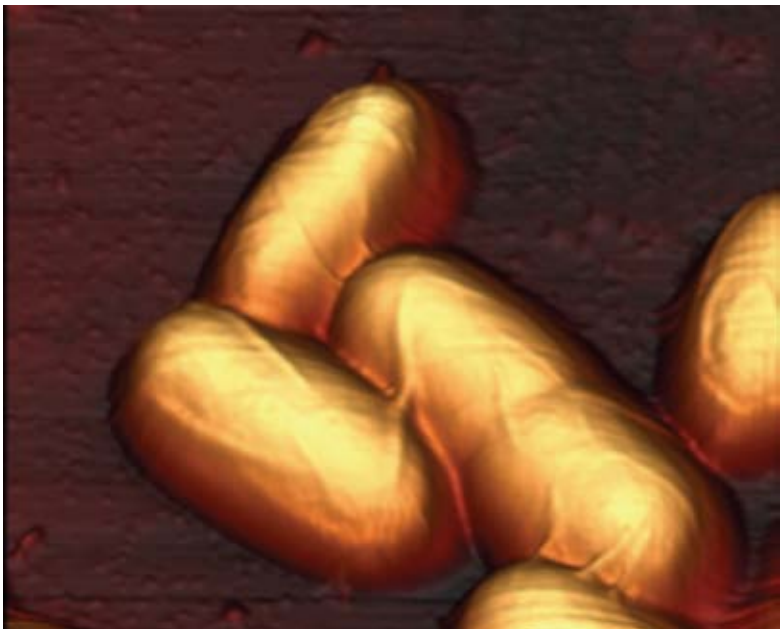
Prof. Joan Bausells Centro Nacional de Microelectrónica de Barcelona-CSIC, Spain

Prof. Antonio Juárez, University of Barcelona, Spain

Scientific equipment and techniques

- Cypher Atomic Force Microscope (Asylum Research)
- Nanowizard 4 Bio-Atomic Force Microscope (JPK)
- Cervantes Atomic Force Microscope (Nanotec Electronica)
- Easy Scan 2 Atomic Force Microscope (Nanosurf)
- AxioImager A1m Reflection Optical Microscope (Zeiss) equipped with a AxioCam ERc5s (Zeiss)
- CompactStat portable electrochemical interface and impedance analyzer (Ivium Technologies)
- 2 eLockIn204 4-phase Lock-In amplifiers (Anfatec)
- Keithley 6430 sub-femtoAmp remote sourcemeter (Keithley)

Atomic Force Microscopy topography image of living *Enetero Agregative E. Coli* bacterial cells on a gelatin coated mica substrate in HEPES buffer solution. The image has been obtained in dynamic jumping mode.



Nanoprobes and nanoswitches

Group leaders: Pau Gorostiza (ICREA research professor) and Fausto Sanz

Senior researchers: Ismael Díez, Marina Inés Giannotti, Mireia Oliva

Postdoctoral researchers: Miquel Bosch, Nadim Darwish, Carlo Matera, Xavier Rovira

PhD students: Pep Astola, Albert Cortijos, Aida Garrido, Berta Gumí, Montserrat López, Silvia Pittolo, Marta Pozuelo, Davia Prischich

Masters student: Pepita Pla

Undergraduate students: Federica Botta, Lídia García

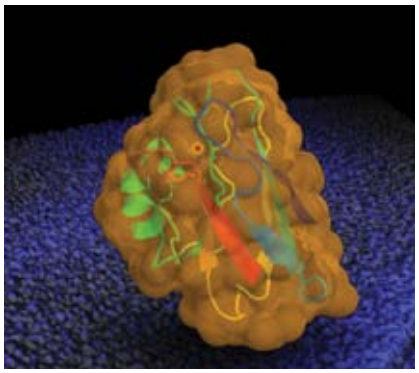
Senior technician: Núria Camarero

Nanoprobes and nanoswitches

The group's research focuses on developing nanoscale tools to study biological systems. These tools include instrumentation based on proximity probes, such as electrochemical tunnelling microscopy and spectroscopy, that we apply to investigate electron transfer in metal oxides and individual redox proteins.

These studies are relevant to the development of biosensors and molecular electronics devices. In particular, based on our development of nanoscale field-effect transistors using individual redox protein, we have recently published a method to measure conductance switching in single redox proteins "wired" between two electrodes.

Another set of nanotools that we are developing is based on molecular actuators that can be switched with light, such as azobenzene, which can be chemically attached to biomolecules in order to optically control their activity. We have demonstrated for the first time two-photon stimulation of neurons and astrocytes with azobenzene-based photoswitches. We have also developed several bioactive compounds that have been engineered to be regulated by light. These "optopharmacological" compounds include peptide inhibitors of protein-protein interactions involved in clathrin-mediated endocytosis, and two ligands of G protein-coupled receptors (adenosine and metabotropic glutamate receptors), which are important therapeutic targets.



Crystal structure of redox protein azurin (Protein Data Bank entry: 1AZU) displaying its solvent accessible surface (gold) superimposed on the tertiary structure (rainbow) and a red sphere indicating the copper ion. When an atomically flat gold electrode is coated with azurin, the protein can be imaged under potentiostatic control by electrochemical tunneling microscopy (3D rendering of a 100x100nm^2 area shown in blue), and its electron transfer properties can be investigated by current-distance spectroscopy (Juan Manuel Artés *et al.*, 2011, *ACS Nano*).

Research projects

- **THERALIGHT** Therapeutic Applications of Light-Regulated Drugs (2013-2015)
PI: **Pau Gorostiza**
ERC

- Grup de recerca consolidat (2014-2016)
PI: **Fausto Sanz**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (SGR 2014)

- **Single-BioET** Single-molecule junction capabilities to map the electron pathways in redox bio-molecular architectures (2012-2015)
PIs: **Ismael Díez** and **Pau Gorostiza**
Marie Curie FP7-PEOPLE-IRG (International Re-integration Grants)

- **MODULIGHTOR** Moduladores fotoconmutables sintéticos para manipular remotamente proteínas endógenas: fotocontrol *in vivo* de canales iónicos pentaméricos (2015-2018)
PI: **Pau Gorostiza**
MINECO Nacional /Acciones de Programación Conjunta Internacional

- Inhibición fotoselectiva de interacciones proteína-proteína para el estudio de redes interactómicas y el desarrollo de nuevas terapias (2015-2018)
PI: **Pau Gorostiza**
Fundación Ramon Areces

- **OPTOPHARMACOLOGY** Therapeutic applications of optopharmacology (2014-2016)
PI: **Pau Gorostiza**
MINECO (CTQ2013-43892-R)

Collaborations with other research centres

Prof. Amadeu Llebaria Institut de Química Avançada de Catalunya (IQAC-CSIC)

Prof. Ernest Giralt Dept. de Química Orgànica, Universitat de Barcelona

Prof. Miquel Àngel Pericàs Institut Català d'Investigació Química (ICIQ), Tarragona

Dr. Piotr Bregestovski Institut de Neurobiologie de la Mediterraneé (INMED), Marseille

Dr. Mireia Oliva Dept. de Farmàcia i Tecnologia Farmacèutica, Universitat de Barcelona

Dr. Artur Llobet Dept. Patología y Terapéutica Experimental, Universitat de Barcelona

Dr. Joan Torrent Escola Universitària d'Òptica i Optometria de Terrassa, Spain

Prof. Dirk Trauner Chemistry Dept., UC Berkeley, USA

Prof. Carles Solsona Pathology and Experimental Therapeutics Dept, UB

Prof. Francisco Ciruela ICREA / Universitat de Barcelona, Spain

Prof. Jesús Giraldo & **Dr. Jordi Hernando** Universitat Autònoma de Barcelona, Spain

Publications

- Martín-Quirós, A., Nevola, L., Eckelt, K., Madurga, S., Gorostiza, P. and Giralt, E. (2015). Absence of a stable secondary structure is not a limitation for photoswitchable inhibitors of β-Arrestin/β-Adaptin 2 protein-protein interaction. *Chemistry & Biology*, 22 (1): 31-37

- Andrade, F., Neves, J. D., Gener, P., Schwartz, S., Ferreira, D., Oliva, M. and Sarmento, B. (2015). Biological assessment of self-assembled polymeric micelles for pulmonary administration of insulin. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 11 (7): 1621-1631

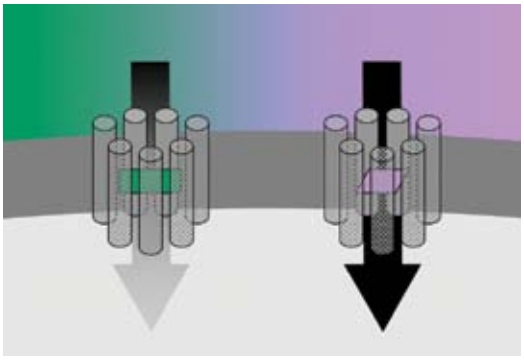
- Aragonès, A. C., Darwish, N., Im, J., Lim, B., Choi, J., Koo, S. and Díez-Pérez, I. (2015). Fine-tuning of single-molecule conductance by tweaking both electronic structure and conformation of side substituents. *Chemistry – A European Journal*, 21 (21): 7716-7720

- Gascón-Moya, M., Pejoan, A., Izquierdo-Serra, M., Pittolo, S., Cabrè, G., Hernando, J., Alibés, R., Gorostiza, P. and Busque, F. (2015). An optimized glutamate receptor photoswitch with sensitized azobenzene isomerization. *The Journal of Organic Chemistry*, 80 (20): 9915-9925

- Ponce, I., Aragonès, A. C., Darwish, N., Pla-Vilanova, P., Oñate, R., Rezende, M. C., Zagal, J. H., Sanz, F., Pavez, J. and Díez-Pérez, I. (2015). Building nanoscale molecular wires exploiting electrocatalytic interactions. *Electrochimica Acta*, 179 611-167

- Hoyo, J., Guaus, E., Torrent-Burgués, J. and Sanz, F. (2015). Electrochemistry of LB films of mixed MGDG: UQ on ITO. *Bioelectrochemistry*, 104 26-34

- Abadías, C., Serés, C. and Torrent-Burgués, J. (2015). AFM in peak force mode applied to worn siloxane-hydrogel contact lenses. *Colloids and Surfaces B: Biointerfaces*, 128 61-66
- Gumi-Audenis, B., Sanz, F. and Giannotti, M. I. (2015). Impact of galactosylceramides on the nanomechanical properties of lipid bilayer models: an AFM-force spectroscopy study. *Soft Matter*, 11 (27): 5447-5454
- Hoyo, J., Guaus, E., Torrent-Burgués, J. and Sanz, F. (2015). Biomimetic monolayer films of digalactosyldiacylglycerol incorporating plastoquinone. *Biochimica et Biophysica Acta - Biomembranes*, 1848 (6): 1341-1351
- Pla-Vilanova, P., Aragonès, A. C., Ciampi, S., Sanz, F., Darwish, N. and Diez-Perez, I. (2015). The spontaneous formation of single-molecule junctions via terminal alkynes. *Nanotechnology*, 26 381001
- Andrade, F., Fonte, P., Oliva, M., Videira, M., Ferreira, D. and Sarmento, B. (2015). Solid state formulations composed by amphiphilic polymers for delivery of proteins: Characterization and stability. *International Journal of Pharmaceutics*, 486 (1-2): 195-206
- Hoyo, J., Guaus, E., Torrent-Burgués, J. and Sanz, F. (2015). Biomimetic monolayer films of monogalactosyldiacylglycerol incorporating plastoquinone. *Journal of Physical Chemistry B*, 119 (20): 6170-6178
- Giannotti, M. I., Cabeza de Vaca, I., Artés, J. M., Sanz, F., Guallar, V. and Gorostiza, P. (2015). Direct measurement of the nanomechanical stability of a redox protein active site and its dependence upon metal binding. *The Journal of Physical Chemistry B*, 119 (36): 12050-12058



Schematic representation of a light-regulated drug bound to a 7-transmembrane receptor. Under violet illumination, the drug is inactivated and the receptor produces normal intracellular signaling. In the dark or under green light, the drug inhibits the receptor and interferes with signaling in a reversible way. (Pittolo, S. *et al,* 2014).

Scientific equipment and techniques

- iMic molecular imaging system
- Electrochemical scanning tunnelling microscope (STM) for molecular imaging
- Asylum Research Molecular Force Probe
- Multimode SPM Nanoscope III (SCT-UB)
- Autolab potentiostat
- Patch clamp setup with Heka EPC10 amplifier
- Molecular Imaging Electrochemical STM

- Gumí-Audenis, B., Carlà, F., Vitorino, M. V., Panzarella, A., Porcar, L., Boilot, M., Guerber, S., Bernard, P., Rodrigues, M. S., Sanz, F., Giannotti, M. I. and Costa, L. (2015). Custom AFM for X-ray beamlines: *in situ* biological investigations under physiological conditions. *Journal of Synchrotron Radiation*, 22 1364-1371 (2015).
- Brazil, R. (2015). Drugs on demand. *Chemistry & Industry*, 79 (2): 36-39

Book Sections

- Artés, J. M., Hihath, J. and Diéz-Pérez, I. Biomolecular electronics. In: "Molecular Electronics: An Experimental and Theoretical Approach" (ed. Baldea, I.). Pan Stanford Publishing, Singapore. 325: 281-324

Biomedical signal processing and interpretation

Group leader: Raimon Jané

Senior researchers: José Antonio Fiz, Beatriz Giraldo, Jordi Solà, Abel Torres

Postdoctoral researchers: Leonardo Sarlabous

PhD students: Luis Estrada, Manuel Lozano, Javier Rodríguez, Oiane Urra

Masters students: Sara Argerich, Yolanda Castillo, Roger Gallart

Research technicians: Maria Puy Ruiz de Alda, Mirella López

Biomedical signal processing and interpretation

The group's research addresses the design and development of advanced signal processing techniques and the interpretation of biomedical signals to improve non-invasive monitoring, diagnosis, disease prevention and pathology treatment.

Our main objective is to improve diagnosis capability through the characterization of physiological phenomena and to enhance early detection of major cardiac and respiratory diseases and sleep disorders.

We propose and design new signal processing algorithms and develop new biosignal databases, with the collaboration of our hospital partners. To validate the clinical information of new surface signals, we have developed specific invasive/non-invasive protocols and animal models. The group focuses its research in a translational way to promote the transfer of our scientific and technological contributions. Currently, our prototypes are used in hospitals for research purposes and for future industrial developments.

Highlights in 2015

Obstructive Sleep Apnea and Sleep Disorders

- A novel method to estimate cardiorespiratory phase synchronization in OSA patients during sleep and awake states (*IEEE-EMBC* 2015, 7708-7711) with the Hospital Germans Trias i Pujol, Badalona.

Chronic Obstructive Pulmonary Disease and Asthma

- Novel method based on sample entropy for efficiency estimation of mechanical activation of inspiratory muscles in COPD patients (*Eur Resp Journal* 2015, 46(6): 1808-1811), with the Hospital Germans Trias i Pujol, Badalona, and the Hospital del Mar, Barcelona.
- Automatic detection of continuous adventitious respiratory sounds using ensemble empirical mode decomposition and instantaneous frequency (*J Biomed Health Inf* 2015, early online version).
- Non-invasive estimation of neural respiratory drive from diaphragm electromyographic signals using fixed sample entropy (*J Biomed Health Inf* 2015, early online version).
- Novel methods to estimate the respiratory signal derived from EMG signal (*IEEE-EMBC* 2015, 1703-1706) and smart-phone built-in accelerometer (*IEEE-EMBC* 2015, 6768-6771).
- Evaluation of sternocleidomastoid muscle activity during respiratory activity by electromyography recorded with concentric ring electrodes (*CASEIB* 2015, 183-186), with the Universidad Politécnica de Valencia.
- Novel approach for analysis of continuous adventitious sound in asthmatic patients by means of the Hilbert spectrum (*CASEIB* 2015, 179-182), with the Hospital Germans Trias i Pujol, Badalona.

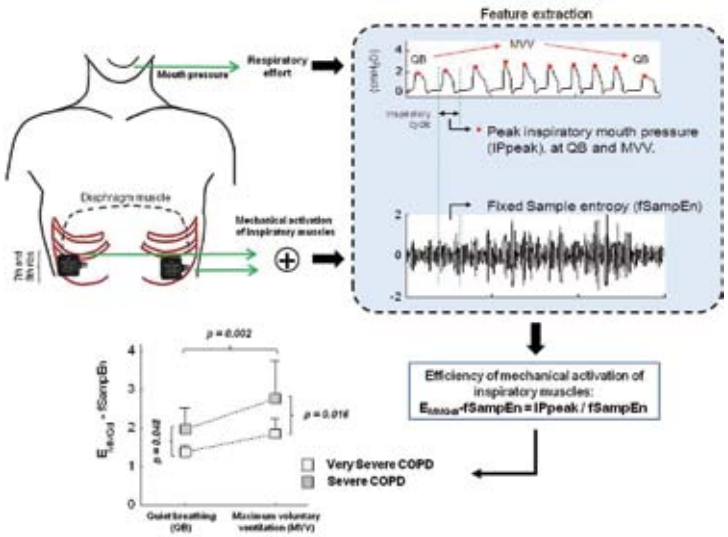
Cardiac and cardiorespiratory diseases and ageing

- Novel method to classify patients undergoing weaning from mechanical ventilation using the coherence between heart rate variability and respiratory flow signal (*Physiological Measurement* 2015, 36 (7): 1439-1452), with the Hospital de Sant Pau, Barcelona.
- Time-varying analysis to detect periodic breathing in climbers ascending to extreme altitude (*Medical & Biological Engineering & Computing* 2015, 53 (8): 699-712), with Zurich Hospital, Switzerland.

- Novel method to estimate cardiorespiratory and cardiovascular interactions in cardiomyopathy patients using joint symbolic dynamic analysis (*IEEE-EMBC* 2015, 306-309), with Hospital Germans Trias i Pujol, Badalona and University of Jena, Germany.
- Novel characterization of patients with ischemic and dilated cardiomyopathy by ECG signals and blood pressure (*CASEIB* 2015, 31-34), with Hospital Germans Trias i Pujol, Badalona and University of Jena, Germany.

Neurorehabilitation and Biofeedback

- Assessment of the impact of visual feedback on the motor control of the upper-limb (*IEEE-EMBC* 2015, 3945-3948).
- Evidence of visual feedback facilitates intermanual transfer of the motor control of arms (*CASEIB* 2015, 503-506)



New non-invasive method of evaluating the efficiency of the respiratory muscles in patients with chronic obstructive pulmonary disease (COPD), using Fixed Sampled Entropy (fSampEn) of respiratory muscle mechanomyogram (MMG). The results indicate that the amplitude of the MMG of patients with severe-to-very severe COPD is closely related to the inspiratory effort, and that the MMG is higher in more severe patients even during quiet breathing, showing a lower efficiency of the respiratory muscles (Sarlabous et al, 2015, *Eur Respir J*).

Publications

- Sarlabous, L., Torres, A., Fiz, J. A., Gea, J., Martínez-Llorens, J. M. and Jané, R. (2015). Efficiency of mechanical activation of inspiratory muscles in COPD using sample entropy. *European Respiratory Journal*, 46 (6): 1808-1811
- Arcentales, A., Caminal, P., Diaz, I., Benito, S. and Giraldo, B. (2015). Classification of patients undergoing weaning from mechanical ventilation using the coherence between heart rate variability and respiratory flow signal. *Physiological Measurement*, 36 (7): 1439-1452
- Garde, A., Giraldo, B. F., Jané, R., Latshang, T. D., Turk, A. J., Hess, T., Bosch, M.-M., Barthelmes, D., Merz, T. M., Hefti, J. P., Schoch, O. D. and Bloch, K. E. (2015). Time-varying signal analysis to detect high-altitude periodic breathing in climbers ascending to extreme altitude. *Medical & Biological Engineering & Computing*, 53 (8): 699-712

Conference Papers

- Estrada, L., Torres, A., Sarlabous, L. and Jané, R. (2015). Respiratory signal derived from the smartphone built-in accelerometer during a Respiratory Load Protocol. *37th Annual International Conference of the IEEE, Milan, Italy (25/08/2015)*, 6768-6771. Published by IEEE
- Estrada, L., Torres, A., Sarlabous, L. and Jané, R. (2015). EMG-derived respiration signal using the fixed sample entropy during an Inspiratory load protocol. *37th Annual International Conference of the IEEE, Milan, Italy (25/08/2015)*, 1703-1706. Published by IEEE
- Giraldo, B. F., Rodriguez, J., Caminal, P., Bayes-Genis, A. and Voss, A. (2015). Cardiorespiratory and cardiovascular interactions in cardiomyopathy patients using joint symbolic dynamic analysis. *37th Annual International Conference of the IEEE, Milan, Italy (25/08/2015)*, 306-309. Published by IEEE

Research projects

- Study on software comparison of audio recordings and correlation to SAHS events (2015-2016)
PI: **Raimon Jané**
R+D contract with Audiodontics in the framework of a SBIR project "System for Monitoring Dental Device Compliance and Efficacy in Treatment of Obstructive Sleep Apnea", funded by the NIH (USA)

- Grup de recerca consolidat (2014-2016)
PI: **Raimon Jané**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (SGR 2014)

- Respiratory sounds analysis (2011-2015)
PI: **Raimon Jané**
Health Sciences Research Institute, Germans Trias I Pujol Foundation

Collaborations with other research centres

Dr. J. Mark Ansermino Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, Canada

Prof. Antonio Bayes Genis Grup ICREC, Servei Cardiología Hospital Universitari Germans Trias i Pujol, Barcelona

Dr. Salvador Benito Hospital de la Santa Creu i Sant Pau, Barcelona

Prof. Dr. Konrad Bloch Pulmonary Division, University of Zurich, Switzerland

Prof. Armin Bolz Institute of Biomedical Engineering, University of Karlsruhe, Germany

Prof. Manuel Doblaré Grupo de Mecánica Estructural y Modelado de Materiales, Universidad de Zaragoza, Spain

Prof. Guy Dumont Department of Electrical and Computer Engineering, University of British Columbia, Vancouver, Canada

Prof. Ramon Farré Unitat de Biofísica i Bioenginyeria, Facultat de Medicina, Barcelona

Dr. Javier García-Casado Instituto Interuniversitario de Investigación en Bioingeniería y Tecnología Orientada al Ser Humano, Universidad Politécnica de Valencia

Dr. Joaquim Gea Servei Pneumologia, Hospital del Mar-IMIM, Barcelona

Dr. Alfredo Hernández Laboratoire Trataiment du Signal et de l'Image, Université de Rennes 1, Instituto Francés de Salud (INSERM), France

Dr. Eric Laciar Departamento de Electrónica y Automática, Universidad Nacional de San Juan, Argentina

Prof. Pablo Laguna Instituto de Investigación de Aragón (I3A), Universidad de Zaragoza, Spain

Dr. Barry Mersky Audiodontics, LLC, Bethesda, Maryland, USA

Prof. Dr. Thomas Penzel Interdisciplinary Sleep Center, Charité University Hospital, Berlin, Germany

Dr. Josep Morera Prat Servicio de Neumología, Hospital Germans Trias i Pujol, Badalona, Spain

Prof. Winfried J. Randerath Institut für Pneumologie, Klinik Bethanien, Solingen, Germany

Dr. Juan Ruiz Servei de Pneumología de l'Hospital Germans Trias i Pujol de Badalona

Dr. Matthias Schwaibold MCC-Med GmbH & Co. KG, Karlsruhe, Germany

Prof. Dr. Lotfi Senhadji Laboratoire Traitement du Signal et de l'Image (LTSI), Université de Rennes 1, Institut National de la Santé et de la Recherche Médicale (INSERM), France

Prof. Leif Sörnmo Signal processing group, Lund University, Sweden

Prof. Dr. Jaume Veciana Grupo de Nanociencia Molecular y Materiales Orgánicos del Instituto de Ciencia de Materiales de Barcelona (NANOMOL-CSIC), Barcelona

Prof. Andreas Voss University of Applied Sciences, Jena, Germany

Dr. Pierluigi Casale Laboratory for advanced research in microelectronics (IMEC), Eindhoven, The Netherlands

Dr. Francky Catthoor Laboratory for advanced research in microelectronics (IMEC), Leuven, Belgium

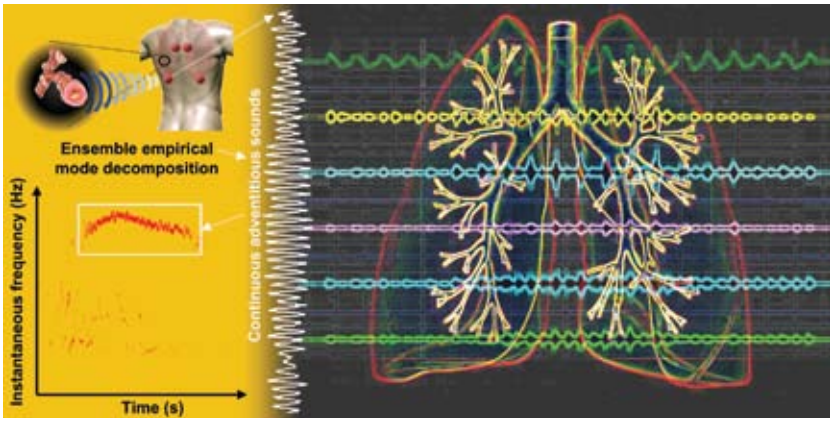
Dr. Miquel Domenech Dep. of Social Psychology, Universitat Autònoma de Barcelona

Dr. Caroline Jolley / Dr. John Moxham King's College London, UK

Scientific equipment and techniques

- Research laboratory with full equipment for acquisition and processing of biomedical signal to test new sensors and to define clinical protocols (preliminary tests and control subjects)
- Non-invasive Vital Signs Monitor for small lab animals (mice and rats) (Mouse-Ox Plus)
- BIOPAC system for multichannel cardiac and respiratory biomedical signal acquisition
- Databases of biomedical signals from hospitals and animal laboratories
- Snoring analyzer equipment (SNORYZER)
- Sensors, electrodes and microphones to obtain cardiac, respiratory, neural, muscular and sleep biomedical signals
- Polisomnographic equipment available in the Sleep Laboratory of collaborator hospital
- Beat to beat arterial blood pressure and haemodynamic monitor equipment
- Computing server for high performance biomedical signals

Novel method for differentiating normal from adventitious respiratory sounds (RS) to improve the diagnosis of pulmonary diseases. Particularly, continuous adventitious sounds (CAS) are of clinical interest because they reflect the severity of certain diseases. The new method is based on the multi-scale analysis of instantaneous frequency (IF) and envelope (IE) calculated after ensemble empirical mode decomposition (EEMD) of respiratory sounds. (Lozano et al., 2015, *IEEE Journal of Biomedical and Health Informatics*)



- Sola-Soler, J., Giraldo, B. F., Fiz, J. A. and Jané, R. (2015). Cardiorespiratory Phase Synchronization in OSA subjects during wake and sleep states. *37th Annual International Conference of the IEEE, Milan, Italy (25/08/2015)*, 7708-7711. Published by IEEE
- Urra, O., Casals, A. and Jané, R. (2015). The impact of visual feedback on the motor control of the upper-limb. *37th Annual International Conference of the IEEE, Milan, Italy (25/08/2015)*, 3945-3948. Published by IEEE
- Estrada, L., Torres, A., Garcia-Casado, J., Sarlabous, L., Prats-Boluda, G. and Jané, R. (2015). Evaluation of sternocleidomastoid muscle activity by electromyography recorded with concentric ring electrodes. *XXXIII Congreso Anual de la Sociedad Española de Ingeniería Biomédica (CASEIB 2015*, 04/11/2015), 183-186. Published by SEIB, Madrid
- Giraldo, B. F., Rodríguez, J., Arcentales, A., Voss, A., Caminal, P. and Bayes-Genis, A. Caracterización de pacientes isquémicos y dilatados a partir de las señales ECG y de presión sanguínea. *XXXIII Congreso Anual de la Sociedad Española de Ingeniería Biomédica (CASEIB 2015*, 04/11/2015), 31-34. Published by SEIB, Madrid
- Lozano, M., Fiz, J. A. and Jané, R. (2015). Análisis de sonidos adventicios continuos en pacientes asmáticos mediante el espectro de Hilbert. *XXXIII Congreso Anual de la Sociedad Española de Ingeniería Biomédica (CASEIB 2015*, 04/11/2015), 179-182. Published by SEIB, Madrid
- Urra, O., Casals, A. and Jané, R. (2015). Visual feedback facilitates intermanual transfer of the motor control of the dominant arm towards the nondominant arm. *XXXIII Congreso Anual de la Sociedad Española de Ingeniería Biomédica (CASEIB 2015*, 04/11/2015), 503-506. Published by SEIB, Madrid

Microbial biotechnology and host-pathogen interaction

Group leader: Antonio Juárez

Research assistant: Sònia Aznar

Postdoctoral researchers: Manuela Dietrich, Mário Hüttener

Laboratory technician: Mª Carmen Jaramillo

Masters student: Imanol Urcola, Óscar Zhu

Undergraduate student: Alejandro Prieto

Structure and function of bacterial proteins that modulate virulence expression; bacterial plasmids and their role in transmission of multidrug resistance markers; application of nanotools of bacterial biotechnology

1. Structure and function of bacterial proteins that modulate virulence expression

Protein–protein and protein–DNA interactions play key roles in the ability of virulent bacteria to adapt to the host environment and cause disease. A group of proteins is currently the focus of our research: nucleoid-associated proteins (NAPs) that contribute to DNA architecture and modulate gene expression. We are interested in unravelling the role played by two of these proteins – Hha and H-NS – in the regulation of virulence and of plasmid transfer. *Escherichia coli* pathotypes such as enteroaggregative *E. coli* are the subject of our research. Owing to their key modulatory functions, these proteins are interesting targets to combat bacterial infections.

2. Bacterial plasmids and their role in transmission of multidrug resistance markers

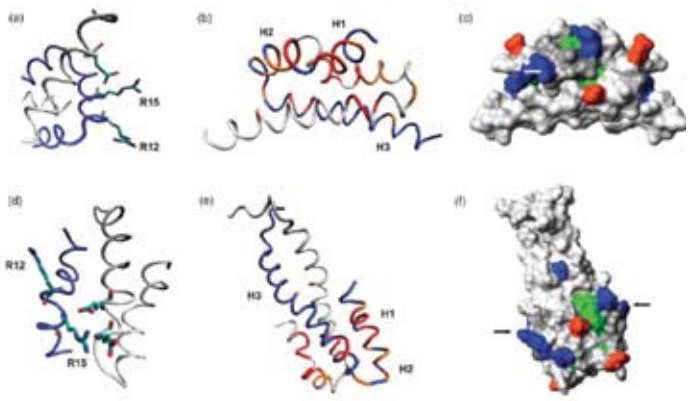
A main concern with bacterial infections is the selection of isolates that are resistant to several antimicrobial drugs. The transmission of the ability of bacterial cells of simultaneously resist several antimicrobial drugs is accomplished, in many instances, by plasmids. These genetic elements can be transmitted from one cell to another, and modify the phenotype of the recipient cell. We have recently shown that multidrug resistance plasmids in Salmonella require specific plasmid proteins to be stably maintained in this microorganism. These proteins could be considered as targets to combat multidrug resistance.

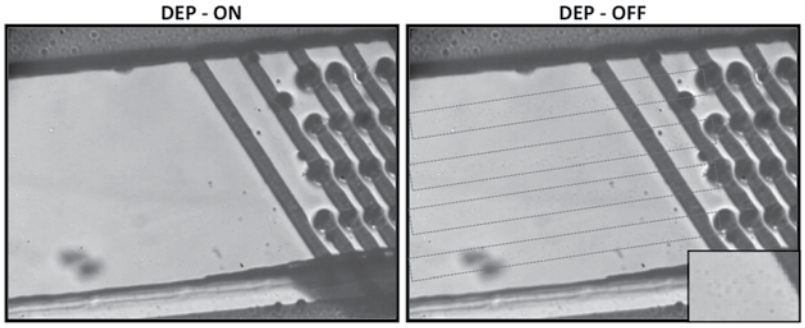
3. Application of nanotools of bacterial biotechnology

3.1. Dielectrophoresis (DEP). We have previously shown that dielectrophoresis can be a valuable tool for bacterial cell sorting and characterization. We are currently using different chip designs (2D and 3D carbon electrodes) to: a) study the effect of electric fields on bacterial cell physiology; b) combine DEP with other molecular protocols for detection and identification of different types of cells. Recent results have shown that DEP chips can be used to increase PCR detection of yeast cells.

3.2. Atomic force microscopy (AFM). Conventional AFM approaches have been shown to be powerful techniques for characterizing both biomaterials and biomolecules. In a joint project with the Nanoscale Bioelectrical Characterization group (page 56), we intend to use electrical-AFM to characterize the bacterial cell envelope. We also plan to use this approach to analyze the structural and physiological properties of bacterial living cells.

Hha perturbing H-NS structure.





Trapping of Escherichia coli cells in a dielectrophoresis chip.

Research projects

- **REGVIRBAC** Regulación de la virulencia bacteriana por proteinas que reconocen conformaciones locales del ADN (2014-2016)
PI: **Antonio Juárez**
MINECO (BIO2013-49148-C2-1-R)

- **FRISELVA** Valoració de subproducte de excorxador (2014-2015)
PI: **Antonio Juárez**
Industrial project with Friselva, S.A.

- **MEJORAVE2** Mejora sanitaria y de productos cármicos de ave (2013-2015)
PI: **Antonio Juárez**
Industrial project with Mevet, S.A / CZ Veterinaria, S.A.

Collaborations with other research centres

Prof. Josep Casadesús Universidad de Sevilla, Spain

Prof. Charles Dorman Trinity College, Dublin

Prof. F. García del Portillo Centro Nacional de Biotecnología, Madrid, Spain

Dr. Gabriel Gomila IBEC (page 68)

Prof. Josep Samitier IBEC (page 117)

Dr. Eduard Torrents IBEC (page 128)

Prof. Mike Hughes University of Surrey, UK

Dr. Rodrigo Martínez-Duarte École Polytechnique Fédérale de Lausanne, Switzerland

Prof. Miquel Pons Organic Chemistry Dept., University of Barcelona, Spain

Publications

- Hüttener, M., Paytubi, S. and Juárez, A. (2015). Success in incorporating horizontally transferred genes: the H-NS protein. *Trends in Microbiology*, 23 (2): 67-69
- Barreiros dos Santos, M., Azevedo, S., Agusil, J. P., Prieto-Simón, B., Sporer, C., Torrents, E., Juárez, A., Teixeira, V. and Samitier, J. (2015). Label-free ITO-based immunosensor for the detection of very low concentrations of pathogenic bacteria. *Bioelectrochemistry*, 101 146-152
- Solórzano, C., Srikumar, S., Canals, R., Juárez, A., Paytubi, S. and Madrid, C. (2015). Hha has a defined regulatory role that is not dependent upon H-NS or StpA. *Frontiers in Microbiology*, 6 Article 773
- Jaramillo, M. d. C., Huttener, M., Alvarez, J. M., Homs-Corbera, A., Samitier, J., Torrents, E. and Juárez, A. (2015). Dielectrophoresis chips improve PCR detection of the food-spoiling yeast *Zygosaccharomyces rouxii* in apple juice. *Electrophoresis*, 36 (13): 1471-1478
- del Moral Zamora, B., Manuel Álvarez Azpeitia, J., Brañas, A. M. O., Colomer-Farrarons, J., Castellarnau, M., Miribel-Català, P. L., Homs-Corbera, A., Juárez, A. and Samitier, J. (2015). Dielectrophoretic concentrator enhancement based on dielectric poles for continuously flowing samples. *Electrophoresis*, 36 (13): 1405-1413
- del Moral Zamora, B., Álvarez Azpeitia, J. M., Oliva Brañas, A. M., Colomer-Farrarons, J., Castellarnau, M., Miribel-Català, P., Homs-Corbera, A., Juárez, A. and Samitier, J. (2015). Continuous flow dielectrophoretic concentrator enhancement based on dielectric poles. *Electrophoresis*, 36 (13): 1405–1413

■ Van Der Hofstadt, M., Hüttener, M., Juárez, A. and Gomila, G. (2015). Nanoscale imaging of the growth and division of bacterial cells on planar substrates with the atomic force microscope. *Ultramicroscopy*, 154 29-36

Scientific equipment and techniques

- Thermocycler (PCR)
- Protein and DNA electrophoresis
- Process of biomolecule production
- Protein expression and purification systems
- Technology of microbial culture facilities
- Dielectrophoresis equipment

Salmonella R27 plasmid

Signal and information processing for sensing systems

Group leader: Santiago Marco

Senior researcher: Agustín Gutiérrez

Research assistant: Rudys Magrans

Postdoctoral researcher: Jordi Fonollosa

PhD students: Ariadna Bartra, Javier Burgués, Lluís Fernández, Sergio Oller, Ana Maria Solórzano

Masters student: Raquel Rodríguez

Undergraduate students: Laia Garrit, Laura Mateu

Research technician: Marta Padilla

Senior technician: Raquel Obregón

Laboratory technicians: Núria Cañaveras, Juan Manuel Jiménez

Current smart instrumentation using multi-sensors and/or spectrometers provides a wealth of data that requires sophisticated signal and data processing approaches in order to extract the hidden information.

In this context, we are interested in intelligent chemical instruments for the detection of volatile compounds and smells.

These systems can be based on an array of nonspecific chemical sensors with a pattern recognition system , taking inspiration from the olfactory system. Some spectrometries, e.g. Ion Mobility Spectrometry, are capable of very fast analysis with good detection limits but poor selectivity. These technologies have been proposed for the fast determination of the volatolome (volatile fraction of the metabolome), instead of the reference technique of gas chromatography – mass spectrometry.

Our group develops algorithmic solutions for the automatic processing of Gas Sensor Array, Ion Mobility Spectrometry (IMS) and Gas Chromatography – Mass Spectrometry (GC-MS) data for metabolomics and food samples.

In a parallel activity, our group is working on the detection of drowsiness in drivers using vehicle dynamic measures.

Our research in 2015 included the following:

Signal and Data Processing for smart chemical Instrumentation:

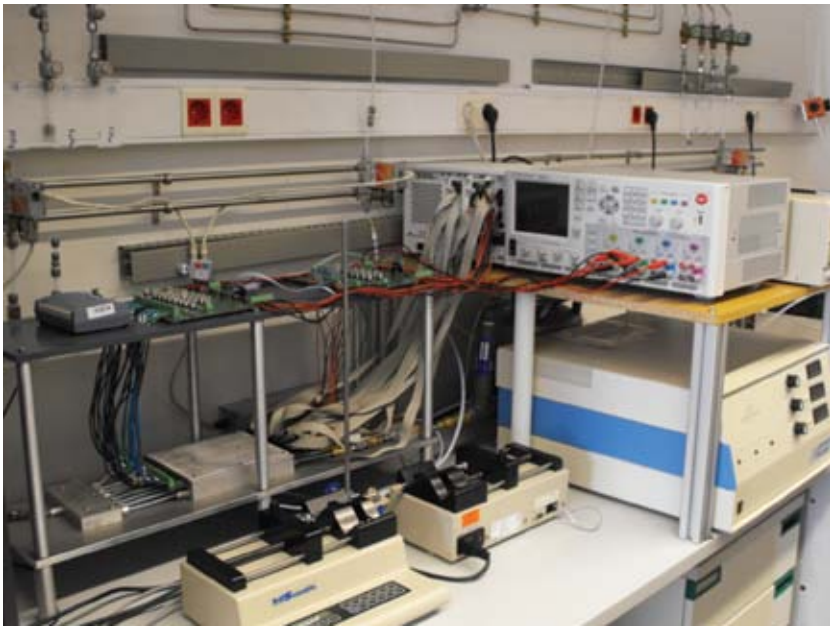
1. In hyphenated techniques based in fast chromatography coelution is a common problem. Usually coelution can be separated using blind source separation techniques if we segment the data portion where coelution occurs. Here we have proposed a methodology for automatic analysis of samples from Gas Chromatography – Ion Mobility Spectrometry based on a sliding window blind source separation.
2. We have proven that Reservoir computing algorithms can compensate the slow response of chemosensors exposed to fast varying concentrations of the target analytes.
3. Inspired by nature (olfactory system), we have characterized how redundancy in chemical sensor arrays improves robustness to diverse types of sensor failures
4. We have built a biomimetic olfactory system implementing controlled sniffing to show that gas flow modulation improves early odorant detection.
5. In collaboration with Universitat de Lleida (Dr. J. Palacin) and University of Örebro (Prof. A. Lilienthal) we are testing chemical source localization algorithms with autonomous robots.

Bioinformatics:

6. The detection of regulatory regions in candidate sequences is essential for the understanding of the regulation of a particular gene and the mechanisms involved. This paper proposes a novel methodology based on information theoretic metrics for finding regulatory sequences in promoter regions. Results This methodology (SIGMA) has been tested on genomic sequence data for *Homo sapiens* and *Mus musculus*. SIGMA has been compared with different publicly available alternatives for motif detection.

Computational Neuroscience:

7. We often learn and recall sequences in smaller segments (or chunks). In collaboration with the University of San Diego, we studied the temporal dynamics of chunking for learning cognitive sequences using a dynamical model of competing nodes arraged to evoke a hierarchical winnerless competition dynamics. The resulting patterns of activities share features observed in behavioural experiments, such as the pauses between boundaries of chunks, their size and duration.



System to test chemical sensor arrays for diversity and redundancy

Research projects

- Grup de recerca consolidat (2014-2016)
PI: **Santiago Marco**
AGAUR, Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya

- **SMART-IMS** Procesado de Señal para Espectroscopia de Movilidad de Iones: Análisis de Fluidos Biomédicos y Detección de Sustancias Tóxicas (2012-2015)
PI: **Santiago Marco**
MINECO

- **SIGVOL** Mejora de la señal para instrumentación química: aplicaciones en metabolómica de volátiles y en olfacción (2015-2017)
PI: **Santiago Marco**
MINECO

- **SENSIBLE** Sensores inteligentes para edificios más seguros (2014-2016)
PI: **Santiago Marco**
MINECO

- **BIOENCODE** Estudio comparativo de la capacidad de codificación de información química de sistemas biológicos y artificiales (2012-2015)
PI: **Agustín Gutiérrez**
MINECO

- **BIOTRANS** Transduccion biomimetica para olfaccion artificial (2013-2015)
PI: **Agustín Gutiérrez**
MINECO, Europa Excelencia

- **SAFESENS** Sensor Technologies for Enhanced Safety and Security of Buildings and its Occupants (2014-2017)
PI: **Santiago Marco**
ENIAC project (European project with a mix of public-private funding)

Publications

- Fonollosa, J., Neftci, E. and Rabinovich, M. (2015). Learning of chunking sequences in cognition and behavior. *PLoS Computational Biology*, 11 (11): e1004592
- Ziyatdinov, A., Fonollosa, J., Fernánndez, L., Gutierrez-Gálvez, A., Marco, S. and Perera, A. (2015). Bioinspired early detection through gas flow modulation in chemo-sensory systems. *Sensors and Actuators B: Chemical*, 206 538-547
- Fonollosa, J., Sheik, S., Huerta, R. and Marco, S. (2015). Reservoir computing compensates slow response of chemosensor arrays exposed to fast varying gas concentrations in continuous monitoring. *Sensors and Actuators B: Chemical*, 215 618-629
- Fernandez, L., Marco, S. and Gutierrez-Galvez, A. (2015). Robustness to sensor damage of a highly redundant gas sensor array. *Sensors and Actuators B: Chemical*, 218 296-302
- Maynou, J., Pairo, E., Marco, S. and Perera, A. (2015). Sequence information gain based motif analysis. *BMC Bioinformatics*, 16 (1): 377
- Ziyatdinov, A., Fonollosa, J., Fernández, L., Gutiérrez-Gálvez, A., Marco, S. and Perera, A. (2015). Data set from gas sensor array under flow modulation. *Data in Brief*, 3 131-136

Conference Papers

- Oller-Moreno, S., Singla-Buxarrais, G., Jiménez-Soto, J. M., Pardo, A., Garrido-Delgado, R., Arce, L. and Marco, S. (2015). Sliding window multi-curve resolution: Application to gas chromatography - Ion Mobility Spectrometry. 15th International Meeting on Chemical Sensors, Buenos Aires, Argentina (01/10/2015). Published by Elsevier

- Fonollosa, J., Neftci, E., Huerta, R. and Marco, S. (2015). Evaluation of calibration transfer strategies between Metal Oxide gas sensor arrays. EUROSENSORS 2015, Freiburg, Germany (06/09/2015). Published by Elsevier

- Sensor test for indoor air quality and safety applications (2015-2016)
PI: **Santiago Marco**
Industrial Project with BSH Electrodomesticos, Spain

- Analisis de tapones de corcho por espectroscopia de movilidad de iones (2015-2016)
PI: **Santiago Marco**
Industrial Project with 3control, Spain

- Analysis of a Volatolomics dataset (2015)
PI: **Santiago Marco**
Industrial Project with Technion

- **SOMNO-ALERT** Detecció de Somnolència (2010-2015)
PI: **Santiago Marco**
Industrial Project with Ficomirrors

Collaborations with other research centres

Dr. Lourdes Arce
Dept. Química Analítica, Universidad de Córdoba, Spain

Dr. Alexandre Perera
Centre de Recerca en Enginyeria Biomèdica, Universitat Politècnica de Catalunya, Barcelona, Spain

Dr. J. Fonollosa and Prof. Ramon Huerta
Biocircuits Lab, University of California in San Diego, USA

Prof. J. W. Gardner
Microsensors and Bioelectronics Lab, Dept. of Electric and Electronic Engineering, University of Warwick, UK

System to test chemical chemical sensors for malodour detection

Prof. Achim Lilienthal and Dr. Marco Trincavelli
Mobile Robotics and Olfaction Lab, University of Örebro, Sweden

Dr. Ivan Montoliu
Nestlé Institute of Health Sciences, Laussane, Switzerland

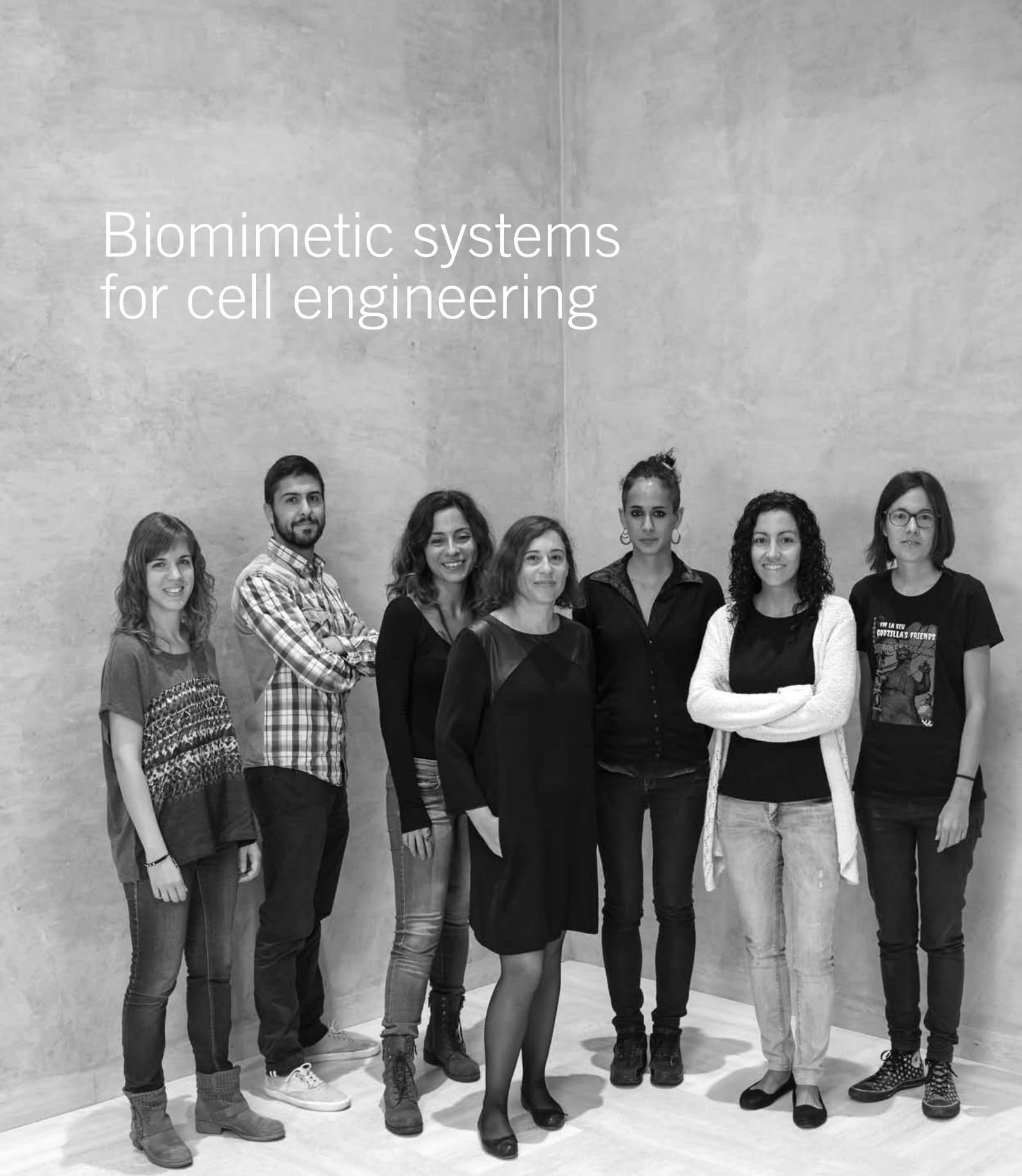
Dr. Jordi Palacín
Robotics Lab, Universitat de Lleida, Spain

Scientific equipment and techniques

- Gas chromatograph/mass spectrometer (Thermoscientific) with robotic head-space sampler
- 2 Infusion pumps K-systems
- 6 channel vapor generator plus humidity control (Owlstone, UK)
- Ion Mobility Spectrometer: Gas Detector Array (Airsense Analytics GmbH)
- Computing and General Purpose Electronic Instrumentation
- Field Asymmetric Ion Mobility Spectrometer (Owlstone, UK)
- Corona Discharge Ion Mobility Spectrometer (3QBD, Israel)
- Ultraviolet Ion Mobility Spectrometer (Gas Dortmund, Germany)

SAFESENS project aims to produce personal health monitors for emergency personnel including toxic hazards detection

Biomimetic systems for cell engineering



Junior group leader: Elena Martínez

PhD students: Gizem Altay, Albert Garcia, Verónica Hortigüela, Enara Larrañaga, Maria Valls, Anna Vila

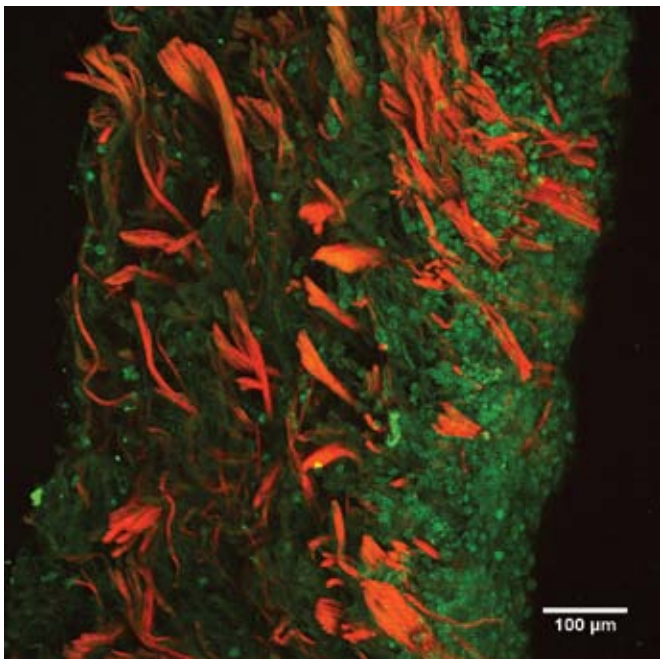
Master student: Jari Iannucci

Undergraduate students: Claudia Insa, Gabriela Korbelová, Ariadna Nistal

In vitro assay platforms involving human cells are increasingly important to study tissue development, tissue regeneration, construct models of disease or develop systems for therapeutic screening that predict the human *in vivo* context.

The main conceptual problem of the standard *in vitro* cell-based assays is that they rely on two dimensional monolayer cellular cultures, which fail to replicate the complexity of living systems. There is an urgent need to create technological platforms with complex cell culture systems that mimic better the tissue-like cellular microenvironment.

Our lab is interested in the development of new biomimetic systems for cell-based assays that account for the structural, physiological and biochemical features of the *in vivo* cellular microenvironment. Specifically, we develop systems that mimic the heterogeneity of the tissue extracellular matrix for cell engineering. Advanced designs include the structural anisotropy intrinsic to tissues such as heart muscle or bone, the binding of specific ligands and the capability of generating gradients of regulatory signals. These biomimetic systems will provide the interface between biological questions and engineering tools to (i) develop new insights into environmental regulation of cells, (ii) investigate diseases, and (iii) develop new therapies for regenerative medicine.



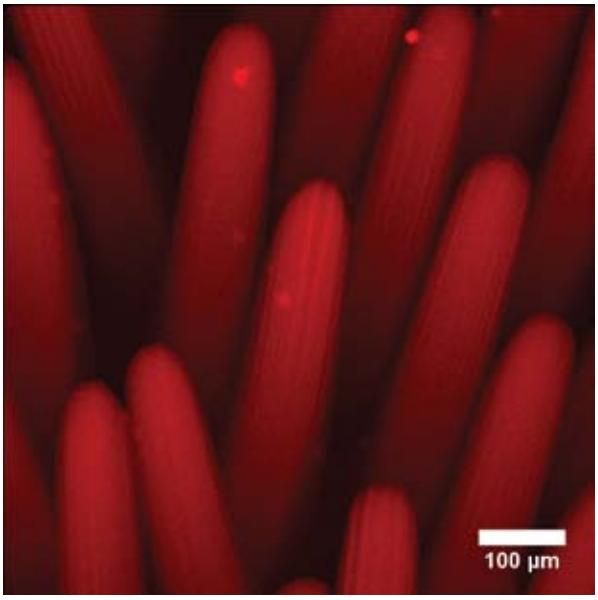
Cross-section of a cardiac tissue construct cultured in a perfusion bioreactor with electrical stimulation. A primary culture of neonatal rat cardiomyocytes was seeded in a 3D collagen-elastin matrix. Collagen fibers (orange) were imaged using two-photon second harmonic generation (SHG), and elastin fibers (green) using autofluorescence. As cells have a high degree of autofluorescence they are also shown in green, densely packed in the right part of the image.

Publications

- Galan, T., Lagunas, A., Martinez, E. and Samitier, J. (2015). Fabrication of bioactive polypyrrole microelectrodes on insulating surfaces by surface-guided biocatalytical polymerization. *RSC Advances*, 5 (82): 67082-67088
- Estévez, M., Martínez, E., Yarwood, S. J., Dalby, M. J. and Samitier, J. (2015). Adhesion and migration of cells responding to microtopography. *Journal of Biomedical Materials Research - Part A*, 103 (5): 1659-1668
- Lagunas, A., Martinez, E. and Samitier, J. (2015). Surface-bound molecular gradients for the high throughput screening of cell responses. *Frontiers in Bioengineering and Biotechnology*, 3 Article 132

Book Sections

- Comelles, J., Hortigüela, V., Martínez, E. and Riveline, D. (2015). Methods for rectifying cell motions *in vitro*: Breaking symmetry using microfabrication and microfluidics. In: "Methods in Cell Biology - Biophysical Methods in Cell Biology" (ed. Wilson, L. and Tran, P.). Academic Press, Santa Barbara, USA. 125: p437-452
- de Oñate, L., Garreta, E., Tarantino, C., Martínez, E., Capilla, E., Navarro, I., Gutiérrez, J., Samitier, J., Campistol, J. M., Muñoz-Cánovas, P. and Montserrat, N. (2015). Research on skeletal muscle diseases using pluripotent stem cells. In: "Muscle Cell and Tissue" (ed. Sakuma, K.). InTech, Rijeka, Croatia. p333-357



Hydrogel microstructures mimicking villi of the small intestinal tissue. They have been fabricated of PEGDA polymer and functionalized with labelled protein (in red).

Research projects

- **MINAHE5** (Bio)funcionalización de Micro- y NanoHerramientas en Suspensión para Aplicaciones en Células Vivas (2015-2017)
  PI: **Maria Lluïsa Pérez**
  MINECO
- **COMIET** Engineering Complex Intestinal Epithelial Tissue Models (2015-2020)
  PI: **Elena Martínez**
  ERC Consolidator Grant
- **GLAM** Glass-Laser Multiplexed Biosensor (2015-2019)
  PI: **Elena Martínez**
  European Commission (H2020) – PHC-10-2015

Collaborations with other research centres

Prof. Josep Samitier IBEC (page 117)

Prof. Ángel Raya / Dr. Samuel Ojosnegros Center of Regenerative Medicine in Barcelona (CMRB), Barcelona

Dr. Núria Montserrat IBEC (page 98)

Dr. Daniel Riveline ISIS/IGBMC, Strasbourg (France)

Dr. Matthew Dalby University of Glasgow, Glasgow (UK)

Prof. Eduard Batlle Institut de Recerca Biomédica (IRB), Barcelona

Prof. Fernando Albericio Institut de Recerca Biomédica (IRB), Barcelona

Prof. Jordi Martorell Institut de Ciències Fotòniques (ICFO), Castelldefels (Spain)

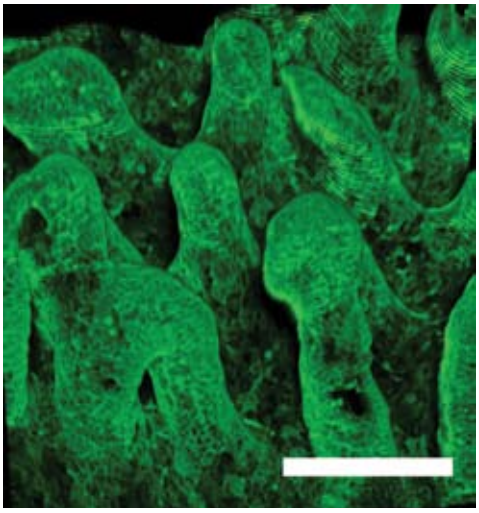
Prof. Pablo Loza Institut de Ciències Fotòniques (ICFO), Castelldefels (Spain)

Prof. Martí Gich Institut de Ciència de Materials de Barcelona (ICMAB), Bellaterra (Spain)

Prof. Rosa Villa CNM-SCIC, Bellaterra (Spain)

Scientific equipment and techniques

- Micro and nanofabrication techniques:
  - Biomolecule gradients produced by microfluidics
  - Large-area nanostructured polymer surfaces produced by diblock copolymers
  - 3D microstructures on hydrogel materials
  - Mini-bioreactor for 3D cell culture
- Characterization techniques:
  - Surface Plasmon Resonance (SPR) measurements on polymer materials
  - Atomic Force Microscope (AFM) expertise
  - Optical Microscopes (white light/epifluorescence)
  - Focused Ion Beam (FIB) / Scanning Electron Microscopy (SEM) of biological specimens
- Equipment:
  - Biological safety cabinet (class II)
  - High precision syringe pumps
  - Peristaltic pumps
  - Access to the Nanotechnology Platform (IBEC Core Facilities): equipment for hot embossing lithography, polymer processing and photolithography, chemical wet etching, e-beam evaporation and surface characterization (TOF-SIMS)
  - Access to the Scientific and Technological Centers (University of Barcelona): equipment for surface analysis (XPS, AFM, XRD) and microscopy techniques (SEM, TEM, confocal)



Caption: 3D rendering of villi-like microstructures fabricated of an hydrogel and seeded with Caco-2 cells. Scale bar = 200 µm.

iPSCs & activation of endogenous tissue programs for organ regeneration

Junior group leader: Núria Montserrat

Senior researchers: Elena Garreta, Federico González

PhD students: Lorena De Oñate, Laura Siles

Masters student: Andrés Marco

Laboratory assistant: Mireia Samitier

Senior technician: Carolina Tarantino

The generation of induced pluripotent stem cells (iPSCs), especially the generation of patient-derived pluripotent stem cells suitable for disease modelling *in vitro*, opens the door for the potential translation of stem-cell related studies into the clinic.

Successful replacement, or augmentation, of the function of damaged cells by patient derived differentiated stem cells would provide a novel cell-based therapy for diseases. Since iPSCs resemble human embryonic stem cells (hESCs) in their ability to generate cells of three germ layers, patient-specific iPSCs offer definitive solutions for the ethical and histo-incompatibility issues related to hESCs. Indeed human iPSC (hiPSC)-based autologous transplantation is heralded as the future of regenerative medicine.

One of our aims is to generate and correct disease-specific hiPSCs for disease modelling and drug screening. The combination of gene-editing based methodologies together with the development of novel protocols for cell differentiation into relevant tissues/organs, provides a unique scenario for modelling disease progression, and the identification of molecular and cellular mechanisms leading to organ regeneration (Figure 1). In this regard we are particularly interested in generation of transgene-free and disease free patient derived hiPSCs for disease modelling and the discovery of novel therapeutic targets.

We believe that the recovery of tissue function should not be restricted to the development of cell replacement therapies. In this regard, in our laboratory we take advantage of organisms that possess the ability to regenerate such as zebrafish, in order to understand which molecular and cellular pathways lead to organ regeneration. Surprisingly, studies in neonatal mice have demonstrated that soon after birth this organism posses the capability to regenerate its heart. Taking advantage of such preliminary observations we are translating such analysis in order to understand if the mammalian neonatal kidney still posses the capability to regenerate, and more importantly, if we are able to dissect the epigenetic and cellular mechanisms leading to those responses.

Lastly, and in an effort to fully develop *in vitro* and *ex vivo* platforms for organ regeneration, in our lab we are focused in the development of reporter cell lines for different transcription factors essential for tissue-specific commitment and differentiation (i.e: renal and cardiac lineages). The possibility to combine pluripotent stem cell lines together with decellularized matrices, functionalized biomaterials and *ex vivo* organoids offers and unprecedented opportunity for the immediate generation of patient-specific *in vitro* and *ex vivo* platforms for disease modelling and organ regeneration (Figure 2).

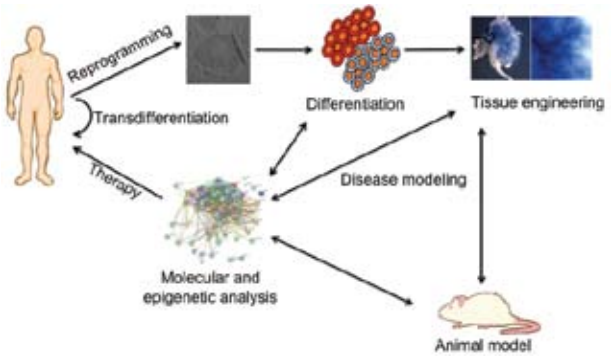


Figure 1: Patient induced pluripotent stem cells (iPSCs) represent an unprecedented tool for the generation of *in vitro* platforms for disease modelling and the definition of protocols for pluripotent stem cells differentiation. Transdifferentiation also offers the possibility to generate auto-compatible cells with no need to undergo to pluripotent stage. In these scenarios the correction of the genetic defect(s) leading to disease may help to understand the molecular and cellular mechanisms driving disease gestation and progression, and more importantly, to identify novel mechanisms leading to organ regeneration. The combination of gene editing methodologies with defined protocols for tissue differentiation helps us to generate *in vitro* systems for drug screening and disease modelling.

Publications

- Reddy, P., Ocampo, A., Suzuki, K., Luo, J., Bacman, S., Williams, S., Sugawara, A., Okamura, D., Tsunekawa, Y., Wu, J., Lam, D., Xiong, X., Montserrat, N., Esteban, C., Liu, G.-H., Sancho-Martinez, I., Manau, D., Civico, S., Cardellach, F., del Mar O'Callaghan, M., Campistol, J., Zhao, H., Campistol, J., Moraes, C. and Izpisua Belmonte, Juan C. (2015). Selective elimination of mitochondrial mutations in the germline by genome editing. *Cell*, 161 (3): 459-469

Book Sections

- de Oñate, L., Garreta, E., Tarantino, C., Martínez, E., Capilla, E., Navarro, I., Gutiérrez, J., Samitier, J., Campistol, J. M., Muñoz-Cánovas, P. and Montserrat, N. (2015). Research on skeletal muscle diseases using pluripotent stem cells. In: "Muscle Cell and Tissue" (ed. Sakuma, K.). InTech, Rijeka, Croatia. p333-357

Research projects

- **TRATENFREN** Desarrollo de nuevas estrategias para el tratamiento de la enfermedad renal (2015-2017)
PI: **Núria Montserrat**
MINECO

- Regenerative medicine for Fanconi anemia: generation of disease-free patient-specific iPS (2013-2016)
PI: **Núria Montserrat**
Fundació La Marató de TV3

- **REGMAMKID** How to regenerate the mammalian kidney (2015-2020)
PI: **Núria Montserrat**
ERC-StG

Collaborations with other research centres

Juan Carlos Izpisua Belmonte Salk Institute for Biological Studies

Dr. Josep Maria Campistol Plana Experimental Laboratory of Nephrology and Transplantation, Hospital Clínic, Barcelona

Peter Hohestein The Roslin Institute, University of Edinburgh

Dr. Pere Gascón Vilaplana Head of Oncology Service/Molecular and Translational Oncology Laboratory, IDIBAPS

Gloria Calderon President, Embryotools SL

Pura Muñoz Cánovas Departament de Ciències Experimentals i de la Salut, Universitat Pompeu Fabra

Dr. Pedro Guillén Director Clínica Cemtro, Madrid

Dr. Francisco Fernández Avilés Head of Cardiology Service, Hospital General Universitario Gregorio Marañón, Madrid

Dr María Eugenia Fernández Unit of Cell Production, Hospital Gregorio Marañón, Madrid

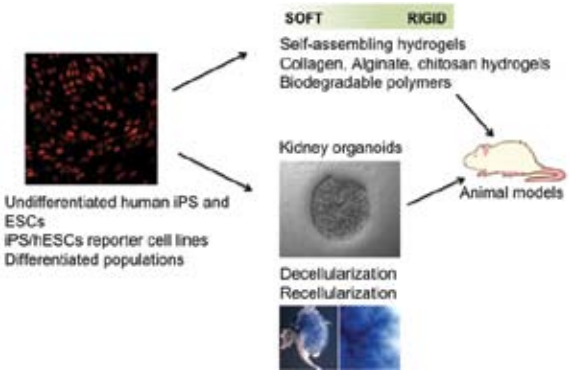


Figure 2: Induced pluripotent stem cells (iPSCs) resemble human embryonic stem cells (hESCs) in their ability to generate cells of the three germ layers of the embryo. This capacity can help us to understand the molecular and cellular cues driving cell fate. Our aim is to generate reporter cell lines from patient iPSCs in order to develop robust protocols for pluripotent stem cells differentiation. Moreover, the combination of patient differentiated populations together with functionalized biomaterials, *ex vivo* approaches (i.e: organoids), and decellularized tissue matrices, offers and unprecedented strategy for organ regeneration.

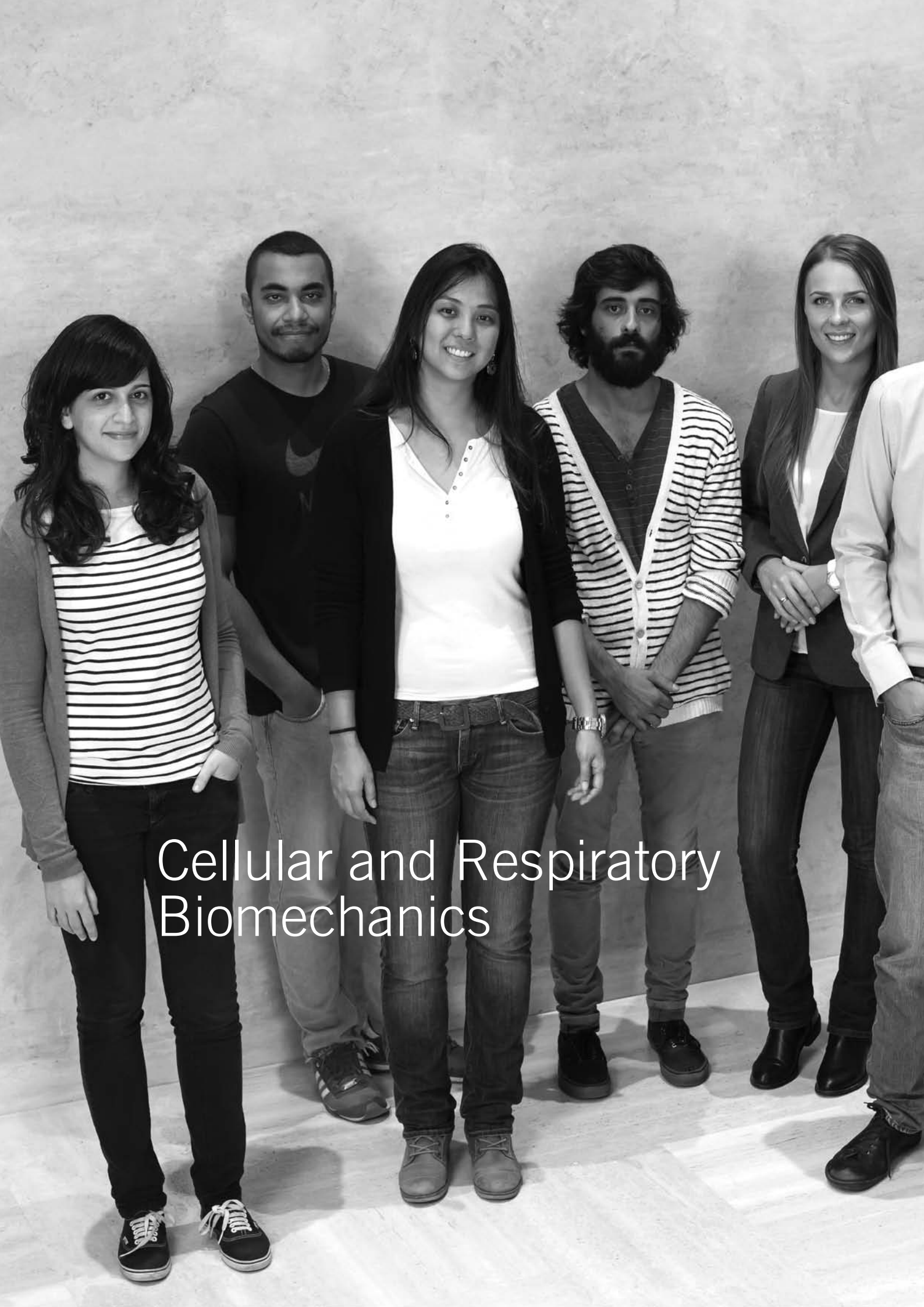
Joaquin Gutiérrez Fruitós University of Barcelona

Dr. Elena Martínez Biomimetic systems for cell engineering, IBEC (page 94)

Dr. Cristina Eguizabal Argaiz Centro Vasco de Transfusion y Tejidos Humanos (CVTTH), Bizkaia

Scientific equipment and techniques

- Real Time QuantStudio 5
- SimpliAmp thermocycler
- Eppendorf 5415D centrifuge
- Allegra X-15 R centrifuge
- BioUltra 6 Telstar culture Hood 2x
- Binder CB 60 incubators 2x
- Bioruptor Pico sonicator
- Thermomixer C thermal block
- Leica DMS1000 and DMIL Led microscopes
- Leica MZ 10F magnifying glass
- Safe Imager 2.0 transilluminator



Cellular and Respiratory Biomechanics

Group leader: Daniel Navajas

Junior group leader: Pere Roca-Cusachs

Postdoctoral researchers: Jordi Alcaraz, Alberto Elosegui

PhD students: Noelia Campillo, Víctor González, Ignasi Jorba, Anita Joanna Kosmalska, Roger Oria

Masters students: Manuel Jiménez, Eduard Quer

The research of our groups is focused on biomechanics; that is, the study of the mechanisms and physiological implications underlying mechanical force in biology. This research is organized into two different research lines.

The biophysical mechanobiology line, led by Prof. Pere Roca-Cusachs, studies the basic physical and molecular mechanisms by which cells detect and respond to forces. The respiratory biomechanics line, led by Prof. Daniel Navajas, studies the mechanical behavior of the respiratory system, and how it is altered in respiratory diseases.

Biophysical mechanobiology (Pere Roca-Cusachs, Junior Group Leader)

Every time we blink, move a hand, draw a breath, or walk, cells in our body exert, transmit, withstand, and detect forces. This mechanical interaction with the environment determines how cells proliferate, differentiate, and move, and regulates development, tumorigenesis or wound healing. Just like biochemical stimuli initiate signaling cascades, mechanical forces affect the links and conformation of a network of molecules connecting cells to the extracellular matrix.

Our research aims precisely at unraveling the mechanisms that these molecules use to detect and respond to mechanical stimuli like forces or tissue rigidity, triggering downstream cell responses. To this end, we combine biophysical techniques like magnetic tweezers, Atomic Force Microscopy, traction microscopy, and microfabricated force sensors with molecular biology, advanced optical microscopy, and theoretical modelling. Using this approach, we have recently unveiled a molecular mechanism that cells employ to detect and respond to the rigidity of their environment, which could be crucial in breast tissue and breast cancer (Elosegui-Artola et al., 2014, *Nature Materials*). We have also shown that cell membranes can use purely physical principles to adapt their shape in response to mechanical forces (Kosmalska et al., 2015, *Nat. Commun.*) Previously, we revealed the different mechanical roles of several adhesion molecules: whereas some are responsible for withstanding forces, others detect and transmit those forces (Roca-Cusachs et al., 2013, *PNAS*, and Roca-Cusachs et al., 2009, *PNAS*). Ultimately, when we determine the molecular mechanisms that communicate cells with their environment, we will understand how forces determine development when things go right, and tumor formation when they go wrong.

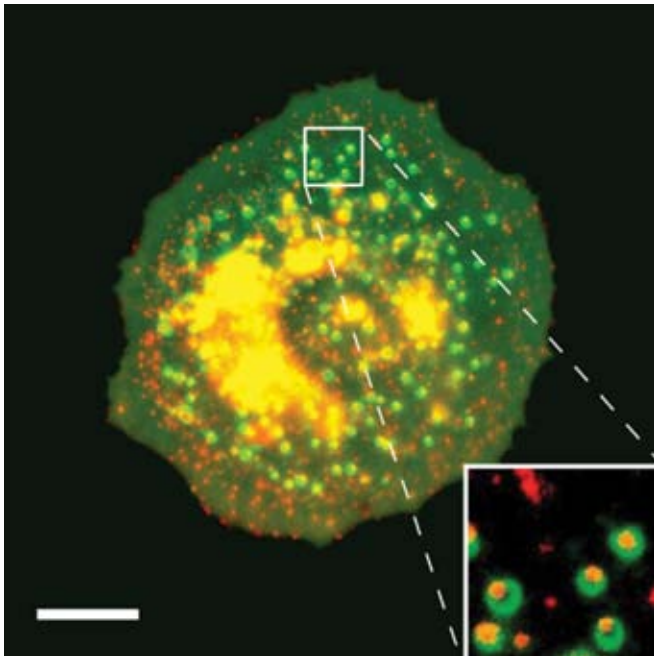
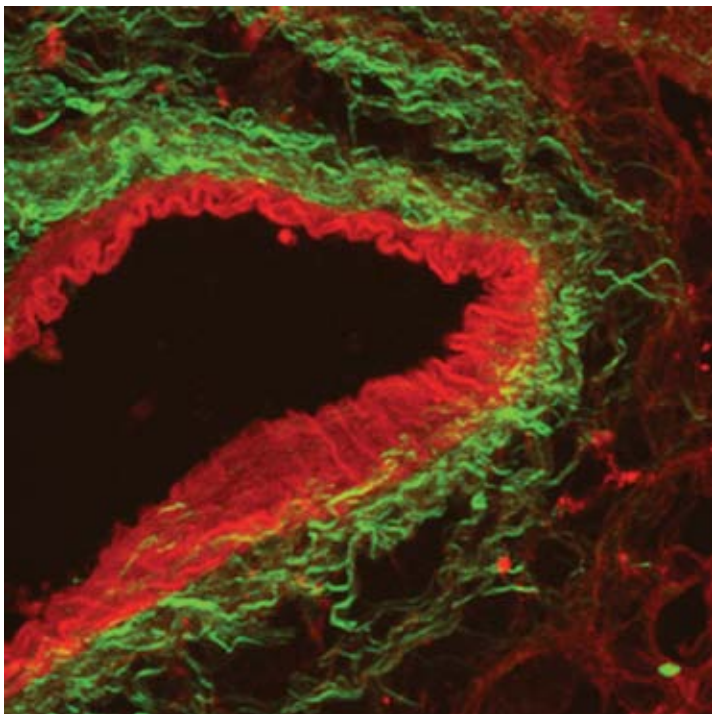


Image of membrane structures created by mouse embryonic fibroblasts after mechanical stimulation by stretch and hypo-osmotic shock. Scale bar is 20 µm.

Respiratory biomechanics (Daniel Navajas)

Our goal is to gain a deeper understanding of cellular and respiratory biomechanics in order to improve the diagnosis and treatment of respiratory diseases. The work is organized into two interrelated areas, focused on respiratory mechanics at both the systemic and the cellular level. We use basic and translational approaches in a multidisciplinary framework involving close cooperation with clinical groups. At the systemic level, we study the mechanical properties of airways and lung tissues and the mechanical dysfunctions associated with respiratory diseases. In the last period, our research has been mainly addressed to the study of sleep apnea syndrome (SAOS). We have improved continuous positive airway pressure devices for SAOS treatment. By using a novel murine model of SAOS we have shown that SAOS induces early release of mesenchymal stem cells (MSCs). We have also shown that injection of MSCs reduces SAOS-induced inflammation. We have revealed that cancer progression is associated with intermittent hypoxia. At the cellular level, we have developed an AFM technique to probe micro/nano-mechanical properties of the extracellular matrix (ECM) of decellularized tissue scaffolds. This innovative approach allowed us to reveal for the first time the local mechanical properties of the lung and heart cell niche. We have implemented several protocols for lung and heart decellularization and assessed the effect in mechanical and histological properties of the scaffold. By using induced pluripotent stem cells (iPSCs) we have shown that low O2 tension enhances the generation of lung progenitor cells.

Vessel section from a decellularized lung showing the tunica intima, rich in elastin (red), and the tunica adventitia, with high concentration of collagen fibers (green). The image was obtained by two-photon and second harmonic generation microscopy. Melo *et al. Tissue Eng Part C*, 2014)



Publications

- Bazellières, E., Conte, V., Elosegui-Artola, A., Serra-Picamal, X., Bintanel-Morcillo, M., Roca-Cusachs, P., Muñoz, J. J., Sales-Pardo, M., Guimerà, R. and Trepat, X. (2015). Control of cell-cell forces and collective cell dynamics by the intercellular adhesome. *Nature Cell Biology*, 17 (4): 409-420
- Kosmalska, A. J., Casares, L., Elosegui-Artola, A., Thottacherry, J. J., Moreno-Vicente, R., González-Tarragó, V., Del Pozo, M. Ã., Mayor, S., Arroyo, M., Navajas, D., Trepat, X., Gauthier, N. C. and Roca-Cusachs, P. (2015). Physical principles of membrane remodelling during cell mechanoadaptation. *Nature Communications*, 6 7292
- Stanisavljevic, J., Loubat-Casanovas, J., Herrera, M., Luque, T., Peña, R., Lluch, A., Albanell, J., Bonilla, F., Rovira, A., Peña, C., Navajas, D., Rojo, F., García De Herreros, A. and Baulida, J. (2015). Snail1-expressing fibroblasts in the tumor microenvironment display mechanical properties that support metastasis. *Cancer Research*, 75 (2): 284-295
- Crosas-Molist, E., Meirelles, T., López-Luque, J., Serra-Peinado, C., Selva, J., Caja, L., Gorbenko Del Blanco, D., Uriarte, J. J., Bertran, E., Mendizábal, Y., Hernández, V., García-Calero, C., Busnadiego, O., Condom, E., Toral, D., Castellà, M., Forteza, A., Navajas, D., Sarri, E., Rodríguez-Pascual, F., Dietz, H. C., Fabregat, I. and Egea, G. (2015). Vascular smooth muscle cell phenotypic changes in patients with marfan syndrome. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 35 (4): 960-972
- da Palma, R. K., Campillo, N., Uriarte, J. J., Oliveira, L. V. F., Navajas, D. and Farré, R. (2015). Pressure- and flow-controlled media perfusion differently modify vascular mechanics in lung decellularization. *Journal of the Mechanical Behavior of Biomedical Materials*, 49, 69-79

Research projects

- Precondicionamento biofísico de células madre mesenquimales para el tratamiento de la lesión pulmonar aguda provocada por sobreventilación en modelo animal (2015-2017)
PI: **Daniel Navajas**
Fondo de Investigación Sanitaria (FIS), MINECO (PI14/00280)

- Mechanical signaling driving stem cell differentiation in the lung. Lung-on-a-chip model (2012-2015)
PI: **Daniel Navajas**
Fondo de Investigación Sanitaria, Ministerio de Ciencia e Innovación (PI11/00089)

- Stromal stiffness in tumor progression (2014-2017)
PI: **Pere Roca-Cusachs**
Fundació la Marató de TV3

- Red de Excelencia en Mecanobiología (2014-2016)
PI: **Pere Roca-Cusachs**
"REDES DE EXCELENCIA", MINECO

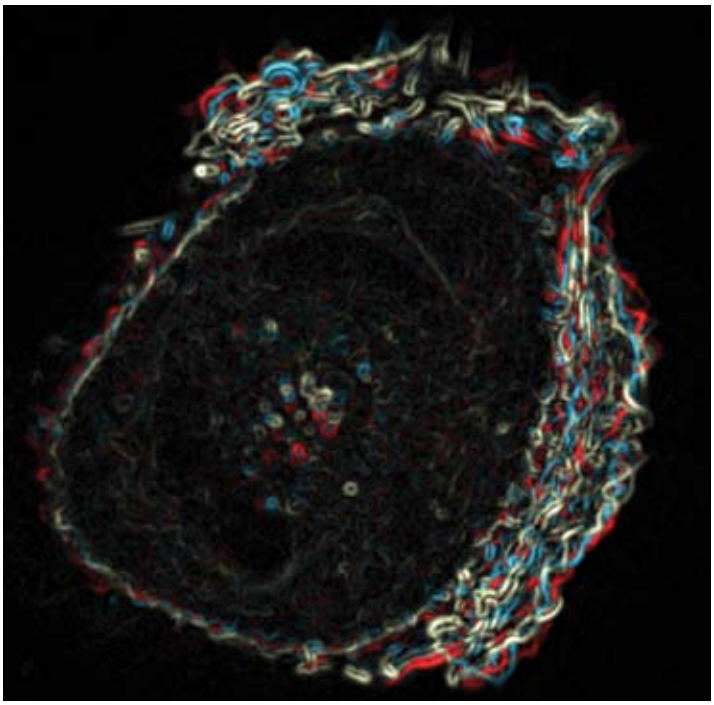
Collaborations with other research centres

Prof. Ramon Farré Unit of Biophysics and Bioengineering, Dept. Physiological Sciences, School of Medicine, University of Barcelona/IDIBAPS, Barcelona, Spain

Prof. J. M. Montserrat Service of Pneumology, Hospital Clinic/IDIBAPS, Barcelona, Spain

Prof. M. Sheetz Biological Sciences, Columbia University New York, USA

Movement of the actin cytoskeleton of a breast myoepithelial cell, shown by superimposing images of the actin cytoskeleton in different timeframes.



Prof. A. Artigas Intensive Care Service, Hospital Sabadell, Spain

Prof. A. Pedotti Bioengineering Dept., Politecnico di Milano, Italy

Prof. J. Cortiella Laboratory of Tissue Engineering and Regenerative Medicine, University of Texas Medical Branch, Galveston, USA

Prof. James Hone Mechanical Engineering, Columbia University, USA

Prof. Miguel Ángel del Pozo Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

Dr. Nils Gauthier Mechanobiology Institute, Singapore

Scientific equipment and techniques

- Fluorescence resonance energy transfer (FRET) microscopy
- Confocal Microcopy
- Traction Microscopy
- Live cell fluorescence microscopy
- Cell stretching
- Cell culture
- Magnetic Tweezers
- Atomic Force Microscopy
- Surface Micro/Nano-patterning

- Perea-Gil, I., Uriarte, J. J., Prat-Vidal, C., Gálvez-Montón, C., Roura, S., Llucià-Valldeperas, A., Soler-Botija, C., Farré, R., Navajas, D. and Bayes-Genis, A. (2015). *In vitro* comparative study of two decellularization protocols in search of an optimal myocardial scaffold for recellularization. American *Journal of Translational Research*, 7 (3): 558-573
- Torres, M., Rojas, M., Campillo, N., Cardenes, N., Montserrat, J. M., Navajas, D. and Farré, R. (2015). Parabiotic model for differentiating local and systemic effects of continuous and intermittent hypoxia. *Journal of Applied Physiology*, 118 (1): 42-47
- da Palma, R. K., Farré, R., Montserrat, J. M., Gorbenko Del Blanco, D., Egea, G., de Oliveira, L. V. F., Navajas, D. and Almendros, I. (2015). Increased upper airway collapsibility in a mouse model of Marfan syndrome. *Respiratory Physiology & Neurobiology*, 207, 58-60

Control of stem cell potency

Group leader/ICREA research professor: Ángel Raya

Postdoctoral researchers: América Martínez, Mario Notari, Marianna Vitaloni

PhD students: Carlos Félix Calatayud, Juan Crespo, Claudia Di Guglielmo, Anna Garcia, Isil Tekeli, Juan Luís Vázquez

Senior technician: Yvonne Richaud

Laboratory technician: Cristina García

Research technician: Senda Jiménez

Control of stem cell potency

During embryo development, the potency of the zygote is deployed through coordinated and stereotypical changes in cell behaviors and processes of tissue patterning, ultimately resulting in the formation of an entire, highly complex organism in a relatively short period of time.

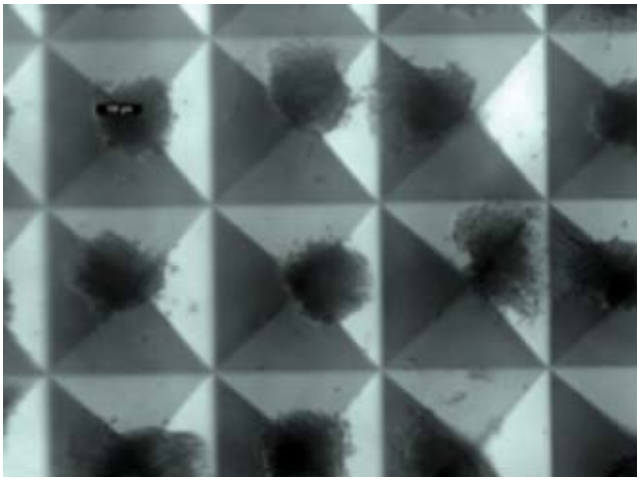
Throughout this process, the developmental potency of individual cells, i.e. their ability to give rise to cells of a different type than their own, is progressively lost, so that somatic cells in adult individuals retain very limited potency (such as in rare adult stem cells) or show no potency at all.

Our laboratory is interested in understanding the mechanisms that govern the degree of potency of human somatic cells, and how it can be experimentally increased for conditions where doing so may be of biomedical relevance. Specifically, the context in which we investigate these issues is mainly centred on the paradigm of cardiac regeneration/repair.

Heart-related diseases are the main cause of mortality in the world, with ischemic heart disease being the single most frequent condition accounting for the death toll. This results from the very limited ability of the mammalian heart to regenerate on its own, and underscores the pressing biomedical need to finding ways for potentiating this ability (heart regeneration) and/or providing new cardiac cells to replace the lost or damaged ones (heart repair). We pursue the first approach by studying the process of heart regeneration in the zebrafish, an organism with a remarkable capacity for regeneration. Natural regeneration is a biologically fascinating phenomenon in which somatic cells may regain developmental potency, and we hope that understanding the molecular and cellular mechanisms that control this process will help devising strategies to potentiate the regeneration of adult mammalian hearts.

For achieving heart repair, in turn, our research is aimed at generating functional human heart muscle cells that could be used for transplantation. For this purpose, we investigate ways to manipulate the developmental potency of human somatic cells so they become pluripotent (i.e. regain the potency of cells in the early embryo), and then study how these so-called induced pluripotent stem cells (iPSC) can be instructed to differentiate into functional cardiomyocytes. In addition, since iPSC can be generated from disease-carrying cells, many laboratories including ours are exploring the possibility of using patient-specific iPSC to generate disease-relevant cell types in which to investigate the pathogenic mechanisms of disease initiation and/or progression.

Overall, our research takes advantage of a variety of experimental paradigms (zebrafish heart regeneration, human iPSC generation and differentiation), approached from a multi-disciplinary perspective, ranging from bioengineering approaches to 3D stem cell differentiation to single-cell genetic lineage tracing analyses and genetic manipulation of human cells, aimed at tackling important current issues in biology and biomedicine, such as the mechanisms that control the establishment and maintenance of developmental potency, the initiation and progression of the regenerative process, and the differentiation and functional maturation of human cardiomyocytes, and the development of genuinely human models of human disease.



Human iPS cells aggregated to form embryoid bodies

Research projects

- **REGEN_HEART** Aproximación de bioingeniería a la regeneración/reparación cardiaca (2013-2015)
PI: **Ángel Raya**
MINECO, Investigación fundamental no orientada.

- Industrial Biological Biomaterials Doctorate (2013-2016)
PI: **Ángel Raya**
European Commission, MARIE CURIE - ITN

- Grup de recerca consolidat (2009-2014)
PI: **Ángel Raya**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (SGR 2009)

- Perpetuing NF+1/- and NF1-/- plexiform neurofibroma-derived tumor cells through the generation of induced pluripotent stem (iPS) cells (2014-2015)
PI: **Ángel Raya**
JHU SCHOOL OF MEDICINE Neurofibromatosis Therapeutic Acceleration Program (NTAP)

Collaborations with other research centres

Anne Weber/Anne Dubart Inserm, Le Kremlin-Bicêtre Cedex, France

Manuel Galiñanes Hospital Universitari Vall d'Hebron, Barcelona, Spain

Patrizia Dell'Era Università degli Studi di Brescia, Italy

Miquel Vila Institut de Recerca, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Eduard Tolosa Hospital Clínic, Barcelona, Spain

Pedro Muniesa Facultad de Veterinaria, Zaragoza, Spain

Publications

- Gálvez-Montón, C., Fernandez-Figueras, M. T., Martí, M., Soler-Botija, C., Roura, S., Perea-Gil, I., Prat-Vidal, C., Llucià-Valldeperas, A., Raya, A. and Bayes-Genis, A. (2015). Neoinnervation and neovascularization of acellular pericardial-derived scaffolds in myocardial infarcts. *Stem Cell Research and Therapy*, 6 (1): 108

- Martorell, L., Corrales, I., Ramirez, L., Parra, R., Raya, A., Barquinero, J. and Vidal, F. (2015). Molecular characterization of ten F8 splicing mutations in RNA isolated from patient's leucocytes: Assessment of in silico prediction tools accuracy. *Haemophilia*, 21 (2): 249-257

- Notari, M., Pulecio, J. and Raya, A. (2015). Update on the pathogenic implications and clinical potential of microRNAs in cardiac disease. *BioMed Research International*, 2015 Article ID 105620

- Torrent R, De Angelis Rigotti F, Dell'Era P, Memo M, Raya A, Consiglio A. (2015). Using iPS cells toward the understanding of Parkinson's disease. *J Clin Med* 4:548-66

- Canals, I., Soriano, J., Orlandi, J.G., Torrent, T., Richaud-Patin, Y., Jiménez-Delgado, S., Merlin, S., Follenzi, A., Consiglio, A., Vilageliu, L., Grinberg, D., Raya, A. (2015). Activity and high-order effective connectivity alterations in Sanfilippo C patient-specific neuronal networks. *Stem Cell Rep* 5:546-57

- Fernández-Santiago R, Carballo-Carbajal I, Castellano G, Torrent R, Richaud Y, Sánchez-Danés A, Vilarrasa-Blasi R, Sánchez-Pla A, Mosquera JL, Soriano J, López-Barneo J, Canals JM, Alberch J, Raya Á, Vila M, Consiglio A, Martín-Subero JI, Ezquerra M, Tolosa E. (2015). Aberrant epigenome in iPSC-derived dopaminergic neurons from Parkinson's disease patients. *EMBO Mol Med* 7:1529-46

José López Barneo Instituto de Biomedicina (IBiS), Sevilla, Spain

Daniel Grinberg/Lluïsa Vilageliu University of Barcelona, Spain

Rafael Garesse Instituto de Investigaciones Biomédicas "Alberto Sols"/UAM, Spain

Antonia Follenzi Universita' del Piemonte Orientale, Novara, Italy

Sheng Ding Scripps Research Institute, La Jolla, USA

Jordi Barquinero Institut de Recerca, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Jordi Alberch/Josep M. Canals Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Spain

Jerónimo Blanco/Núria Rubio Centro de Investigación Cardiovascular CSIC-ICCC, Barcelona, Spain

Francisco J. Blanco Complejo Hospitalario Universitario A Coruña, Spain

Antonella Consiglio Institute of Biomedicine of the University of Barcelona (IBUB), Spain

Ludovic Jullien Ecole Normale Supérieure, Paris, France

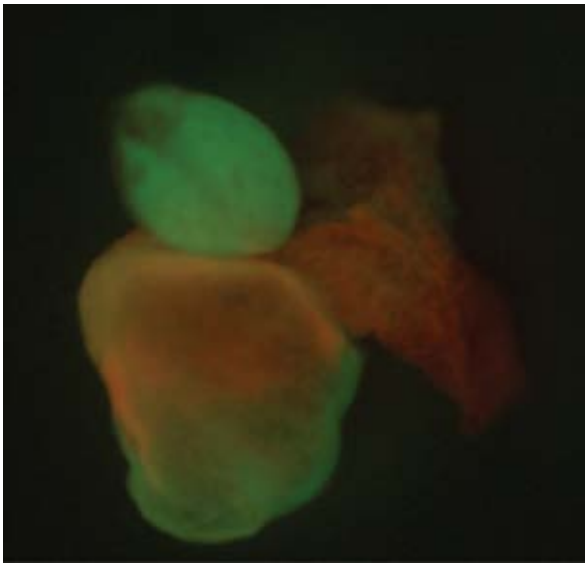
Ana Maria Cuervo Albert Einstein College of Medicine, Bronx, USA

Lorenzo Monserrat Complejo Hospitalario Universitario A Coruña, Spain

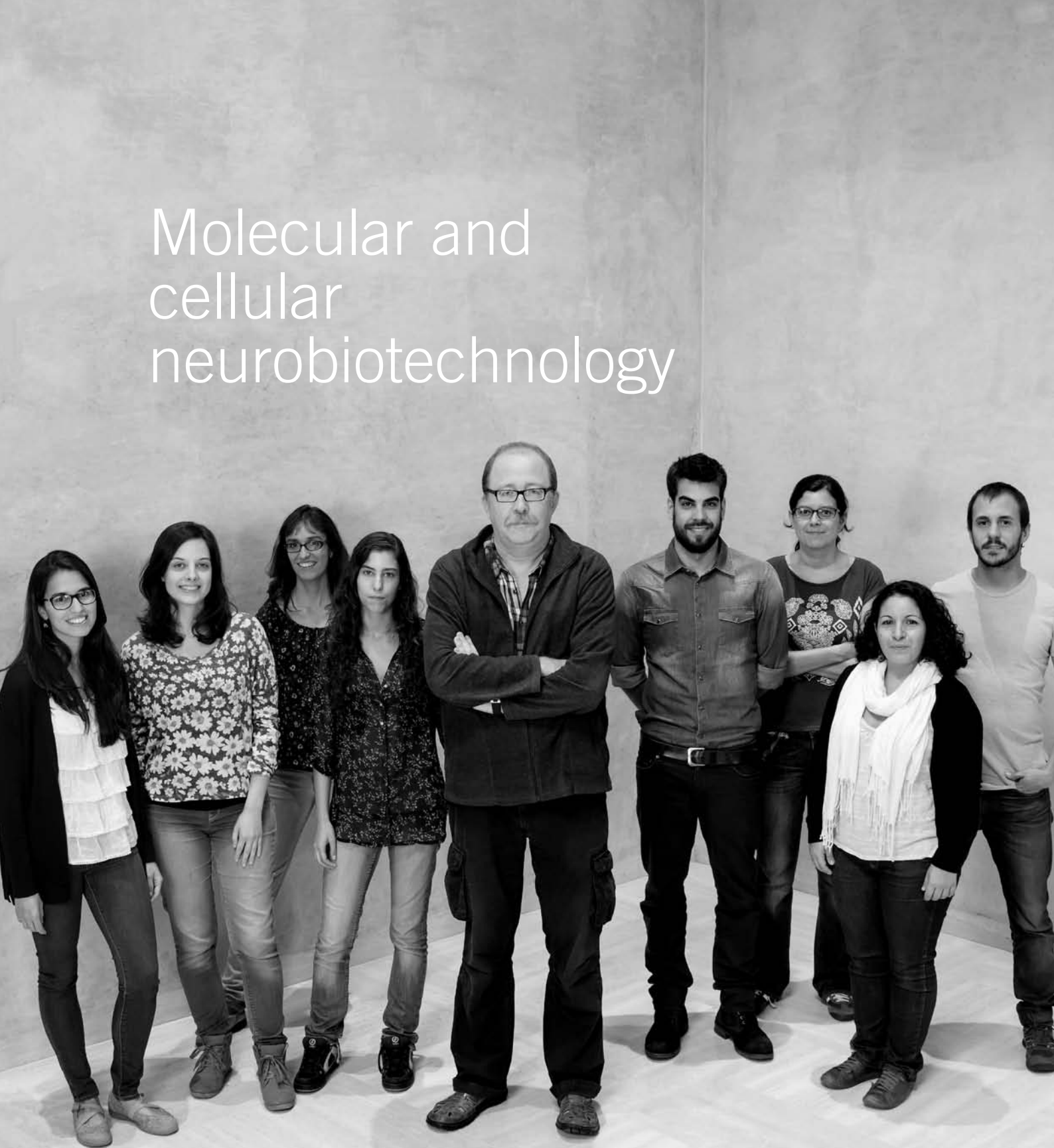
Scientific equipment and techniques

- hES/iPS cell culture station
- Zebrafish transgenesis
- Molecular biology facilities
- Stereomicroscope for picking hES colonies
- Cell culture facilities

Heart of a transgenic zebrafish showing mosaic recombination



Molecular and cellular neurobiotechnology



Group leader: José Antonio Del Río

Senior researcher: Rosalina Gavín

Postdoctoral researchers: Vanessa Gil, Ariadna Pérez

PhD students: Agata Mata, Andreu Matamoros, Laura Urrea

Masters students: Laia Lidón, Ana López, Montserrat Salguero, Lorena Sueiro

Undergraduate students: Anna Prieto

Laboratory assistant: Miriam Segura

Our research interests are focused on four main aspects of developmental neurobiology and regeneration:

1) Role of PrPc in epilepsy

Rapid progressive dementia such us fast Alzheimer´s disease or prionopathies are characterized by myoclonus and epilepsy. In humans, a decrease in the cellular prion protein PrPc can be observed in these diseases. In a collaboration between 4 laboratories (JM Torres (INIA), Giuseppe Legname (SISSA), Isidre Ferrer (UB) and Franc Llorens (Germany)) we determined the role of PrPc in epilepsy. We determined that in absence of the protein neural excitability increases and neurons become more sensitive to kainate or glutamatergic insults. These effects can be seen in 4 different models of Prion diseases with different genetic background.Results were published in Scientific Reports.

2) Cell therapy and pharmacological treatment to potentiate axon regeneration in lesioned central nervous system

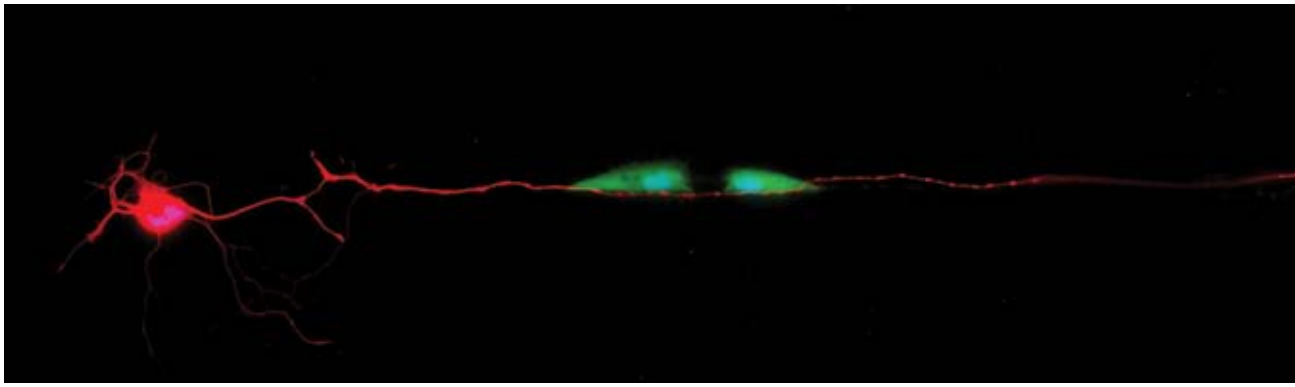
In the last year we have focused on genetically modifying olfactory ensheathing cells (OECs) to increase their survival and migration in the lesioned spinal cord. Results were published in Cellular and Molecular Life Science. In our experiments, OECs were genetically modified to overexpress the ectodomain of Nogo Receptor to increase their migration in inhibitory substrates. Current experiments by our group in collaboration with Profs J. Rogers and J. Fawcett (UK) aim to modify these cells to be able to degrade the second inhibitory molecules present in lesioned spinal cord: the chondroitin sulphate proteoglycans.

3) Neurodegenerative diseases

We recently determined the role of a natural neural protein PrPc in the evolution of Alzheimer's disease (published in Molecular Neurobiology). Results point to PrPc as neuroprotective factor in Alzheimer's. Further experiments will continue in this direction, and also will be expanded to Parkinson's disease. Our hypothesis is that PrPc is a cross-link protein between different neurodegenerative diseases presenting taupathy. In addition, we determined that the N-terminal domain of the protein is the responsible of these neuroprotective effects.

4) Development of new lab on a chip devices for neurobiological research

We recently developed a new device able to reproduce axon lesioning *in vitro* in a single chip (published in RSC Advances). Current experiments of our group in collaboration with groups of IBEC and CIBER-BBN aimed at developing new lab on chip devices to mimics and modulate particular neurobiological processes. For example: cortico-spinal chips to develop genetic studies; molecular gradient generation for migrating neurons and *in silico* 3D modeling for neurodegenerative diseases (Alzheimer chip).



Research projects

- **NEURODEV** Nuevas funciones de PlexinD1/Sema3E, PrP^C y las proteínas asociadas a la mielina durante el desarrollo de la corteza cerebral de roedores y en neurodegeneración (2013-2015)
PI: **José Antonio del Río**
MINECO, BFU2012-32617

- Modalitat B - Grup de Recerca Consolidat (2009-2015)
PI: **José Antonio del Río**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca (SGR 2014-2016)

- Red Nacional de Priones (2015-2017)
PI: **José Antonio del Río**
MINECO

- Role of the cellular prion protein as "cross-talk" protein between α-syn/ LRRK2 and p-Tau in sporadic and familiar Parkinson's disease (2015-2018)
PI: **José Antonio del Río**
Fundació La Marató de TV3

- **DEMTEST** Biomarker based diagnosis of rapid progressive dementias – optimization of diagnostic protocols (2012-2015)
PI: **José Antonio del Río**
Instituto de Salud Carlos III

Collaborations with other research centres

Prof. Javier de Felipe Instituto Cajal, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

Dr. Fernando de Castro Hospital Nacional de Parapléjicos, Toledo, Spain

Dr. Adolfo Lopéz de Munain Hospital de Donostia, San Sebastian, Spain

Dr. Jokin Castilla CiC Biogune, Bilbao, Spain

Prof. Jose Manuel García Verdugo Facultad de Ciencias, Universidad de Valencia, Spain

Prof. Jose Manuel García Aznar Nanotechnology Institute, Zaragoza, Spain

Prof. Fernando Albericio Institute for Research in Biomedicine (IRB), Barcelona

Dra. Miriam Royo Institute for Research in Biomedicine (IRB), Barcelona

Corticospinal axon (red) follows axonal guidance cues of olfactory ensheathing cells (green) *in vitro.*

Publications

- Reginensi, D., Carulla, P., Nocentini, S., Seira, O., Serra-Picamal, X., Torres-Espín, A., Matamoros-Angles, A., Gavín, R., Moreno-Flores, M. T., Wandosell, F., Samitier, J., Trepat, X., Navarro, X. and del Río, J. A. (2015). Increased migration of olfactory ensheathing cells secreting the Nogo receptor ectodomain over inhibitory substrates and lesioned spinal cord. *Cellular and Molecular Life Sciences*, 72 (14): 2719-2737

- Carulla, P., Llorens, F., Matamoros-Angles, A., Aguilar-Calvo, P., Espinosa, J. C., Gavín, R., Ferrer, I., Legname, G., Torres, J. M. and del Río, J. A. (2015). Involvement of PrPC in kainate-induced excitotoxicity in several mouse strains. *Scientific Reports*, 5, 11971

- Vergara, C., Ordóñez-Gutiérrez, L., Wandosell, F., Ferrer, I., del Río, J. A. and Gavín, R. (2015). Role of PrPC expression in tau protein levels and phosphorylation in alzheimer's disease evolution. *Molecular Neurobiology*, 51 (3): 1206-1220

- Perez-Balaguer, A., Ortiz-Martínez, F., García-Martínez, A., Pomares-Navarro, C., Lerma, E. and Peiró, G. FOXA2 mRNA expression is associated with relapse in patients with Triple-Negative/Basal-like breast carcinoma. *Breast Cancer Research and Treatment*, 153 (2): 465-474

- Llorens, F., Zafar, S., Ansoleaga, B., Shafiq, M., Blanco, R., Carmona, M., Grau-Rivera, O., Nos, C., Gelpí, E., del Río, J. A., Zerr, I. and Ferrer, I. (2015). Subtype and regional regulation of prion biomarkers in sporadic Creutzfeldt-Jakob disease. *Neuropathology and Applied Neurobiology*, 41 (5): 631-645

Dr. Elisabeth Engel (page 58), **Prof. Josep Samitier** (page 117), **Prof. Xavier Trepat** (page 132)

Prof. Ángel Raya Center of Regenerative Medicine in Barcelona (CMRB), Barcelona

Prof. Jesús Ávila and **Prof. Francisco Wandosell** Consejo Superior de Investigaciones Científicas (CSIC), Universidad Autónoma de Madrid, Spain

Prof. Isidro Ferrer Institut d'Investigació Biomèdica de Bellvitge, University of Barcelona, Spain

Prof. Marc Tessier-Lavigne Genentech, Inc., South San Francisco, USA

Prof. Fanny Mann Developmental Institute of Marseille Luminy, Université de la Méditerranée, Marseille, France

Prof. Yutaka Yoshida Division of Developmental Biology, Cincinnati Children's Research Foundation, Cincinnati, Ohio, USA

Prof. Jean Leon Thomas Developmental neurobiology, Yale University

Prof. Masato Hagesawa Faculty of Medicine, Tokyo

Scientific equipment and techniques

- Neural stem cell culture
- Microscopy facility (Olympus BX61 and Olympus IX71 with LCi culture and OKOlab systems)
- Electroporation system (BTX 600)
- Pressure microinjection system
- Protein expression and purification systems
- Technology of neuronal culture facilities (2D and 3D)
- Lentiviral production and characterization
- Gradient thermocycler (PCR)
- Protein and DNA electrophoresis
- *In situ* hybridization oven

Nanobioengineering

Group leader: Josep Samitier

Senior researchers: David Caballero, Mònica Mir

Research assistant: Xavier Coromina

Postdoctoral researchers: Margarita Alvira, Anna Lagunas

PhD students: Maider Badiola, Luís Botaya, Roberto Paoli, Wilmer Alfonso Pardo, Luís Rigat

Masters students: Iago López, Iro Tsintzou

Undergraduate students: Anna Agustí, Lluis Figueras, Neus García, Laura Pérez, Ferran Plana, Cristina Tabas

Research technician: Samuel Dulay

Laboratory technicians: Miriam Funes, David Izquierdo, Judit Pérez

The Nanobioengineering group is a truly multidisciplinary team composed by researchers coming from very diverse backgrounds (chemistry, physics, material science, electronic engineering, pharmacy and molecular biology) working together in applying nanotechnology for the development of new biomedical systems and devices, mainly for diagnostic purposes, and integrated microfluidic Organ-on-Chip devices for the study of organ physiology, disease etiology, or drug screening.

The main research activities of the group include the engineering and biochemical functionalization of biomaterials integrated with microfluidics systems. The bioengineered microdevices are used to study cell responses to biomolecular compounds applied to Organ-on-Chip devices, or for the development of new lab-on-a-chip based biosensors.

The goal is to fabricate microsystems containing living cells that recapitulate tissue and organ level functions *in vitro* and new portable diagnosis devices that can be used as Point-of-Care systems. The projects carried out by the group are focused on clinical and industrial problems and are related to four convergent research lines:

1. Biosensors and Lab-on-a-Chip devices for clinical diagnosis and food safety applications

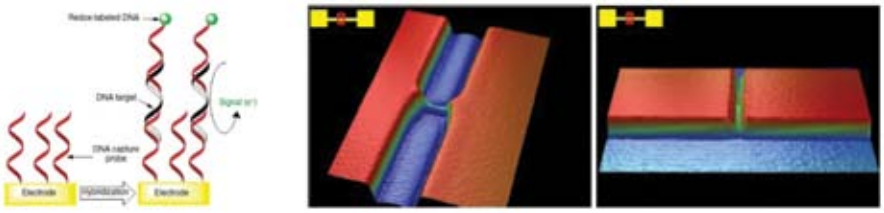
- DNA sensors and platform arrays for cancer biomarker detection.
- Antibody-based sensors for pathogenic microorganisms' detection.
- Sensor array for *in vivo* hypoxia and ischemia monitoring.
- Sensors to mimic the chemical detection of plant roots for robotic applications.
- Microfluidic chip for reagent handling in POC diagnosis devices.
- Microfluidic chip using hydrodynamic forces for cell counting and sorting. Application for detection of circulating tumors cells (CTC).

2. Nanotechnology applied to biomolecule interaction studies and micro/nano-environments for regenerative medicine applications

- Development of bioengineered micro/nanoenvironments with a topography and chemical composition controlled at the nanoscale for cell behavior studies (adhesion, proliferation, differentiation).
- Biophysical description of cellular phenomena (cell migration, differentiation) using micro/nanotechnologies, cell biology tools and soft matter physics.
- Study of magnetite - Amyloid-Beta interaction in Alzheimer disease.

3. Microfluidic systems for biological studies and Organ-on-Chip devices

- Microfluidic chip for blood/plasma filtering.
- Spleen-on-a-chip development.
- Nanoporous-based systems for kidney-on–a-chip developments.
- Engineering microfluidic platforms for neurobiological studies.



Nano-gap DNA sensors.

Research projects

- **PLANTOID** Innovative Robotic Artefacts Inspired by Plant Roots for Soil Monitoring (2012-2015)
  PI: **Josep Samitier**
  EU- FP7-ICT-FET-Open

- **OligoCODEs** Universal Diagnostic Platforms Based On Oligonucleotide Codified Nanoparticles and DNA Microarray Sensor Devices (2013-2015)
  PI: **Josep Samitier**
  MINECO

- Grup de recerca consolidat (2009-2014)
  PI: **Josep Samitier**
  Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (SGR 2009)

- **LABINACHIP** Nuevos métodos para la fabricación de dispositivos microfluídicos (2014-2015)
  PI: **Josep Samitier**
  Industrial project with Tallers Fiestas S.L

- **ELECTRA-G** (2014-2016)
  PI: **Josep Samitier**
  Conveni GENOMICA S.A.U.

Collaborations with other research centres

Prof. Fernando Albericio Institut de Recerca Biomédica (IRB), Barcelona, Spain

Dr. José Antonio Andrades, Universidad de Málaga, Spain

Prof. Joan Bausells Centro Nacional de Microelectrónica (CNM-CSIC), Barcelona

Prof. Albert van den Berg University of Twente, The Netherlands

Prof. Andre Bernard Institut für Mikro- und Nanotechnologie (MNT-NTB), Buchs, Switzerland

Prof. H. Börner Max Planck Institute of Colloids and Interfaces, Golm, Germany

Prof. Josep Maria Canals University of Barcelona, Spain

Dr. Matthew Dalby University of Glasgow, Glasgow, UK

Prof. Paolo Dario Scuola Superiore Sant'Anna (SSSA), Pontedera, Italy

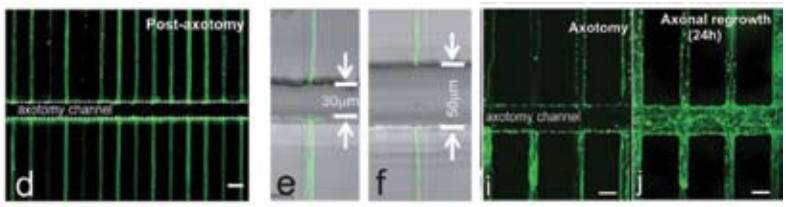
Prof. Ramón Eritja Institut de Recerca Biomédica (IRB), Barcelona, Spain

Prof. E. Faszewski Wheelock College, Boston, USA

Publications

- Galán, T., Prieto-Simón, B., Alvira, M., Eritja, R., Götz, G., Bäuerle, P. and Samitier, J. (2015). Label-free electrochemical DNA sensor using "click"-functionalized PEDOT electrodes. *Biosensors and Bioelectronics*, 74 751-756
- Galán, T., Prieto-Simón, B., Alvira, M., Eritja, R., Götz, G., Bäuerle, P. and Samitier, J. (2015). Label-free electrochemical DNA sensor using "click"-functionalized PEDOT electrodes. *Biosensors and Bioelectronics*, 74 751-756
- Reginensi, D., Carulla, P., Nocentini, S., Seira, O., Serra-Picamal, X., Torres-Espín, A., Matamoros-Angles, A., Gavín, R., Moreno-Flores, M. T., Wandosell, F., Samitier, J., Trepat, X., Navarro, X. and del Río, J. A. (2015). Increased migration of olfactory ensheathing cells secreting the Nogo receptor ectodomain over inhibitory substrates and lesioned spinal cord. *Cellular and Molecular Life Sciences*, 72 (14): 2719-2737
- Teller, S., Tahirbegi, I. B., Mir, M., Samitier, J. and Soriano, J. (2015). Magnetite-Amyloid-β deteriorates activity and functional organization in an *in vitro* model for Alzheimer's disease. *Scientific Reports*, 5 17261
- Caballero, D. and Goetz, J. G. (2015). Foreword: Physics of cell migration. *Cell Adhesion & Migration*, 9 (5): 325-326
- Zaffino, R. L., Galan, T., Pardo, W. A., Mir, M. and Samitier, J. (2015). Nanoprobes for enhanced electrochemical DNA sensors. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, 7 (6): 817-827
- Barreiros dos Santos, M., Azevedo, S., Agusil, J. P., Prieto-Simón, B., Sporer, C., Torrents, E., Juárez, A., Teixeira, V. and Samitier, J. (2015). Label-free ITO-based immunosensor for the detection of very low concentrations of pathogenic bacteria. *Bioelectrochemistry*, 101 146-152

- Tong, Z., Segura-Feliu, M., Seira, O., Homs-Corbera, A., Del Río, J. A. and Samitier, J. (2015). A microfluidic neuronal platform for neuron axotomy and controlled regenerative studies. *RSC Advances*, 5 (90): 73457-73466
- Rigat, L., Homs-Corbera, A. and Samitier, J. (2015). Highly hydrophilic microfluidic device prototyping using a novel poly(dimethylsiloxane)-based polymeric mix. *RSC Advances*, 5 (10): 7423-7425
- Galan, T., Lagunas, A., Martinez, E. and Samitier, J. (2015). Fabrication of bioactive polypyrrole microelectrodes on insulating surfaces by surface-guided biocatalytical polymerization. *RSC Advances*, 5 (82): 67082-67088
- Estévez, M., Martínez, E., Yarwood, S. J., Dalby, M. J. and Samitier, J. (2015). Adhesion and migration of cells responding to microtopography. *Journal of Biomedical Materials Research - Part A*, 103 (5): 1659-1668
- Pardo, W. A., Mir, M. and Samitier, J. (2015). Signal enhancement in ultraflat electrochemical DNA biosensors. Electrophoresis, 36 (16): 1905-1911
- Jaramillo, M. d. C., Huttener, M., Alvarez, J. M., Homs-Corbera, A., Samitier, J., Torrents, E. and Juárez, A. (2015). Dielectrophoresis chips improve PCR detection of the food-spoiling yeast *Zygosaccharomyces rouxii* in apple juice. *Electrophoresis*, 36 (13): 1471-1478
- del Moral-Zamora, B., Punter-Villagrassa, J., Oliva-Brañas, A. M., Álvarez-Azpeitia, J. M., Colomer-Farrarons, J., Samitier, J., Homs-Corbera, A. and Miribel-Català, P. L. (2015). Combined dielectrophoretic and impedance system for on-chip controlled bacteria concentration: application to *Escherichia coli*. *Electrophoresis*, 36 (9-10): 1130-1141
- del Moral Zamora, B., Manuel Álvarez Azpeitia, J., Brañas, A. M. O., Colomer-Farrarons, J., Castellarnau, M., Miribel-Català, P. L., Homs-Corbera, A., Juárez, A. and Samitier, J. (2015). Dielectrophoretic



Proximal segments of axons showing regeneration formation in compartmentalized microfluidic devices

Prof. G. Fuhr FhG Biomedicine, St. Ingbert, Germany

Dr. Juan C. Izpisúa Centro de Medicina Regenerativa (CMRB), Barcelona, Spain

Dr. Nicole Jaffrezic Université Claude Bernard Lyon 1, France

Dr. Graham Johnson Uniscan Instruments Ltd, Buxton, UK

Dr. Mª Pilar Marco Institute of Chemical and Environmental Research, Barcelona

Prof. Jean-Louis Marty Université de Perpignan Via Domitia, France

Prof. Barbara Mazzolai IIT Center for Micro-BioRobotics (CMBR), Pontedera, Italy

Dr. Edith Pajot Biology of Olfaction and Biosensors group (BOB) at INRA, Jouy-en-Josas, France

Dr. M. Lluïssa Pérez Dept. Farmacología, University of Barcelona, Spain

Dr. Hernando del Portillo Centro de Investigación en Salud Internacional de Barcelona (CRESIB), Barcelona, Spain

Dr. Jaume Reventós Hospital Vall d'Hebrón, Barcelona, Spain

Prof. L. Reggiani Nanotechnology Laboratory, INFM, Lecce, Italy

Prof. Daniel Riveline Laboratory of Cell Physics ISIS/IGBMC, Strasbourg

Prof. M. Sampietro Politecnico di Milano, Italy

Prof. Molly M. Stevens Imperial College, London, UK

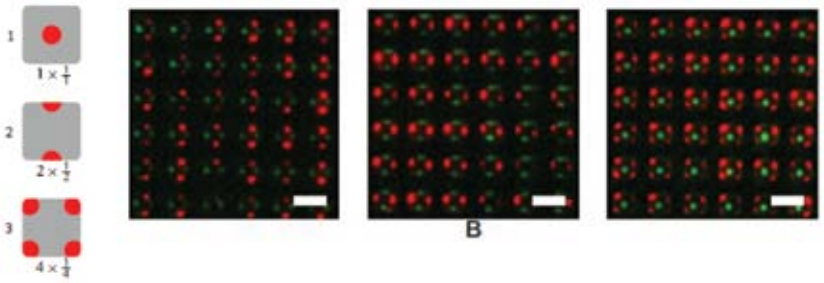
Dr. Christophe Vieu Laboratoire d'analyse et d'architectures des systèmes (LAAS-CNRS), Toulouse, France

Industry partners:

Biokit S.A. (Werfen group); Genomica S.A.U. (Zeltia group); Tallers Fiestas S.L.; Enantia S.L.; Microfluidic ChipShop GmbH

Scientific equipment and techniques

- Nanofabrication and nanomanipulation
  - Automatized microcontact printing system (custom-made)
- Characterization
  - Surface Plasmon Resonance (SPR)
  - Potentiostates
  - Optical Waveguide Lightmode Spectroscope (OWLS)
  - Atomic Force Microscope (AFM)

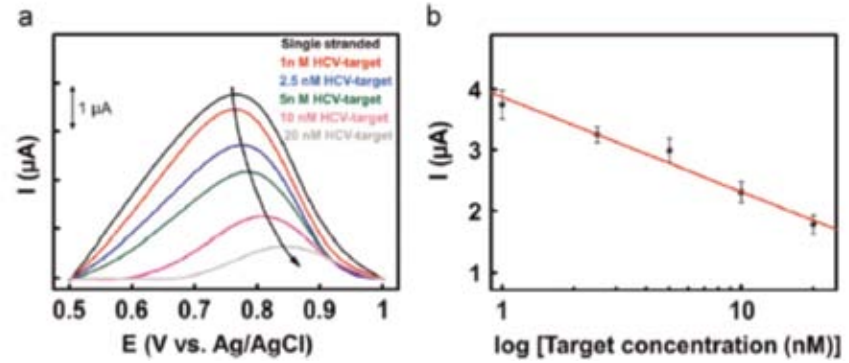


Fluorescence images of multi patterns fabricated with pyramidal PDMS stamp.

- Optical Microscopes (white light/epifluorescence)
- Impedance spectroscopes
- Precision Impedance Analyzer
- Sub-femtoamp Remote SourceMeter Instrument

- Molecular/cell biology
  - Biological safety cabinet (class II)
  - Microwell plate readers
  - Protein and DNA electrophoresis systems
  - Nanodrop spectrophotometer
  - CO^2 incubator for cells: Galaxy® 48 S, 48 L, 230 V/50/60 Hz, Estándar
  - Cell culture cabin: Cabina De Seguridad Biológica, Modelo Bioii-Advance 3
- Microfluidics
  - High precision syringe pumps
  - Peristaltic pumps

Sensor for Hepatitis C Virus using azide-PEDOT electrodes.



concentrator enhancement based on dielectric poles for continuously flowing samples. *Electrophoresis*, 36 (13): 1405-1413

- Del Moral Zamora, B., Álvarez Azpeitia, J. M., Oliva Brañas, A. M., Colomer-Farrarons, J., Castellarnau, M., Miribel-Català, P., Homs-Corbera, A., Juárez, A. and Samitier, J. (2015). Continuous flow dielectrophoretic concentrator enhancement based on dielectric poles. *Electrophoresis*, 36 (13): 1405–1413
- Barniol-Xicota, M., Escandell, A., Valverde, E., Julián, E., Torrents, E. and Vázquez, S. (2015). Antibacterial activity of novel benzopolycyclic amines. *Bioorganic and Medicinal Chemistry*, 23 (2): 290-296
- Paéz Aviles, C., Juanola-Feliu, E., Tahirbegi, I. B., Mir, M., Gonzalez-Piñero, M. and Samitier, J. (2015). Innovation and technology transfer of medical devices fosterd by cross disciplinary communities of practitioners. *International Journal of Innovation Management*, 19 (6): 1540012

Book Sections

- de Oñate, L., Garreta, E., Tarantino, C., Martínez, E., Capilla, E., Navarro, I., Gutiérrez, J., Samitier, J., Campistol, J. M., Muñoz-Cánovas, P. and Montserrat, N. (2015). Research on skeletal muscle diseases using pluripotent stem cells. In: "Muscle Cell and Tissue" (ed. Sakuma, K.). InTech, Rijeka, Croatia. p333-357

Smart nano-bio-devices

Group leader/ICREA research professor: Samuel Sánchez

PhD students: Jaideep Katuri, Tammy Sue Wuen Leung, Ana Candida Lopes, Jemish Parmar

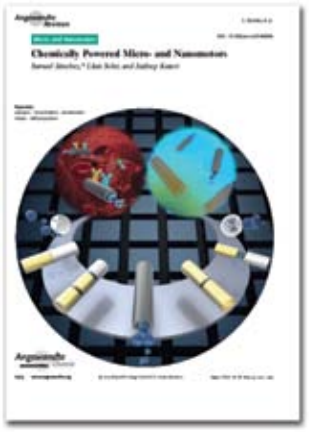
Laboratory technician: Ariadna Pérez

Our group has particular interest in the design of miniaturized devices that bridge functional materials and bio-related applications.

The main research topics are self-propelled micro-nanorobots, compact on-chip electrochemical (bio)sensors and biophysics of cells in confined spaces.

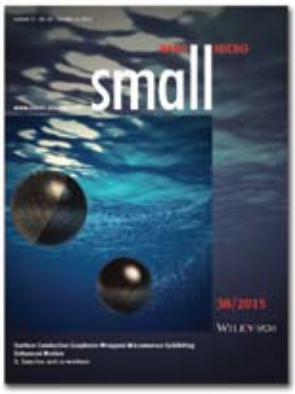
1. Self-propelled Micro-nanorobots

- Environmental applications of MicroRobots using tubular microjets. Self-propelled microrobots have the ability to remove pollutant on-the-fly from contaminated water autonomously or by actuating them with an external force. We engineer tubular microjets scalable from 5 µm up to 500 µm in length containing an inner catalytic material for generation of gas bubbles that provides propulsive thrust and mixes the solution where they swim. Active surface and functionalization of micro-nanorobots enables a versatile approach for removal and capture of a wide range of pollutants from water such as organics and heavy metals. (Collaboration with UAB, Spain and NTU Singapore)



- Spherical Janus micro- and nanomotors. We synthesize half coated silica Janus nano- and micromotors of sizes ranging from 40 nm up to 5 µm in diameter. Micro/nano motors capable of cargo loading and active motion under proper guidance promise a new generation of targeted drug delivery systems. The use of graphene as coating material provides an enhancement on the speed of micromotors. The use of enzymes for propulsion of mesoporous silica nanomotors opens future ventures for biocompatible targeted drug delivery vehicles. (Collaboration with MPI-IS and MPI-FKF Stuttgart, NTU Singapore, La Sapienza, Italy and POSTECH Korea)
- Bio-hybrid microswimmers. Either by electrodeposition or by using 3D printing methods, we developed bio-hybrid microswimmers for drug delivery. Swimmers incorporate motile cells such as E. Coli to power artificial materials for future controlled drug delivery.

2. Biophysics of cells in microfabricated 3D scaffolds

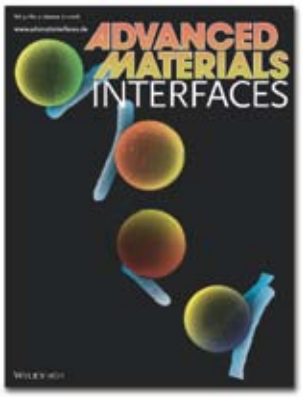


- The microfabrication of rolled-up microtubular structures on a substrate serve as 3D scaffolds for the detection and scrutinization of single cell inside the 3D space which would capture more of the complexity present in tissue scaffold. Cell division, migration and dynamics in confined spaces were studied (Collaboration with the Gurdon Institute, Cambridge; The Johns Hopkins University and IFW Dresden).

3. Compact Integrated (bio)sensors

- Part of the group activities are based on the shrinkage of “Lab-on-a-chip” to “Lab-in-a-tube” micro-analytical systems which can delicately control the positioning of single cells inside micro-tubular structures integrated on-chip. The detection of cancer HeLa cells by ultracompact impedimetric sensor was reported. These sensors could detect single cells in flow and imaged by optical microscopy at the same time. (Collaboration with IFW Dresden and The Johns Hopkins University)

Research projects



- **LT-NRBS** Lab-in-a-tube and Nanorobotic biosensors (2013-2017)
PI: **Samuel Sánchez**
European Research Council (ERC-StG)

- Motion of chemically active objects in confined spaces (2013-2015)
PI: **Samuel Sánchez** and Mikola Tasinkevych
German Research Foundation (DFG) (at MPI-IS)

- Mesoporous Silica Micro/Nano-motors as Active Drug Delivery Vehicles (2014-2016)
PI: Ma Xing (hosted by **Samuel Sánchez** at MPI-IS)
Alexander von Humboldt Foundation

- LOC-Systems based on Nano/Micromachines for Food Safety Applications (2014-2016)
PI: Diana Vilela (hosted by **Samuel Sánchez** at MPI-IS)
Alexander von Humboldt Foundation

Collaborations with other research centres

Prof. D.P. Kim National Center of Applied Microfluidic Chemistry, Department of Chemical Engineering, POSTECH (Pohang University of Science and Technology), Korea

Prof. D.S. Kim Department of Mechanical Engineering, POSTECH, Pohang, Korea

Prof. M. Rümmeli Sungkyunkwan (SKKU) University, Seoul, Korea / IFW Dresden, Germany

Prof. P. Fischer Molecular, Micro- and Nano- machines, Max-Planck Institute for Intelligent Systems, Stuttgart, Germany

Prof. S. Dietrich, Dr. M. Popescu, M. Tasinkevych, Dr. W. Uspal Theory of Soft Condensed Matter, MPI for Intelligent Systems, Stuttgart, Germany

Prof. M. Sitti Physical Intelligence department, MPI for Intelligent Systems

Prof. C. Bechinger Faculty 2 of Physics, University of Stuttgart, Germany

Prof. C. Holm and Dr. J. de Graaf Faculty of Mathematics, University of Stuttgart, Germany

Dr. L. Ionov Leibniz Institute for Polymer Research, Dresden, Germany (now at Georgia University, USA)

Prof. O.G. Schmidt, Dr. A-K. Meyer, Mrs.V. Magdanz Institute for Integrative Nanosciences, Leibnitz Institute for Solid State and Materials Research, Dresden, Germany

Dr. A-K. Meyer Division of Neurodegenerative Diseases and Center for Regenerative Therapies Dresden (CRTD) Technische Universität Dresden, Germany

Prof. A. Richter Institut für Halbleiter- und Mikrosystemtechnik, Technische Universität Dresden, Dresden, Germany

Dr. B. Friedrich Max Planck Institute for the Physics of Complex Systems, Dresden, Germany

Publications

- Ma, X., Jannasch, A., Albrecht, U. R., Hahn, K., Miguel-López, A., Schäffer, E. and Sánchez, S. (2015). Enzyme-powered hollow mesoporous Janus nanomotors. *Nano Letters*, 15 (10): 7043-7050
- Ma, X., Hahn, K. and Sánchez, S. (2015). Catalytic mesoporous janus nanomotors for active cargo delivery. *Journal of the American Chemical Society*, 137 (15): 4976-4979
- Sánchez, S., Soler, L. and Katuri, J. (2015). Chemically powered micro- and nanomotors. *Angewandte Chemie - International Edition*, 54 (4): 1414-1444
- Ma, X., Katuri, J., Zeng, Y., Zhao, Y. and Sánchez, S. (2015). Surface conductive graphene-wrapped micromotors exhibiting enhanced motion. *Small*, 11 (38): 5023–5027
- Choudhury, U., Soler, L., Gibbs, J., Sánchez, S. and Fischer, P. (2015). Surface roughness-induced speed increase for active Janus micromotors. *Chemical Communications*, 51 8660-8663 (2015).
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- Stanton, M. M., Trichet-Paredes, C. and Sánchez, S. (2015). Applications of three-dimensional (3D) printing for microswimmers and bio-hybrid robotics. *Lab on a Chip*, 15 (7): 1634-1637
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- Paxton, W., Sánchez, S. and Nitta, T. (2015). Guest editorial: Special issue micro- and nanomachines. *IEEE Transactions on Nanobioscience*, 14 (3): 258-259
- Khalil, I. S. M., Magdanz, V., Sánchez, S., Schmidt, O. G. and Misra, S. (2015). Precise localization and control of catalytic janus micromotors using weak magnetic fields. *International Journal of Advanced Robotic Systems*, 12 (2): 1-7

Scientific equipment and techniques

- Autolab Galvostat/potentiostat (Metrohm)
- Dynamic light scattering (Wyatt)
- Langmuir Blodgett (KSV NIMA)
- Inverted Fluorescent microscope with cell incubator, galvo stage for 3D tracking (Leica DMi8); Upright microscope (Leica)
- Video camera (1000+ fps) (Hamamatsu)
- High speed camera (10000+ fps) (Vision Research)
- CCD video camera (100fps) (Thorlabs)
- Centrifuge (Eppendorf)
- UV- Visible spectrometer (Analytik Jena)
- 3D printer (Formlabs)
- Wave form source; Voltage amplifier (Tabor Electronics)
- DC power supply (Hameg)
- Oscilloscope (Rigol)
- Testtube heater; Eppendorf tube Shaker (Hach)
- Oxygen Plasma cleaner (Deiner Electronics)
- TOC Analyser (Analytik Jena)

Bacterial infections: antimicrobial therapies

Junior group leader: Eduard Torrents

PhD students: Aida Baelo, Anna Crespo, Lucas Pedraz

Masters student: Michael Brennan, Ana Jareño, Alba Pérez

Research technician: Pep Astola

Infectious diseases constitute a tenacious and major public health problem all over the world. The emergence and increasing prevalence of bacterial strains that are resistant to available antibiotics demand the discovery of new therapeutic approaches.

In addition, there is an urgent need for reliable and rapid detection of infecting bacteria and its pattern of resistance to antibiotics.

Bacterial DNA synthesis open new horizons in the discovery of new antibacterial targets due to remarkably differences to the eukaryotic system. The enzyme ribonucleotide reductase (RNR) catalyzes the reduction of ribonucleotides to the corresponding deoxyribonucleotides (dNTP) and thereby provides the building blocks for DNA synthesis and repair. The balance of the different dNTPs has to be carefully regulated and the RNR enzymes as well as its expression play important roles. In the bacterial world it is not known which transcriptional regulators are required to control the expression of the different RNR genes, their role in virulence and during bacterial biofilm formation.

Our lab aims to investigate new antimicrobial therapies to combat bacterial infections with different objectives:

- First, to establish the molecular basis for the regulation of RNR genes, their importance in virulence and biofilm formation;
- Second, the identification and screening of new molecules for the highly selective inhibition of bacterial RNR;
- Third, by using nanomedicine techniques the development of novel and specific nanoparticles to deliver existing antibiotics or new identify antimicrobial drugs, especially when the bacteria are growing in biofilm, close to the physiological conditions of the disease and where the current chemotherapy fails;
- Finally, we will use lab-on-a-chip technology to deeply elucidate mechanisms to combat bacterial forming biofilm as well as new approaches to identify multiresistant bacteria to different antibiotics.

We believe these projects will be beneficial to society since we explore the use of different bioengineering approaches to elucidate ways to diagnose and eradicate multi-drug resistant bacteria.

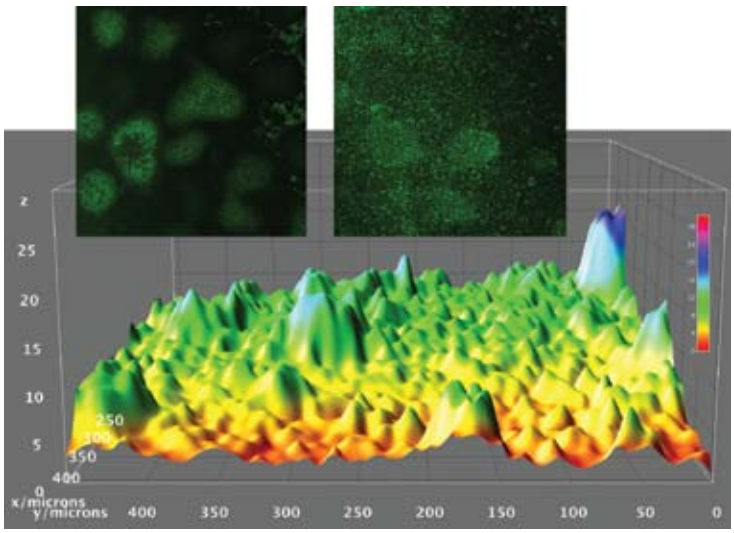

Figure 1: Surface plot analysis of *Pseudomonas aeruginosa* wild-type PAO1 days. Biofilms were grown in a continuous flow cell system and visualized under confocal microscopy.

Publications

- Baelo, A., Levato, R., Julián, E., Crespo, A., Astola, J., Gavaldà, J., Engel, E., Mateos-Timoneda, M. A. and Torrents, E. (2015). Disassembling bacterial extracellular matrix with DNase-coated nanoparticles to enhance antibiotic delivery in biofilm infections. *Journal of Controlled Release*, 209 150-158
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- Dreux, N., Cendra, M. d. M., Massier, S., Darfeuille-Michaud, A., Barnich, N. and Torrents, E. (2015). Ribonucleotide reductase NrdR as a novel regulator for motility and chemotaxis during adherent-invasive *Escherichia coli* infection. *Infection and Immunity*, 83 (4): 1305-1317
- Julián, E., Baelo, A., Gavaldà, J. and Torrents, E. (2015). Methylhydroxylamine as an efficacious antibacterial agent that targets the ribonucleotide reductase enzyme. *PLoS ONE*, 10 (3): e0122049
- Crespo, A., Pedraz, L. and Torrents, E. (2015). Function of the *Pseudomonas aeruginosa* NrdR transcription factor: Global transcriptomic analysis and its role on ribonucleotide reductase gene expression. *PLoS ONE*, 10 (4): e0123571
- Jaramillo, M. d. C., Huttener, M., Alvarez, J. M., Homs-Corbera, A., Samitier, J., Torrents, E. and Juárez, A. (2015). Dielectrophoresis chips improve PCR detection of the food-spoiling yeast *Zygosaccharomyces rouxii* in apple juice. *Electrophoresis*, 36 (13): 1471-1478

Structural superposition of NrdA (class I) and NrdD (class III) subunits of ribonucleotide reductase.

Research projects

- **RNRpathotarget** Redes reguladoras de la expresión génica de las distintas ribonucleotidil reductasas en bacterias (2012-2015)
PI: **Eduard Torrents**
MINECO

- Inhibición de la síntesis del ADN bacteriano como diana contra organismos patogenos en enfermos de fibrosis quistica (2012-2015)
PI: **Eduard Torrents**
Federacion Española de Fibrosis Quística "PABLO MOTOS"

Collaborations with other research centres

Prof. Fernando Albericio Institut de Recerca Biomèdica (IRB), Barcelona, Spain

Dr. Elisabeth Engel IBEC (page 58)

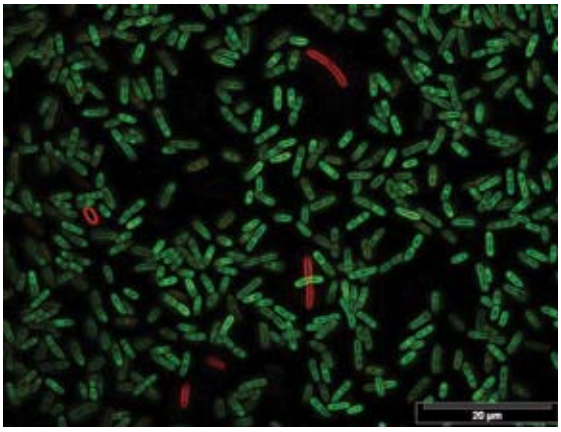
Dr. Esther Julián Dept. de Genètica i de Microbiologia, Universitat Autònoma de Barcelona, Spain

Prof. Britt-Marie Sjöberg Dept. Molecular Biology and Functional Genomics, Stockholm University, Sweden

Dr. Nicolas Barnich Pathogénie Bactérienne Intestinale, Université Clermont 1, Clermont-Ferrand, France

Dr. Joan Gavaldà Infectious diseases, Vall d'Hebrón Hospital and Research Institute, Barcelona, Spain

Prof. Víctor Puntes Inorganic nanoparticles group, Institut Català de Nanociència i Nanotecnología, Barcelona, Spain

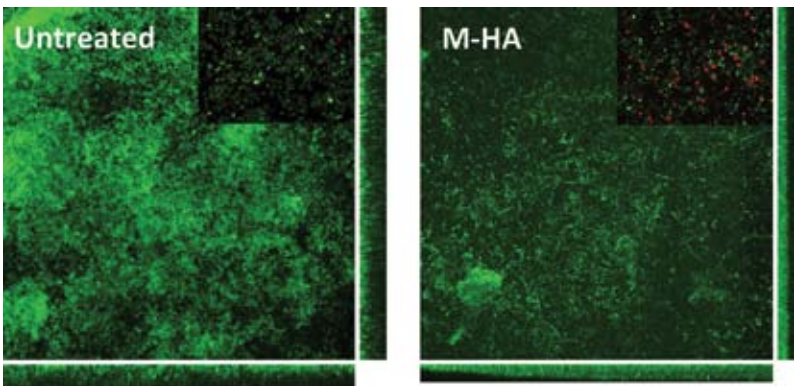


Pseudomonas aeruginosa treated with novobiocin.

Scientific equipment and techniques

- Continuous flow system model for bacterial biofilm development
- Single Channel Fiber-Optic Oxygen Meter with microsensor
- Gradient thermocycler (PCR)
- Molecular biology facilities
- Protein and DNA electrophoresis
- Bacterial expression systems for heterologous protein production
- Protein purification systems (FPLC; Biologic DuoFlow System From Bio-Rad)
- Technology of microbial culture facilities.
- Pressure microinjection system
- *Drosophila melanogaster* as a model host for bacterial infections

Figure 3: Disassembling the existing *P. aeruginosa* biofilm by adding methylhydroxylamine (M-HA).



- Barniol-Xicota, M., Escandell, A., Valverde, E., Julián, E., Torrents, E. and Vázquez, S. (2015). Antibacterial activity of novel benzopolycyclic amines. *Bioorganic and Medicinal Chemistry*, 23 (2): 290-296

Conference Papers

- Basas, J., Rojo, E., Gomis, X., Sierra, J. M., Torrents, E., Almirante, B. and Gavaldà, J. (2015). Actividad de anidulafungia vs. anfotericina b liposomal frente a C. *Parapsilopsis* creciendo en biopelículas en distintos materiales. *XIX Congreso de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC), Sevilla, Spain.* Published by Elsevier
- Torrents, E. (2015). Tratamientos antimicrobianos dirigidos. ¿Es posible la nanomedicina en las enfermedades infecciosas? *XIX Congreso de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC), Sevilla, Spain.* Published by Elsevier

Integrative cell and tissue dynamics

Group leader/ICREA research professor: Xavier Trepat

Postdoctoral researchers: Juan Francisco Abenza, Vito Conte, Anna Labernadie, Andrea Malandrino, Raimon Sunyer, Léo Valon, Romaric Vincent, Dobryna Zalvidea

PhD students: Agustí Brugués, Laura Casares, Simón García, Ernest Latorre, Carlos Pérez, Pilar Rodríguez, Marina Uroz

Masters student: Carlos Ureña

Undergraduate student: Guillem Güell

Laboratory technician: Natalia Castro

The ability of eukaryotic cells to migrate within living organisms underlies a wide range of phenomena in health and disease.

When properly regulated, cell migration enables morphogenesis, host defense and tissue healing. When regulation fails, however, cell migration mediates devastating pathologies such as cancer, vascular disease and chronic inflammation.

Our research focuses on understanding the fundamental biophysical mechanisms underlying migration both at the single cell level and at the tissue level.

Making cellular forces visible

To study cell and tissue dynamics we develop new technologies to measure physical forces at the cell-cell and cell-matrix interface. By combining these technologies with computational analysis of cell shape and velocity we obtain a full experimental characterization of epithelial dynamics during tissue growth, wound healing and cancer cell invasion.

Mechanical waves and collective cell guidance

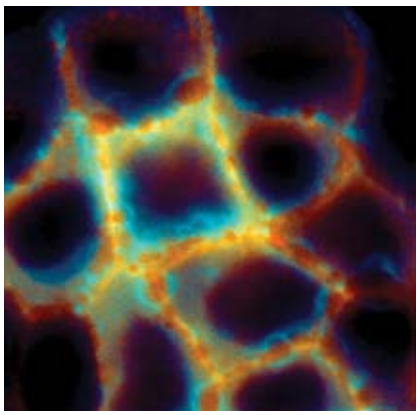
Our new tools led to the discovery of a mechanical wave – which we called “X-wave” – that propagates through expanding cell sheets. This mechanical wave is a natural candidate to trigger mechanotransduction pathways during wound healing, morphogenesis, and collective cell invasion in cancer. We also discovered a new mechanism, plithotaxis, by which cells align their shape and migration velocity to minimize intercellular shear stresses.

Microfabrication and wound healing

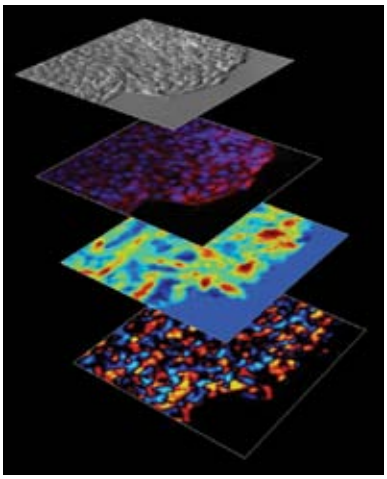
Using microfabrication technologies, we designed new ways to decipher the mechanisms of wound healing. By doing so we uncovered a new understanding of how cells move and work together to close a gap in a tissue. We showed that a new mechanism applies in which cells assemble supracellular contractile arcs that compress the tissue under the wound. By combining experiments and computational modeling, we showed that contractions arising from these arcs make the wound heal in a quicker and more robust way.

Fracking epithelial layers

Epithelial sheets must be malleable enough to adopt functional shapes during morphogenesis and to quickly self-repair after damage. Yet, they must be resilient enough to ensure organ compartmentalization and to protect organisms against environmental pathogens. To study the mechanisms that regulate this fine balance between malleability and integrity we develop tools to map epithelial tension during tissue stretching. By combining these tools with computational modeling we determined the mechanisms of epithelial fracture. Intriguingly, one of such mechanisms is hydraulic fracturing or “fracking”.



Fracking in epithelial layers: the small fractures between cells, in blue, close within minutes



Our lab has developed techniques to simultaneously map cell velocities, cytoskeletal structure, intercellular stresses, and cell-substrate tractions (from top to bottom).

Research projects

- **GENESFORCEMOTION** Physical Forces Driving Collective Cell Migration: From Genes to Mechanism (2009-2014)
PI: **Xavier Trepat**
European Research Council IDEAS Starting Grants

- **TENSIONCONTROL** Multiscale regulation of epithelial tension (2015-2019)
PI: **Xavier Trepat**
European Research Council - CoG

- **MICROGRADIENTPAGE** Micro Gradient Polyacrylamide Gels for High Throughput Electrophoresis Analysis (2014-2015)
PI: **Xavier Trepat**
European Research Council - PoC

- **CAMVAS** Coordination and migration of cells during 3D Vasculogenesis (2014-2017)
PI: **Xavier Trepat**
MARIE CURIE - IOF

- **ADHESIONFORCE** The mechanome of epithelial adhesion: unveiling the mechanisms of intercellular force detection, resistance, and transmission (2013-2015)
PI: **Xavier Trepat**
MINECO

- **CAFFORCE** Physical forces driving fibroblast-led cancer cell migration (2014-2015)
PI: **Xavier Trepat** (fellow: **Anna Labernadie**)
Marie Curie Intra-European Fellowships

- Mechanics of Monolayer Migration (2011-2016)
Co-Investigator: **Xavier Trepat** (PI: Jeffrey Fredberg, Harvard School of Public Health)
National Institutes of Health, USA

Publications

- Casares, L., Vincent, R., Zalvidea, D., Campillo, N., Navajas, D., Arroyo, M. and Trepat, X. (2015). Hydraulic fracture during epithelial stretching. *Nature Materials*, 14 (3): 343-351

- Bazellières, E., Conte, V., Elosegui-Artola, A., Serra-Picamal, X., Bintanel-Morcillo, M., Roca-Cusachs, P., Muñoz, J. J., Sales-Pardo, M., Guimerà, R. and Trepat, X. (2015). Control of cell-cell forces and collective cell dynamics by the intercellular adhesome. *Nature Cell Biology*, 17 (4): 409-420

- Vedula, S. R. K., Peyret, G., Cheddadi, I., Chen, T., Brugués, A., Hirata, H., Lopez-Menendez, H., Toyama, Y., Neves de Almeida, L., Trepat, X., Lim, C. T. and Ladoux, B. (2015). Mechanics of epithelial closure over non-adherent environments. *Nature Communications*, 6 6111

- Ravasio, A., Cheddadi, I., Chen, T., Pereira, T., Ong, H. T., Bertocchi, C., Brugues, A., Jacinto, A., Kabla, A. J., Toyama, Y., Trepat, X., Gov, N., Neves de Almeida, L. and Ladoux, B. (2015). Gap geometry dictates epithelial closure efficiency. *Nature Communications*, 6 7683

- Kosmalska, A. J., Casares, L., Elosegui-Artola, A., Thottacherry, J. J., Moreno-Vicente, R., González-Tarragó, V., Del Pozo, M. Ã., Mayor, S., Arroyo, M., Navajas, D., Trepat, X., Gauthier, N. C. and Roca-Cusachs, P. (2015). Physical principles of membrane remodelling during cell mechanoadaptation. *Nature Communications*, 6 7292 (2015).

- Vincent, R., Bazellières, E., Pérez-González, C., Uroz, M., Serra-Picamal, X. and Trepat, X. (2015). Active tensile modulus of an epithelial monolayer. *Physical Review Letters*, 115 (24): 248103 (2015).

- Lucantonio, A., Noselli, G., Trepat, X., DeSimone, A. and Arroyo, M. (2015). Hydraulic fracture and toughening of a brittle layer bonded to a hydrogel. *Physical Review Letters*, 115 (18): 188105

- García, S., Sunyer, R., Olivares, A., Noailly, J., Atencia, J. and Trepat, X. (2015). Generation of stable orthogonal gradients of chemical concentration and substrate stiffness in a microfluidic device. *Lab on a Chip*, 15 (12): 2606-2614
- Brask, J. B., Singla-Buxarrais, G., Uroz, M., Vincent, R. and Trepat, X. (2015). Compressed sensing traction force microscopy. *Acta Biomaterialia*, 26 286-294
- Reginensi, D., Carulla, P., Nocentini, S., Seira, O., Serra-Picamal, X., Torres-Espín, A., Matamoros-Angles, A., Gavín, R., Moreno-Flores, M. T., Wandosell, F., Samitier, J., Trepat, X., Navarro, X. and del Río, J. A. (2015). Increased migration of olfactory ensheathing cells secreting the Nogo receptor ectodomain over inhibitory substrates and lesioned spinal cord. *Cellular and Molecular Life Sciences*, 72 (14): 2719-2737
- Vizoso, M., Puig, M., Carmona, F. J., Maqueda, M., Velásquez, A., Gomez, A., Labernadie, A., Lugo, R., Gabasa, M., Rigat-Brugarolas, L. G., Trepat, X., Ramírez, J., Reguart, N., Moran, S., Vidal, E., Perera, A., Esteller, M. and Alcaraz, J. (2015). Aberrant DNA methylation in Non Small Cell Lung Cancer associated fibroblasts. *Carcinogenesis*, 32 (12): 1453-1463
- Mrkonjić, S., Garcia-Elias, A., Pardo-Pastor, C., Bazellières, E., Trepat, X., Vriens, J., Ghosh, D., Voets, T., Vicente, R. and Valverde, M. A. (2015). TRPV4 participates in the establishment of trailing adhesions and directional persistence of migrating cells. *Pflugers Archiv European Journal of Physiology*, 467 (10): 2107-2119
- Zaritsky, A., Welf, E. S., Tseng, Y.-Y., Angeles Rabadán, M., Serra-Picamal, X., Trepat, X. and Danuser, G. (2015). Seeds of locally aligned motion and stress coordinate a collective cell migration. *Biophysical Journal*, 109 (12): 2492-2500

- Grup de recerca consolidat (2014-2016)
PI: **Xavier Trepat**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya

Collaborations with other research centres

Julien Colombelli / Eduard Batlle Institute for Research in Biomedicine (IRB) Barcelona

Roger Guimerà Univeristat Rovira i Virgili, Tarragona, Spain

Roberto Mayor University College London, UK

Erik Sahai Cancer Research, UK

Benoit Ladoux Université Paris 7, France

Jim Butler & Jeff Fredberg Harvard University, Boston

Scientific equipment and techniques

- Soft Lithography
- Micro/Nano fabrication
- Cell stretching
- Live Confocal Microcopy
- Magnetic Tweezers
- Magnetic Twisting Cytometry
- Monolayer stress microscopy
- Traction microscopy

- Perrault, C., Brugues, A., Bazellieres, E., Ricco, P., Lacroix, D. and Trepat, X. (2015). Traction forces of endothelial cells under slow shear flow. *Biophysical Journal*, 109 (8): 1533-1536

Book Sections

- Serra-Picamal, X., Conte, V., Sunyer, R., Muñoz, J. J. and Trepat, X. (2015). Mapping forces and kinematics during collective cell migration. In: "Methods in Cell Biology - Biophysical Methods in Cell Biology" (ed. Wilson, L. and Tran, P.), Academic Press, Santa Barbara, USA. 125: 309-330


P&G

Core Facilities

Core Facilities

Nanotechnology Platform Coordinator
Mateu Pla-Roca

Nanotechnology Platform Technicians
Judit Linacero,
Marina Cazorla

Head of Core Facilities
Isabel Oliveira

Laboratory Assistant
Alicia Nadal

CORE FACILITIES

IBEC provides its researchers with extensive research facilities and a scientific–technical infrastructure distributed over interdisciplinary open lab spaces. It is designed and managed to facilitate research and promote the cooperation and exchange of knowledge between IBEC scientists.

In this way, researchers share not only the space itself but also the equipment, bench space, and qualified technical staff, thereby helping to reduce research costs.

Apart from routine laboratory equipment, the Core Facilities provide additional sophisticated, state-of-the-art equipment to support the groups' research. They are organized into two different categories: in-house equipment (only for internal users) and the Nanotechnology Platform (open to external users).

In-house equipment

- Chromatography System Biologic LP – Bio-Rad
- Spectrophotometer – Nanodrop
- Multimode microplate reader Infinite M200 Pro – Tecan
- Spectrophotometer UV-Visible – Shimadzu
- Microplate Reader Benchmark Plus – Bio-Rad
- StepOnePlus Real Time PCR System – Applied Biosystems
- DNA Engine Thermal Cycler – Bio-Rad
- T100 Thermal Cycler – Bio-Rad
- GeneAmp PCR System 9700
- ImageQuant LAS 4000 mini – GE Healthcare
- GelDoc XR+ System – Bio-Rad

Not pictured:

Cristina Rivero, Laboratory Technician, until June 2015

Oriol Rius, Vocational student, January-June 2015

Tania Bordoy, Undergraduate student, until March 2015

Laboratory Technician
Laura Gómez

Laboratory Technician
Ramona Bravo

Laboratory Technician
Jenifer González

Laboratory Technician
Miriam Funes

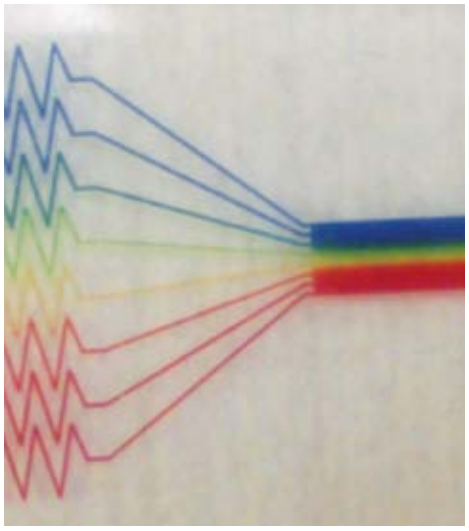
Nanotechnology Platform

The Nanotechnology Platform is part of the institute's long-term strategic plan to create new Core Facilities in nano-microfabrication for biomedical applications.

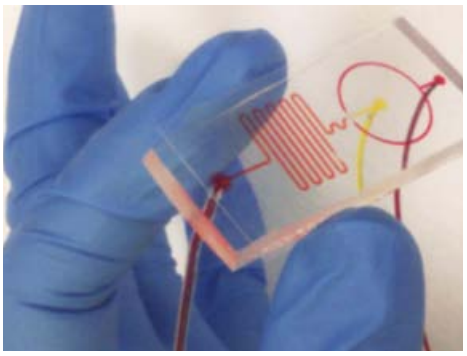
Currently, the platform is an accessible and versatile research facility featuring 100m^2 of class 10,000 cleanroom space offering state-of-the-art equipment for the fabrication and characterization of micro- and nanodevices and structures.

Our aim is to facilitate advanced research support by providing services in the fields of micro and nanofabrication for all academic and industrial researchers. Some of the areas of application include bioengineering, BioMEMS, materials science, tissue engineering, optic and biomaterials and microfluidics.

IBEC's Nanotechnology Platform offers scientific and technological support that includes the design, development and analysis of devices, materials, and processes, so that academic researchers and companies alike may use the platform to develop their innovative ideas.



Left: PDMS Microfluidic device for chemical gradient generation. Below: PDMS Microfluidic device for droplet generation



Platform publications

- Fernandéz-Remolar, D., Santamaria, J., Amis, R., Parro, V., Gómez-Ortiz, D., Izawa, M.R.M., Banerjee, N.R., Rodríguez, R.P., Rodriguez, N., Lopez-Martinez, N. (2015). Formation of iron-rich shelled structures by microbial communities. *Journal of Geophysical Research: Biogeosciences* 120(1), 147-168

Users' publications

- García, S., Sunyer, R., Olivares, A., Noailly, J., Atencia, J., and Trepat, X. (2015). Generation of stable orthogonal gradients of chemical concentration and substrate stiffness in a microfluidic device. *Lab. Chip* 15, 2606–2614
- Tong, Z., Segura-Feliu, M., Seira, O., Homs-Corbera, A., Río, J.A.D., and Samitier, J. (2015). A microfluidic neuronal platform for neuron axotomy and controlled regenerative studies. *RSC Adv.* 5, 73457–73466
- Galán, T., Pietro-Simón, B., Alvira, M., Eritja, R., Götz, G., Bäurle, P., Samitier, J. (2015). Label-free electrochemical DNA sensor using "click"-functionalized PEDOT electrodes. *Biosensors and Bioelectronics* 74, 751-756.

Users

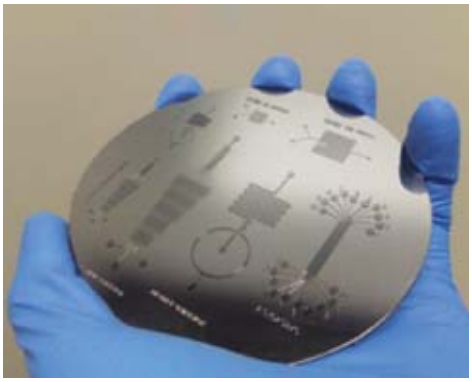
- Infinitec Activos S.L.
- ViaFactor BV
- Advanced Nanotechnologies, S.L.
- BSH Electrodomésticos España, S.A.
- Cosingo - Image Optic Spain, S.L.
- Technoform Bautec Iberica, S.L.
- BCN Peptides, S.A.

Services

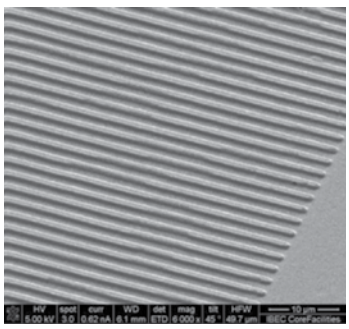
- Access to 10,000 class cleanroom.
- Training on and self-use of the following equipment: interferometer, profilometer, optical microscope, spin-coater, plasma cleaner and mask aligner (photolithography).
- Training on microfluidic chips design, fabrication and interfacing with pumping systems.

- Fabrication:
  - Design and fabrication of customized microfluidic chips using photolithography and replica molding (rapid prototyping in PDMS silicone).
  - E-beam lithography technique for the manufacture of micro- and nano-structures.
  - Replication of micro-nanostructures in thermoplastic polymers by nanoimprint lithography
  - Fabrication of Cr photomasks for photolithographic processes
  - RIE and wet-etching for silicon and glass micro- nanoestrcuturation
  - Thin layer deposition of materials (Au, Al, Ti, Cr, SiO2, Al2O3, etc.)
  - Microelectrodes
  - Fabrication of SU-8 molds for microcontact printing and micromolding in capillaries
  - Medium density microarrays (proteins and DNA)
- Characterization:
  - Sample characterization using ToF-SIMS:
    - Complete mass spectra of surfaces of organic and inorganic materials
    - Chemical mapping of elements and molecular distribution
    - Depth profile, implantation profiles and interface analysis.
  - SEM morphological and topographical characterization
  - Surface topographic analysis by using optical interferometry and mechanical profilometry.
  - Optical characterization of samples with bright and dark field.
  - Contact angle measurements of wettability properties of surfaces

Mold on a silicon wafer fabricated using photolithography containing seven microfluidic systems

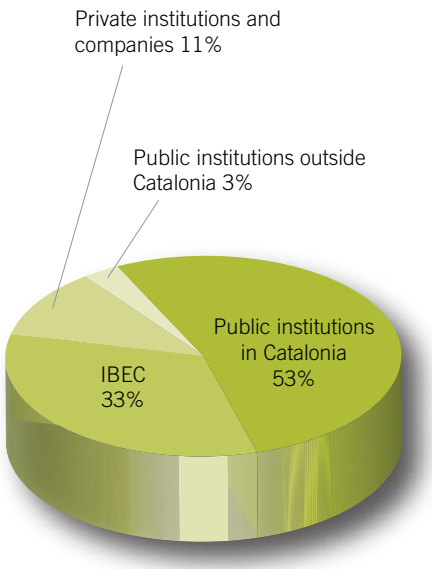


Polylactic acid (PLA) with 1 micrometer wide and 500 nm tall microstructures fabricated using hot-embossing



Equipment

- Time-of-Flight Ion Mass Spectroscopy (ToF-SIMS)
- Ultra-High Resolution Field Emission Scanning Electron Microscopy (SEM)
- E-beam Lithography (EBL)
- Nanoimprint Lithography (NIL)
- UV-Photolithography Mask-aligner
- Direct Write Laser
- Thermal and E-beam metal evaporator
- Reactive Ion Etching (RIE)
- Interferometer
- Profilometer
- Chemical Bath
- 2 Spinners
- Plasma Cleaner
- Optical microscope
- UV lamp
- Contact angle
- Microarrayer



Nanotechnology platform users in 2015

Activities in 2015

During our three years of operation, 62 researchers from ten IBEC groups, 96 researchers from 25 other public institutions, and 18 from ten private companies have become users of the Nanotechnology Platform. In 2015 the average of users and services performed by the platform was 23 and 159 per month, respectively.

In 2015 the Nanotechnology Platform performed several activities, such as:

- Introductions on micro- and nanofabrication techniques to bachelor students in Biotechnology (University of Barcelona), masters in Nano-Microbioengineering (University of Barcelona) and students from Cambridge University invited by ETSEIB (Escola Tècnica Superior d'Enginyeria Industrial, UPC).
- Participated in the programme "Joves i Ciencia 2015", enabling a student to perform some successful developments on microfluidics device assembling.
- Organized an equipment demonstration on a new optical perfilometer system from Zeta Instruments.
- Presented "Nanotechnology Platform Capabilities", an overview of our services, to Health tech cluster meeting (http://healthtechcluster.com/); Reig Jofre representatives (www.reigjofre.com/en/); University Joseph Fournier representatives (www.ujf-grenoble.fr/).

The Nanotechnology Platform is listed on BioCores@BCN, an online tool launched by the CRG which is part of the pan-European initiative Core for Life, which aims to help scientists and other customers find the local scientific service, technique or equipment they need for their biomedical or life sciences research.

The platform is also an active member of the ICTS (Infraestructuras Científicas y Técnicas Singulares) map as part of NANOBIOSIS (Infraestructuras Integradas de Producción y Caracterización de Nanomateriales, Biomateriales y Sistemas en Biomedicina), an integrated platform for research-oriented medical applications.

For more information about the Nanotechnology Platform, or to register as a user, please visit http://www.ibecbarcelona.eu/services/ or follow us on LinkedIn.

- Fundació CTM Centre Tecnològic
- Institut Químic de Sarrià
- Universidad Politécnica de Madrid
- Universidad de Zaragoza
- Universidad de Valladolid
- Universidad Miguel Hernandez
- University of Barcelona (UB)
- Technical University of Catalonia (UPC)
- Centre de Recerca en Enginyeria Biomèdica (CREB)
- Fundació Institut de Recerca en Energia de Catalunya (IREC)
- Instituto de Investigación Sanitaria - Fundación Jimenez Diaz
- Institut de Recerca Biomedica (IRB)
- Institut de Microelectronica de Barcelona (CNM)
- Centre de investigación en nanociencia i nanotecnologia (CIN-2)
- Institut Català de Nanociència i Nanotecnologia (ICN2)
- Institut de Ciència de Materials de Barcelona (ICMAB)
- Institut de Biologia Molecular de Barcelona (IBMB-CSIC)
- Universitat Autónoma de Barcelona (UAB)
- Institute of Environmental Assessment and Water Research (IDAEA-CSIC)
- Institut de Quimica Avançada de Catalunya (IQAC-CSIC)
- Fundació IGTP - Ciencies de la Salut Germans Trias i Pujol

New users (2015):

- Seat, S.A.
- GP-Pharm, S.A.
- Bio-model
- D+T Microelectrónica, A.I.E.
- Fundació Institut de Recerca en Energía de Catalunya (IREC)
- Institut de Ciéncies Fotòniques (ICFO)
- Fundació Centre de Regulació Genòmica (CRG)

Networking

Research partnerships

The model implemented in the creation of IBEC as result of research groups of the University of Barcelona and the Polytechnic University of Catalonia collaborating together and being affiliated to IBEC to conduct their research through our institute has been reinforced over the years with our policy on research partnerships, in which collaborative research is the core aim.

Besides the affiliated staff at the universities, IBEC has a remarkable number of group leaders – five out of seventeen – that are also ICREA research professors, as well as many research staff members affiliated with CIBER.

Affiliated groups

UNIVERSITAT DE BARCELONA

- Nanoscale Bioelectrical Characterization (page 68)
- Nanoprobes and Nanoswitches (page 72)
- Microbial Biotechnology and Host-Pathogen Interaction (until December 2015) (page 84)
- Signal and Information Processing for Sensing Systems (page 89)
- Cellular and Respiratory Biomechanics (page 102)
- Molecular and Cellular Neurobiotechnology (page 113)
- Nanobioengineering (page 117)

UNIVERSITAT POLITÈCNICA DE CATALUNYA

- Robotics (until September 2015) (page 52)
- Biomaterials for Regenerative Therapies (page 58)
- Biomedical Signal Processing and Interpretation (page 78)

ICREA

ICREA

The Catalan Institution for Research and Advanced Studies (ICREA) is supported by the Catalan Government to recruit top scientists for the Catalan R&D system to lead new research groups, strengthen existing ones and set up new lines of research.

The foundation works closely with Catalan universities and research centres through long-term agreements that allow ICREA researchers to participate in research groups in these centres.

In 2015, five of IBEC's group leaders were ICREA research professors:

- Ángel Raya, Control of Stem Cell Potency (until July 2015) (page 108)
- George Altankov, Molecular Dynamics at Cell-Biomaterial Interface (page 47)
- Xavier Trepat, Integrative Cell and Tissue Dynamics (page 132)
- Pau Gorostiza, Nanoprobes and Nanoswitches (page 72)
- Samuel Sánchez, Smart nano-bio-devices (page 122)

Associated researchers

Associated researchers are university professors seconded to IBEC with an agreement signed between their university and the institute who are based in the university premises and working on topics that are of interest or complementary to our research areas. They participate in IBEC's scientific strategy, academic activities and support initiatives, and have the option to submit project proposals and papers with IBEC affiliation.

Recruitment is carried out according to several criteria such as scientific excellence and alignment with IBEC's institutional strategy. Associated researchers are approved by the International Scientific Committee, which evaluates their performance on a regular basis.

Polytechnic University of Catalonia

- Prof. Alícia Casals (from October 2015)
- Prof. Maria Pau Ginebra (from October 2015)

Joint units and other partnerships

Barcelona Global Health Institute (ISGLOBAL)

IBEC and the Barcelona Global Health Institute (ISGLOBAL) signed an official agreement in 2010 to facilitate collaboration in certain areas of common interest. This led to the establishment of a joint unit where both institutions contribute with resources (researchers, spaces, etc) to develop diagnostic and therapeutic nanomedicine-based systems to be applied to malaria (Nanomalaria group, page 64).

Due to the fruitful collaboration, the agreement has been extended up to May 2017 with new objectives for the next two years.

IGTP

A joint research Unit between IBEC and the Hospital Universitari Germans Trias i Pujol (IGTP) is coordinated by Raimon Jané, head of IBEC's Biomedical Signal Processing and Interpretation group (page 78), and the hospital's Miquel Àngel Gasull.

Their results so far have included a collaborative project in respiratory sound analysis. The clinicians performed experiments with patients with asthma and other respiratory diseases, while advanced signal interpretation techniques developed by IBEC's group improved the capability of early diagnosis in these kinds of diseases. This study crystallized in the *PLOS One* paper "Detecting Unilateral Phrenic Paralysis by Acoustic Respiratory Analysis" in 2014. They also developed a new method to evaluate the signals produced by the respiratory muscles to detect and quantify the level of muscular weakness caused by pathologies such as COPD. The study was conducted in the hospital's Respiratory Function Laboratory.

CIBER

Spain's Centro de Investigación Biomédica en Red (CIBER), a legal entity financed by the Instituto de Salud Carlos III, creates large multidisciplinary and multi-institutional networks of research centres that will integrate basic and clinical research.

Several IBEC groups work in programmes within CIBER, such as CIBERBBN, which covers bioengineering, biomaterials and nanomedicine. Research is focused on disease prevention, diagnostics systems and technologies for specific therapies, such as regenerative medicine and nanotherapies. Dr. Xavier Trepat's group has been officially accepted by the CIBER Board as CIBERBBN new group in December 2015 and will start its activity in 2016.

Another programme within CIBER, CIBERES – Centro de investigación en red de enfermedades respiratorias – involves Cellular and Respiratory Biomechanics group leader Daniel Navajas (page 102) and addresses respiratory illnesses.

CIBERNED, which covers neurodegenerative diseases, maintains its own legal personality as it is managed by Fundación CIEN. It is composed of 63 research groups working on basic and clinical research.

Ongoing CIBERBBN projects during 2015

- **CHONDRONANONET** Nanopatterned Cell Carriers for Improved Architectural Communication Networks in Chondrogenesis towards Osteoarthritic Joint Repair
  PI: **Josep Samitier** (coordinator); **Pau Gorostiza**; **Anna Lagunas**

- **E-LEUKEMIA** The nanoconductance of redox proteins of the respiratory chain and its physiopathological implication in leukemia
  PI: **Pau Gorostiza** (coordinator); **Josep Samitier**; **Anna Lagunas**

- **TO-GLIOTHER** Towards Clinical Stem Cell Glioblastoma Therapy
  PI: **Elisabeth Engel**

- **NANO3B** Novel nanocarriers as delivery systems across the Blood-Brain barrier
PI: **Fausto Sanz**

- **NANOXEN++** *Xenopus tropicalis* as an optogenetic and optopharmacological platform
PI: **Pau Gorostiza** (coordinator)

- **BIOSURFACES** Biofunctionalization of titanium implant surfaces
PI: **George Altankov**

- **BIOWOUND** Bioactive materials for wound healing based on controlled ion release
PI: **Soledad Pérez** (scientific coordinator)

- **BIOROTATOR** Tendon Tissue Engineering for Rotator Cuff Tear**s**
PI: **Miguel Angel Mateos** (scientific coordinator)

- **INTER-CARDIO** Computer-assisted interpretation of electrical signals: a step forward in understanding and treating cardiac diseases
PI: **Raimon Jané**

- **OLIGOCODES** Universal Diagnostic Platforms Based On Oligonucleotide Codified Nanoparticles and DNA Microarray Sensor Devices.
PI: **Josep Samitier**

- **MUDIRES-2PSD** Multimodal Diagnosis by Signal Interpretation of the Respiratory System oriented to Pulmonary Diseases and Sleep Disorders
PI: **Raimon Jané** (coordinator); **Daniel Navajas**

- **ULTRASEN-4BIO-2MD** Characterization and evaluation of novel ultrasensitive piezoresistive all-organic sensors for biomedical signals applied to multimodal diagnosis
PI: **Raimon Jané** (coordinator)

- **NANOLYSO** Nanomedicine-based enzyme replacement therapy for the treatment of lysosomal storage disorders
PI: **Fausto Sanz**

- **BIOGELANGIO** Biomimetic extracellular matrices for angiogenic activation and anti-inflammatory activity in regenerative medicine.
PI: **Miguel Angel Mateos** (scientific coordinator)

- **Bioproterial** Biological activity of matrix proteins at the cell-material interface.
PI: **George Altankov**

- **ES-CELLTHERAPY** Use of human pluripotent stem cells as vehicles for localized delivery of therapy to brain tumors.
PI: **Ángel Raya**; **Elisabeth Engel**

- **NACRE** New Approaches for Cartilage Regeneration.
PI: **Ángel Raya**; **Miguel Angel Mateos**

- **NANOMEDIAG** Nanobioanalytical platforms for improved medical diagnosis of infections caused by pathogen microorganisms.
PI: **Josep Samitier**

- **SCAFFTIDE 3D** 3D scaffolds and implants functionalized and reinforced with recombinant protein polymers for regenerative medicine.
PI: **Miguel Angel Mateos**

Ongoing CIBERNED projects during 2015

- Generación de un modelo neuronal dopaminérgico a partir de células madre pluripotentes inducidas de pacientes con enfermedad de Parkinson asociada a mutaciones en el gen LRRK2.
PI: **Ángel Raya**

- Red española de investigación en enfermedades neurológicas PRY-114
PI: **Jose Antonio del Río**

Memoranda of understanding

IBEC pursues opportunities to collaborate on a long-term basis with other world-class national or international research institutes, organisation or other bodies with a collaborative agreement or Memorandum of Understanding (MoU). These formalise the participation of IBEC and the partner institute in cooperative scientific projects, promote the exchange of researchers, aid dissemination of information, the sharing of resources and the organization of joint events and activities.

By 2015, IBEC had MoUs in place with the following organisations:

International

- National Institute for Materials Science (NIMS), Tsukuba, Japan
- Institute of Tissue Regeneration Engineering (ITREN), Dankook University, Korea
- University of Warwick's Centre for Cognitive and Neural Systems, UK
- Interstaatliche Hochschule für Technick Buchs (NTB), Switzerland
- Università degli Studi di Brescia, Italy
- The European Synchroton Radiation Facility (ESFR), France
- Max Planck Institute for Intelligent Systems (MPI-IS), Germany

Local and national

- Fundació Clínic/Hospital Clínic, Barcelona
- Bellvitge Institute for Biomedical Research (IDIBELL), Barcelona
- Vall d'Hebron Research Institute (VHIR), Barcelona
- Fundació Joan Costa Roma (JCRF), Terrassa
- Centre de Medicina Regenerativa de Barcelona (CMRB), Barcelona
- Institut De Recerca I Tecnologia Agroalimentaries (IRTA), Barcelona
- The Barcelona Global Health Institute (ISGLOBAL), the Center for Research in Environmental Epidemiology (CREAL) and the Instituto de Diagnóstico Ambiental y Estudios del Agua (IDAEA-CSIC) to study DDT concentration detection in treated surfaces to tackle malaria
- CIBER (page 147); under a special agreement, IBEC's Nanotechnology Platform (see page 138) is considered an integrated service platform within the CIBERBBN programme, thus facilitating access to all researchers within the network
- The Open University of Catalonia (UOC)
- Escuela Superior de Ingenieros de Caminos, Canales y Puertos de la Universidad de Madrid
- Barcelona Macula Foundation
- University of Barcelona (UB), Barcelona through its Cell Therapy Programme (TCUB) and also the Doctoral Programmes
- Polytechnic University of Catalonia (UPC), Barcelona
- Banc de Sang i Teixits (BST), Barcelona
- Federación de Asociación de Retinosis Pigmentaria (FARPE)

- Fundación de Lucha contra la Ceguera (FUNDALUCE)

Outreach activities and other joint initiatives

- Fundació Catalunya-La Pedrera (for the “Joves i Ciència” and “Professors i Ciència” programmes).
- Barcelona Science Park (PCB) (hosting students under the “Passa l’estiu al parc” initiative and participating in the annual Fira Recerca en Directe).
- Fundació Catalana per la Recerca i la Innovació (FCRI) (for participation in the “Espai Ciència” of the annual Saló de l’ensenyament at Barcelona’s Fira and the city’s “Setmana de la Ciència” festival).
- The council of Sant Feliu de Guíxols (having worked together on a museum exhibit “Curar-se en salut”).
- The Barcelona city council (for ESCOLAB and the Festa de la Ciència).
- BIOcomuniCA’T (for Nit Europea de la Recerca Barcelona).

High school teachers get to grips with cow hearts at IBEC’s 2015 Professors i Ciència workshop

Institutional Initiatives

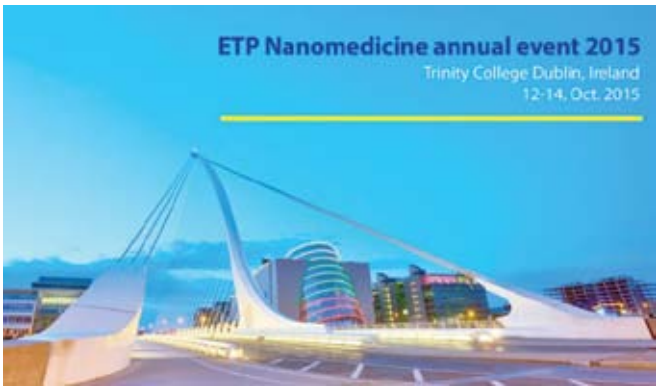
In its role as the country's leading research institute in bioengineering and nanomedicine, IBEC manages or is a partner of national and international initiatives with a range of goals including bringing together entities to network and share resources, providing advice and support, organising events, or acting as a representative, collective voice or expert consultant for stakeholders or funders.

Spanish Nanomedicine Platform (NanoMed Spain)

The Spanish Nanomedicine Platform (NanoMed Spain) is a forum managed by IBEC that brings together public research centres, hospitals, companies and government representatives to unite public and private interests in the development of common strategies. NanoMed Spain represents the interests of its stakeholders in the burgeoning and multidisciplinary area of nanomedicine, and is supported by the Spanish Ministry of Economy and Competitiveness (MINECO), through the Spanish Programme for R+D+I oriented to Societal Challenges.

The activity of NanoMed Spain in 2015 was focused on:

- The continued co-organization of the Annual Conference of the Biomedical Research Technology Platforms (Madrid, 24th-25th March 2014), together with the Spanish platforms for Innovative Medicines, Biotechnology, and Health Technology, with over 200 participants. In the opening ceremony, Josep Samitier, scientific coordinator of the platform, highlighted the leadership of Spain in the field of nanomedicine worldwide and presented the activities carried out by Nanomed Spain. The keynote speaker invited by Nanomed Spain, Lars Montelius, director of the Iberian Nanotechnology Laboratory (INL), spoke of the role of INL in European innovation in nanotechnology. The Spanish Nanomedicine Platform also organized a parallel session focused on the initiative of the European Institute of Technology (EIT), the EIT Health project (page 153), which has a strong Spanish participation.
- Nanomed Spain actively participated in the Forum TRANSFIERE 2015, held in Malaga on 11 and 12 February 2015. At the round table "One-Health", Arantxa Sanz, executive coordinator of Nanomed Spain in 2015, spoke about the challenges in the area of nanomedicine, such as manufacturing of nanodrugs and nanosafety.
- The Spanish Nanomedicine Platform has prepared a report on regional innovation strategies (RIS3) in Spain, with a focus on the regions that include among their priorities nanomedicine, investment in Key Enabling technologies and / or advanced health and medical technologies.
- The Spanish nanomedicine platform participated in the 2nd workshop "Supporting collaboration between KETs Technology Platforms and Promoting the Pan-European access of SMEs to KETs Technology Platforms" held in Brussels on 12th May 2015. The EC project aims at stimulating innovation in SMEs via the identification of technology platforms in the field of KET in Europe and promote cooperation between SMEs and those platforms. Currently, 29 Spanish technology platforms KET are involved.
- As an example of public-private collaboration between Technological Platforms of different fields, Nanomed Spain organized a forum together with Animal Health Platform to foster collaborations on nanomedicine applied to veterinary industry, such as diagnostic tools for framing or nanopharmaceutical formulations for pets. This event took place in Madrid on 15th September 2015.
- The Platform organized and/or participated in several initiatives to promote collaboration between the public and private sector.



This year's European Technological Platform on Nanomedicine (ETPN) annual event took place in Dublin

The European Technological Platform on Nanomedicine (ETPN)

A voting member of the European Technological Platform on Nanomedicine (ETPN) since 2008, IBEC has contributed as an invited expert body, through its director and the Knowledge Exchange Unit, The European Technology Platform on Nanomedicine organised its 2015 Annual Event & General Assembly in Dublin, Ireland. The event took place on 12th-14th October 2015, with local organization being carried out by Trinity College Dublin.

This year's annual event aimed at providing in-depth details on the practical implementation of the ETPN recommendations for a strong translational nanomedicine sector in Europe as well as unveiling future priorities for nanomedical research and innovation, as well as preparing the Nanomedicine Strategic research and Innovation Agenda 2016.

As nanomedicine is indeed entering a concrete implementation phase for the Translation Hub concept developed by the ETP Nanomedicine, notably through the latest calls in Horizon 2020, and is experiencing an increased interest from the research and industrial communities, from national authorities in Europe but also outside Europe, this event has been the opportunity to consolidate the ETPN efforts to shaping a functioning nanomedical sector in Europe for the benefit of patients. In this sense, this year took place the first TAB-in sessions as part of Enabling Nanomedicine Translation (ENATRANS) project aimed at boosting nanomedicine selected projects from the bench to the bedside by experts counselling guidance.

Strategic Alliances

Several organisations exist at a local or national level to consolidate research efforts in particular fields, coordinate and encourage greater visibility for the activities of research centres, or bring together similar entities with a common goal from different regions.

EIT Health

The participation of IBEC as a core partner in the Knowledge Innovation Community (KIC) on Health of the European Institute of Technology (EIT) represents already a recognition of the relevance of the institute in the international arena in health research and innovation, as well as a unique opportunity for its further internationalization. IBEC Director Josep Samitier is member of the Supervisory Board of EIT Health.

EIT Health has formed six co-location centres across Europe: London (UK/Ireland), Stockholm (SCAN), Barcelona (ES), Paris (FR), Heidelberg (GER) and Rotterdam (BENE). The 45 core partners are leading stakeholders throughout Europe from medicine and diagnostics, imaging and other medical technology, the ICT sector, pharmaceutical and consumer goods, insurance companies, biotechnology, health and social care. EIT Health will develop innovative products, education and services addressing the challenge of demographic change in Europe. By 2018, EIT Health is aiming to create 70 start-ups per year and to have 1m students participating in online educational programmes per year.

In the framework of EIT Health, with a total budget of €2.1 billion IBEC will be able to lead and participate in multidisciplinary projects to promote healthy living, to support active ageing and to improve healthcare.

At a Spanish level, IBEC coordinates a Network of Excellence funded by the Ministry of Economy and Competitiveness to reinforce the functioning and the strategic importance of the Spanish co-location centre via specific actions related to (a) active participation in international EIT Health activities, (b) organization of national EIT Health activities, (c) EIT Health project development, (d) dissemination activities of EIT Health objectives and results.

Fundació "La Caixa

Since 2011 IBEC has established an alliance with Fundació "La Caixa" which funded from 2011 to 2014 IBEC's Institutional valorization and technology transfer programme "Diagnosis and therapy systems based on the integration of novel nano-bio-info-cogno-technologies".

Since 2015, IBEC and La Caixa have developed a Joint programme in Healthy Ageing Research. Within this, in July 2015 IBEC launched an internal call for proposals for research projects. Projects are expected to contribute to the development of one of IBEC's focus programmes, Bioengineering for Healthy Ageing, have a translational approach, and be the seed for innovations to be further translated through EIT Health.

After an external selection process, four projects were selected to be developed in 2016-2017:

- Monitoring neurocognitive deficits in Alzheimer's and Parkinson's diseases using saliva or blood-derived biomarkers and multiplexed approach (PI: José Antonio del Rio, page 113)
- Novel m-Health tools for unobtrusive sensing and management improving of Obstructive Sleep Apnea patients at home (PI: Raimon Jane, page 78)
- Dermoglass: Advanced wound healing dressings (PI: Elisabeth Engel, page 58)
- Novel strategies to combat bacterial chronic infections by the development of microfluidics platforms to analyse and treat bacterial growing in biofilms (PI: Eduard Torrents, page 128)

HealthTech Cluster

Since 2014, IBEC has been a member of a new alliance aimed at promoting and contributing to the competitiveness of the health technology sector in Catalonia.

Following in the footsteps of other such initiatives as Biopol'H and Bionanomed Catalunya, the HealthTech Cluster brings together research organisations, companies, hospitals and other bodies to compete globally by promoting innovation and internationalization of partners and improving conditions within the sector.

The cluster is an initiative of ACCIÓ, the Generalitat's Agency of Competitiveness for Companies in Catalonia. This network will focus particularly on partners that are working on developing technologies for healthcare, rather than basic research. The other members include the Universitat Politècnica de Catalunya (UPC) on the research side, Barcelona's Hospital Clínic among the healthcare bodies, and companies such as Telstar and the Sibel Group.

There are around 15,000 people currently employed in the health technologies sector in Catalonia.

Bioinformatics Barcelona (BIB)

July 2015 saw the launch of Bioinformatics Barcelona (BIB), a network of 25 members including universities, research centres, hospitals, major scientific facilities, and pharmaceutical, technology and and bioinformatics companies, which aims to respond to the challenges posed by the growth of big data and position Barcelona as a world leader in bioinformatics.

IBEC participated in the development of the platform, which is supported by the Government of Catalonia and the Obra Social "la Caixa", and which aims to involve all Barcelona organizations working in the field of health and food. BIB will act as a catalyst for initiatives in advanced research and knowledge and technology transfer between research groups, hospitals and the business sector, as well as the development of training programmes in bioinformatics.

HUBc

IBEC is a member of the Health UB Campus (HUBc) project, led by the University of Barcelona, is a recognised Campus of International Excellence that brings together about 30 training institutions, research and knowledge transfer in health sciences, mainly around the campus of the Medical and Hospital San Juan de Dios, the campus Health Sciences with the University Hospital of Bellvitge, ICO, IDIBELL, and Barcelona Innovation Zone.

IBEC Director Josep Samitier held the position of director of HUBc until 2013.

European Innovation Partnership on Active and Healthy Ageing (EIP on AHA)

In 2013, under the umbrella of the HUBc, several research activities at IBEC were accepted as 'commitments' by the European Commission's European Innovation Partnership on Active and Healthy Ageing (EIP on AHA). This policy-influencing initiative alongside H2020 brings together public and private stakeholders to develop new innovations which can improve the quality of life of older people while creating market opportunities for business. Stakeholders work together along six Action Groups on Adherence to medical plan, Falls prevention, Prevention of functional decline and frailty, Integrated care, ICT solutions for independent living and Age-friendly environments.

In December 2015, at the annual Conference of Partners, the six Action Groups produced State-of-play publications highlighting the achievements of their groups both at individual and collective level, key messages to be taken home and lessons for the future. The publications present both the Action Groups in their ways of working as well as the tangible results in this first phase of implementation of the EIP on AHA.

BIOCAT

BIOCAT coordinates, develops and promotes the biotechnology, biomedicine and medical technology sectors in Catalonia, to make the region an international reference in terms of high quality research, competitive networks

and an increasingly dynamic knowledge transfer system. IBEC has worked closely with BIOCAT on such projects as BioNanoMed Catalunya, an alliance of research centres, hospitals and companies launched in 2011 to share know-how and resources and facilitate new developments in nanomedicine.

One of BIOCAT strategic initiatives is B·Debate, which aims to drive top-notch international scientific events to foster debate, collaboration and open exchange of knowledge among experts of renowned national and international prestige in order to tackle complex challenges of high interest in the life sciences. The debates foster the integration of various disciplines of science.

In October 2015, in the framework of B·Debate, IBEC organized the workshop "Future Tools for Biomedical Research. *In vitro, in silico* and *in vivo* Disease Modeling" The workshop gathered international experts from these diverse fields to look at new tools and approaches for basic research and preclinical trials of new drugs, finding new solutions to replace the traditional way of evaluating drug safety – such as the use of animals – and look at how nanotechnology and bioinformatics are enabling the custom design of tailored treatments for individual patients and disease profiles.

Other strategic alliances

During 2015 IBEC continued to be a member or partner of the following organisations or initiatives:

- Associació Catalana d'Entitats de Recerca (ACER). Established in 2003 by the Catalan government's department of Universities, Investigation and Information Society, ACER is an independent association of more than 40 institutions in Catalonia which conduct research as their principal mission. The association's goal is to help establish the region as an international benchmark in scientific and technological research by representing its associated centres, encouraging collaboration and the coordinated exchange of information, promoting synergies with similar agencies related to local, national or international research, and contributing to the improvement of scientific understanding in society. In February 2015 IBEC Director Josep Samitier was named new president of ACER, taking the reins from IFCO director Lluís Torner, who had held the position since 2009.
- CERCA Institute (the Government of Catalonia's means of supervising, supporting and facilitating the activities of Catalan research centres).

The IBEC and BIOCAT-organized B·Debate on Future Tools for Biomedical Research. *In vitro, in silico* and *in vivo* Disease Modeling" took place in October

Technology Transfer

Breakthrough innovation can only happen if research discoveries leave the lab and reach the market and users. Translating discoveries into market-ready products requires effective liaison with industry, as well as knowledge of intellectual property protection and exploitation.

The technologies that meet our criteria for commercialization are developed into products and therapies through collaborations and alliances with other research organizations, companies and clinicians, and by the creation of new start-ups. IBEC researchers are supported by the Technology Transfer Unit along the tech transfer and translation processes.

Entrepreneurs join forces to improve surgeon skills and patient safety

In December 2015, a new spin-off was launched with the aim of developing science and technologies in the medical robotics field to improve surgeons' skills and patient safety. SurgiTrainer SL is a company founded by dedicated entrepreneurs in Alicia Casals's Robotics group (page 52) and a clinical counterpart from the research institute of Hospital de la Santa Creu i Sant Pau (IR-HSCSP), dedicated to the development and production of training systems for endoscopic and laparoscopic surgery.

At the moment the company, a spin-off of IBEC, the Polytechnic University of Catalonia (UPC) and IR-HSCSP, is finalizing an industrial prototype in collaboration with the European Society for Gynaecological Endoscopy (ESGE), with sales due to start very soon.

Clinical-oriented projects selected to focus on translation

The IBEC-La Caixa Joint Programme on Healthy Ageing Research granted four projects based on EIT Health (page 153) objectives. The criteria used to select the projects included translational activities, product-orientation, unmet need identification, scientific excellence and external partners, among others. The four projects are:

- Monitoring neurocognitive deficits in Alzheimer's and Parkinson's diseases using saliva or blood-derived biomarkers and multiplexed approach (PI: José

Xavier Puñet (second from left) and Eduard Torrents (third from right) at the presentation of the first edition of the CaixaImpulse programme

Pau Gorostiza and Head of Technoology Transfer Xavier Rubies at the EBAN meeting in Copenhagen

Antonio del Rio, page 113)

- Novel m-Health tools for unobtrusive sensing and management improving of Obstructive Sleep Apnea patients at home (PI: Raimon Jane, page 78)
- Advanced wound healing dressings (PI: Elisabeth Engel, page 58)
- Novel strategies to combat bacterial chronic infections by the development of microfluidics platforms to analyse and treat bacterial growing in biofilms (PI: Eduard Torrents, page 128)

Each project has been awarded the total amount of the budget requested.

Optimizing RNRbiotics with the CaixaImpulse programme

Bacterial or fungal biofilm-based infections have emerged as a major public health concern, which is critical in chronic infections. Annually, they account for the death of 25000 Europeans with a cost of more than € 1.5 billion/year to the European health service. The development of new antibacterial agents is one of the key goals of public health. In order to address this issue, the group of Bacterial Infections: Antimicrobial Therapies (page 128) is developing new strategies with RNRbiotics, a proprietary chemical library of compounds showing antibacterial activity in inhibiting key pathogenic species. These molecules are protected on PCT/EP2015051755, with the co-ownership of IRB.

Boosted by CaixaImpulse, a funding programme promoted by the Obra Social "la Caixa" and organized jointly with Caixa Capital Risc that aims to promote technology transfer in science, they will be able to optimize the leader molecule and test further efficacy and toxicology both *in vitro* and *in vivo*.

Dermoglass goes pre-clinic thanks to La Caixa

A novel and biodegradable nanotechnology-based wound dressing able to stimulate the re-vascularization of the affected area in chronic wounds, Dermoglass, was selected in the first edition of the CaixaImpulse programme (see above).

Xavier Puñet, a PhD student in the Biomaterials for Regenerative Therapies group (page 58), elaborated a specific valorisation plan together with the Technology Transfer Unit in order to establish the appropriate animal model for chronic wounds in pigs, and will include interviews with medical experts, regulatory issues, scalability analysis and market studies. The final goal is to establish a licence agreement with a leading company from the wound care market.

IBEC ERC grantee meets business angels

IBEC group leader and ICREA research professor Pau Gorostiza was one of nine ERC

Proof of Concept holders to take part in the European Business Angel Network (EBAN) Winter University in Copenhagen.

Pau pitched his project, THERALIGHT: Therapeutic Applications of Light-Regulated Drugs, to the investors from all over the world at the event, which he attended alongside eight other awardees specially selected by the ERC. Together they made up nearly half of the 20 European start-ups hoping to catch the eye of an investor interested in exploring the innovation potential of their findings.

The EBAN Winter University is the global summit on venture finance and innovation in science, space, technology and the creative industries, and provides an opportunity for researchers to interact with industry and attract investments into their start-ups and innovative frontier research.

Intercontinental collaboration to characterize apnoea disorders

A new alliance between IBEC and the North American company Audiodontics has been established in the framework of the Small Business Innovation Research (SBIR) Program in the United States, led by the National Institutes of Health (NIH). It is one of the largest sources of early-stage capital for innovative small companies.

This project consists of developing a mouth-worn tooth microphone that can be used to record night-time breathing sounds. Coupling a specific hardware with speech recognition software, similar to the core speech recognition technology on mobile phones, breath sounds will be analysed. This system will be capable of monitoring oral appliances used in the treatment of sleep apnoea.

GENOMICA-IBEC Joint Unit shows promising results

The Joint Research Unit that joins efforts at IBEC and Genomica S.A.U. (Grupo Zeltia, the leading Spanish company in molecular diagnostics), is advancing fruitfully in various R&D activities related to healthcare.

A mixed team of ten people have participated on several training events, meetings and international workshops, including a short-stay of three months of an IBEC PhD student at Genomica's laboratories. To date, this collaboration has given rise to a PhD thesis, which was obtained taking into account confidentiality issues. The unit, located at IBEC, sees researchers and industry technicians sharing a host of know-how and in-house capabilities to develop and bring to market point-of-care diagnostic products and other medical devices and technologies.

IBEC's researchers in the unit supply the scientific knowledge with their expertise in

IBEC is one of the first members of the HealthTech Cluster

biosensors, micro- and nanofabrication, signal processing and bioengineering, while the members from Genomica's side offer market intelligence, clinical evaluation and regulations, and diagnostics know-how.

It is the first time that IBEC's researchers are physically working together alongside industry personnel, though the institute already has several existing collaborations and research agreements – with companies such as Ferrer International and BSH Electrodomésticos – related to the development of specific projects and the transfer of technologies.

Research Contract with BSH Electrodomesticos

A new joint collaboration with the company BSH Electrodomésticos and the Signal and information processing for sensing systems group (page 89), headed by Santiago Marco, has been consolidated this year. After a previous collaboration up until February, this academic-industrial partnership was further continued and formalized on November 2015 and aims to continue as a stable collaboration with the aim of developing new products and services and improve the company's pre-existing technologies based on the know-how of Santiago Marco's laboratory.

HealthTech Cluster meeting takes place at IBEC

The HealthTech Cluster is an association of companies, hospitals and research institutes working with health technologies in Catalonia. It was created at the end of 2014 and at the end of 2015 had doubled the number of partners involved. IBEC has been involved as an active partner from the very beginning and held one of the Cluster's meetings in their facilities, presenting the different projects and research lines developed by the IBEC researchers. The Technology Transfer team of IBEC was involved in the strategic definition of the Cluster and in the inter-Cluster meetings.

Clinical and translational collaborations

IBEC counts on the collaboration of medical doctors to provide input on the clinical aspects of its research, so that results are easily extended to clinical practice. In this way, IBEC benefits from its privileged position as technological counterpart of the major hospitals in the Barcelona area, four of which (Hospital Clínic, Sant Pau, HSCSP and Bellvitge) are recognized as Biomedical Research Institutes of Excellence by the Spanish government. IBEC's framework agreements and collaborations with these nearby hospitals allow easy access to clinical samples and patients.

Clinical collaborations can be at the research level, with academic publications as the result; translatory, to develop products aimed at reaching the market; or with a spin-off company in mind.

CELLEX collaboration of Nanobioengineering and Robotics groups

This year two IBEC groups, Nanobioengineering (page 117) and Robotics (page 52), joined forces on a project funded by the CELLEX foundation and under the coordination of Dr. Gratacós, head of the Maternal Fetal Medicine Division at the Hospital Clinic. The objective of this multidisciplinary approach, between both institutions, targets the field of fetal medicine and surgery.

On the one hand, the Nanobioengineering group will develop biosensors specifically designed to be applied in the field of fetal medicine. It will seek to develop and apply them in cases where possible infectious diseases in the fetus, tissue ischemia during interventions, or metabolic activity need to be evaluated. The challenge is raised to fit the technology to the dimensions and requirements of fetal endoscopic surgery, and on the development of specific sensors for the detection for certain infecting pathogens and the metabolic activity variations on a fetus.

On the other hand, the Robotics group will develop a guidance system support for prenatal surgery. This robotic assistance will help the surgeon guiding the endoscope and other surgery instruments on a specific anatomical area allowing him to perform high precision operations which are not possible today, such as access to fetal vessels.

Genetic "editing" to fight inherited disease

In the framework of a collaboration led by Juan Carlos Izpisúa at the Salk Institute for Biological Studies (California, US), the group of Núria Montserrat (page 98) had the opportunity to collaborate with researchers at the Hospital Clinic and at the Hospital de Sant Joan de Déu for the development of potential therapeutic tools for preventing the transgenerational transmission of human mitochondrial diseases caused by mutations in mitochondrial DNA (mtDNA). Mitochondrial diseases include a group of maternally inherited genetic disorders caused by mutations in mtDNA. In most of these patients, mutated mtDNA coexists with wild-type mtDNA, a situation known as mtDNA heteroplasmy.

Their paper published in *Cell* in April (see page 10) highlights the benefits of this fruitful collaboration, where basic and translational research teams have merged their different expertise.

Reddy, P. et al (2015). Selective elimination of mitochondrial mutations in the germline by genome editing. Cell *1613, 459-469*

The GLAM project aims to develop a new diagnostic tool to detect biomarkers from biofluids, obtained in a "non invasive" manner, specifically in urine and focusing on genitourinary cancers

A step towards personalized medicine

Currently, differential cancer diagnosis takes place daily in clinical settings for both patient stratification and monitoring patient responses to existing treatments. However, the outcome of this diagnosis is still poor, with many deficiencies and false positives and negatives due to the low sensitivity and specificity of available methodologies. Moreover, as new targeted therapies are available to patients and oncologists, there is a huge need to improve personalised diagnosis and therapy.

This year, the Biomimetic systems for cell engineering group (page 94) initiated the GLAM project, funded by the EU, which aims to develop a new diagnostic tool to detect biomarkers from biofluids, obtained in a non- invasive manner specifically in urine and focusing on genitourinary cancers, to enable oncologists to take better treatment decisions. To this end, GLAM project will develop an integrated device based on novel label-free photonic biosensors with ultra-sensitivity, simplicity of use, portability, multiplexing and low cost by simply applying a drop of urine and reading 10 biomarker levels.

The unique GLAM technology will make the device usable with other biofluids aside of urine, and might also be used to help physicians in personalised medicine in many other biomarker-driven diseases. The clinical validation of the technology will be carried out in the Urology Research Lab at Radboud University Medical Center in Nijmegen, The Netherlands.

A promising alternative for heart regeneration

The Cellular and Respiratory Biomechanics group (page 102) is currently running a collaboration with Dr. Antoni Bayes-Genis, Head of Cardiology at Hospital Germans Trias i Pujol, to improve the biofabrication of tissue patches for regeneration after a heart attack.

Bioartificial tissues reengineered by seeding stem cells in acellular scaffolds offer a promising alternative for heart regeneration; however, stem cell repopulation and differentiation is still limited in its efficiency. Using a biomaterial-based scaffold that mimics the native architecture of the myocardial extracellular matrix (ECM) can enable functional cell attachment and differentiation; however, while decellularized myocardial ECM accomplishes this premise, the decellularization processes may distort or degrade the ECM structure.

"To find an suitable myocardial scaffold for recellularization, we tested detergent- and trypsin-based decellularizing protocols on pig heart samples," says Daniel. "Assessing the scaffolds ultramicroscopically, we found filamentous ECM with preserved fiber disposition and structure in both protocols. This technique could improve the biofabrication of tissue patches for infarcted myocardial regeneration."

Perea-Gil, I., et al (2015). In vitro *comparative study of two decellularization protocols in search of an optimal myocardial scaffold for recellularization.* American Journal of Translational Research *73, 558-573*

Fruitful research into neurodegenerative diseases

The Molecular and Cellular Neurobiotechnology group (page 113) actively continues its collaborations with several clinical groups in Spain and Germany. These collaborations focus on the study of some neurodegenerative diseases: Alzheimer's and Creutzfeldt-Jakob's diseases. Some of their clinical collaborators include:

- **Dr. Gelpí and Dr Grau-Rivera**, Department of Neurology, Hospital Clínic, Barcelona.
- **Dr. Ferrer**, Institute of Neuropathology, IDIBELL-University Hospital Bellvitge, University of Barcelona.
- **Dr. Zerr and Dr. Llorens**, Department of Neurology, Clinical Dementia Center, University Medical School, Georg-August University and German Center for Neurodegenerative Diseases (DZNE), Göttingen, Germany.
- **Dr. López de Munain**, Hospital Universitario Donostia, Neurology Department, San Sebastian, Spain.

As outcomes of these collaborations, they described the evolution and the presence of several biomarkers in the cerebrospinal fluid of dementia patients, as well as *in vitro* and animal models.

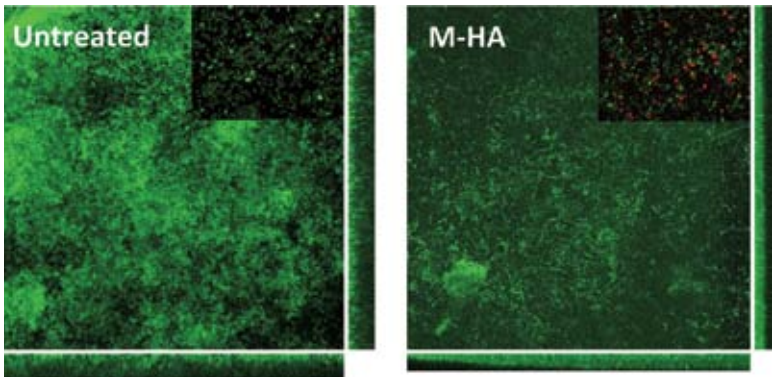
Since November 2015, Prof. del Río has coordinated the National Network of Prions (PRIONETSPAIN) in the framework of the project "Acciones de dinamización Redes de Excelencia" funded by the Spanish Ministry of Economy and Competitiveness (MINECO). In this network, several groups with protracted experience in prion research, including renowned Spanish clinicians, collaborate to develop an outreach, scientific and training programme focused on prion diseases.

Good results from BIOTENDON

BIOTENDON, a collaboration between IBEC's Biomaterials for Regenerative Therapies group and clinicians from the Consorci Sanitari de Terrassa (CST), aims to create a new nanofibrous polymeric scaffold with the appropriate biological signals and committed tendon cells to help surgeons repair rotator cuff tears in the shoulder.

In 2015, the preliminary results of the project, which has been funded under the RecerCaixa programme since 2014, show a good biocompatibility of the mesh when implanted in rabbits, and the formation of new tissue after eight weeks. Not only that, but the mechanical assays demonstrated the good performance of the mesh. The next steps will be to implant the mesh for a longer period to see if the newly formed tissue is tendon-like.

The close collaboration between researchers and clinicians will ensure that the product developed by BIOTENDON meets clinical needs, and represents a substantial benefit for the huge amount of elderly patients suffering from rotator cuff tears.



Disassembling the existing *P. aeruginosa* biofilm by adding M-HA, an enzyme that specifically inhibits bacterial proliferation by inhibiting bacterial DNA replication. The molecule works as a 'radical scavenger' compound to inhibit ribonucleotide reductase, an essential enzyme in DNA replication and repair. This study was the result of a collaboration between Eduard Torrents' Bacterial Infections: Antimicrobial Therapy group at IBEC and VHIR's Infectious Diseases group.

Making waves in bacterial infections

Eduard Torrents' Bacterial Infections: Antimicrobial Therapy group (page 128) has proved to complement that of the Infectious Diseases group led by Drs. Benito Almirante and Joan Gavaldà at Vall d'Hebron Institut de Recerca (VHIR), offering much potential for collaboration since the institutional Memorandum of Understanding between the two centres started in May 2012. For both sides, the close collaboration bridges the gap between fundamental microbiological knowledge and making new therapies available to patients, as well as accelerating the development of activities and maximize the use of resources – such as scientific equipment at IBEC being made available to the clinicians – and knowledge sharing.

During 2015, the groups published two important papers together. One, in the Journal of Controlled Release, which also involved IBEC's Biomaterials for Regenerative Therapies group (page 58), outlines the use of new nanoparticle strategies to combat bacterial infections. The second, in PLoS ONE, identifies of an enzyme that specifically inhibits bacterial proliferation by inhibiting bacterial DNA replication. Both studies open the possibility to treat bacterial infections by *Pseudomonas aeruginosa* and Mycobacterias.

Baelo, A. et al. (2015). "Disassembling bacterial extracellular matrix with DNase-coated nanoparticles to enhance antibiotic delivery in biofilm infections". Journal of Controlled Release*, 209, p150–158*

Julián, E. et al (2015). Methyl-hydroxylamine as an efficacious antibacterial agent that targets the ribonucleotide reductase enzyme. PLoS ONE *10(3): e0122049*

Double results for Robotics

The lack of realistic simulators that can be used for training and the objective evaluation of surgeons led to a Robotics group (page 52) collaboration with the Hospital de Sant Pau to develop a surgical trainer that combines the flexibility of virtual simulators with the realism and objectivity of physical devices and sensing systems. Their robotic trainer, aimed at assisting surgeons to gain skills and evaluate their performance in hysteroscopy, will be part of the training programme of the European Society of Gineacological Endoscopy (ESGE) and has led to the creation of a spin-off, Surgitrainer S.L., for its commercialization.

Secondly, the project Bitrack, which also led to the creation of a spin-off, Rob Surgical Systems S.L., is now in the planning process for clinical validation experiments with the Hospital Vall d'Hebrón and Hospital Clínic. At present the company and the Robotics team are defining the procedure and developing the new performances of the robotic system to achieve the necessary reliability, friendly interactivity and safety to obtain the necessary EC stamp, a necessary step for its meeting all requirements for its regular clinical practice. It is hoped that these trials will be held in November 2016.

The sounds of health

A joint research Unit between IBEC and Hospital Universitari Germans Trias i Pujol (IGTP) is coordinated by Raimon Jané, head of IBEC's Biomedical Signal Processing and Interpretation group (page 78), and the hospital's Manel Puig Domingo, is developing a collaborative project in respiratory sound analysis.

The clinicians performed experiments with patients with asthma and other respiratory diseases, while advanced signal interpretation techniques developed by IBEC's group improved the capability of early diagnosis in these kinds of diseases. The advances of this study were published in the *IEEE Journal of Biomedical and Health Informatics* paper in January 2015, where their non-invasive methodology to assess adventitious respiratory sounds is shown to be able to improve the diagnosis and monitoring of patients with asthma.

The Joint Research Unit also developed, in collaboration with the Hospital del Mar, a new method to evaluate the efficiency of mechanical activation of respiratory muscles to detect and quantify the level of muscular weakness caused by pathologies such as COPD. The results of this study was published in the *European Respiratory Journal* in December.

Lozano, M., et al (2016). Automatic differentiation of normal and continuous adventitious respiratory sounds using ensemble empirical mode decomposition and instantaneous frequency. IEEE Journal of Biomedical and Health Informatics *PP99, 1-1*

Sarlabous, L. et al (2015). Efficiency of mechanical activation of inspiratory muscles in COPD using sample entropy. European Respiratory Journal *466, 1808-1811*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Events and communications

Events and meetings in 2015

Throughout the year

Institutional and scientific projects

Throughout the year, IBEC hosts meetings for the consortia of its ongoing institutional and scientific projects.

Good laboratory practices courses

IBEC's Occupational Risk Prevention Service organized Good Laboratory Practices courses throughout the year, which were mainly aimed at young scientists and students. The courses were given by members of IBEC's Health and Safety Committee who, at the same time, work as laboratory technicians in different research groups. The theoretical part was held by laboratory technicians David Izquierdo and Cristina Rivero, while senior researcher Soledad Pérez, postdoc Senda Jiménez and David Izquierdo developed the practical part. During 2015, the Generalitat published their health and safety indices, which showed IBEC's accident rate is around 30% lower than the mean of the other research institutes in Catalonia.

Scientific Writing courses

Various writing skills courses took place throughout the year. Fourteen people attended "The WHY and HOW of Good Scientific Writing" to help publishing scientists develop a more impartial, analytical view of their own writing behaviour in October and November, and nine scientists benefitted from "Learning to write clearly: the 'how' of good scientific writing" throughout November.

March

■ 6 March

ACER Board of Directors meeting

With IBEC Director Josep Samitier named as new president of the Associació Catalana d'Entitats de Recerca (ACER), the association held its Board of Directors meeting at IBEC. The other members of the Director's Board are ICAC's Joan Gómez Pallarès (Secretary), Ramon Gomis (IDIBAPS), Jordi Galí (CREI) and Josep M. Monfort (IRTA) as members.

2015's Sant Jordi celebration was a case of "Find the Lady"

Events & Communications

The 6th European CellMech Meeting was hosted by IBEC and held at the University of Barcelona's Faculty of Medicine

April

■ 23 April

Sant Jordi

IBECers enjoyed Sant Jordi (23rd April) together this year at a garden party with a difference. In the spirit of internal networking and getting to know new people, each male attendee of the lunchtime gathering in the towers garden of the PCB was given a woman staff member or researcher's name on a slip of paper. They then had to identify her and present her with her Sant Jordi red rose.

■ 30 April

reSearch4Talent

Nearly 60 undergraduate and masters students attended IBEC's reSEARCH4TALENT day on Thursday 30th April. We opened our doors to everyone interested in knowing more about a career as a researcher, giving them the chance to talk to real researchers and ask questions about day-to-day work in the lab, career paths, work-life balance, mobility and more, as well as taking a tour of the IBEC labs and enjoying a "snack 'n' chat" networking session in the PCB garden.

May

■ 6 May

Feria de empresas (UB)

This careers fair, organized by the University of Barcelona's physics and chemistry faculties, helps undergraduate students of these subjects to find out more about potential employers or furthering their studies, as well as improving the university's relations with the business sector. IBEC attended the fair to offer university leavers advice and information about continuing their career at the institute as masters or PhD students.

On 10th March, IBEC also took part in a similar event organized by the Faculty of Industrial Engineering (ETSEIB) of the UPC.

■ 13-15 May

CellMech 2015

The 6th European CellMech Meeting was hosted by IBEC and held at the University of Barcelona's Faculty of Medicine. IBEC group leaders Daniel Navajas, Xavier Trepat and Pere Roca-Cusachs were the organising committee of this year's meeting, one of the premier worldwide conferences on cell mechanobiology. This year's meeting focused in particular on the integration of mechanical processes across scales, from subcellular components to tissues. Topics included innovative experimental approaches to probe cell mechanics and visualize dynamic cellular processes, together with the development of new theoretical and numerical concepts dedicated to cell and tissue engineering.

The conference featured keynote lectures by experts from Europe, the USA, India and Australia, and will also offer the opportunity for young scientists to present their work to a broad and multidisciplinary audience of more than 200 participants.

Ehud Gazit, Director of CERCA Lluís Rovira and Josep Samitier chairing the IBEC/TAU Symposium

■ 18-19 May

IBEC/TAU Symposium

Top scientists from Tel Aviv University (TAU), including Israel's former Chief Scientist of the Ministry of Science and Technology, visited Barcelona in May to take part in a two-day symposium with IBEC. With many similarities between Catalonia and Israel – which are almost neck-and-neck when it comes to research output in *Science* and *Nature*, with over 30 publications per million inhabitants and similar levels of funding under FP7 – this event built on the fact-finding mission of Artur Mas and Barcelona-based scientists to Israel last year and was supported by AGAUR.

Director of CERCA Dr. Lluís Rovira inaugurated the event, entitled "Nanobiotechnology and Nanomedicine: Moving forward the convergence between life sciences, medicine and engineering at the nanoscale", at which group leaders from both sides presented their work and try to identify synergies and opportunities for collaboration. Contributors from TAU include Ehud Gazit, one of the world's leading researchers in nanotechnology, who also holds a Visiting Scientist position at MIT's Center for Biomedical Engineering, and was Chief Scientist of Israel's Ministry of Science and Technology until 2014. From IBEC's side, Josep Samitier, Xavier Fernández-Busquets, Samuel Sánchez, Pau Gorostiza, Gabriel Gomila, Elena Martínez, Elisabeth Engel and Nuria Montserrat and Lorenzo Albertazzi presented their work in front of the 75-strong audience.

■ 25 May

Workshop in gender and diversity

Open to the entire IBEC community, and especially aimed at the members of the Gender and Diversity committee (page 27), this workshop provided the basic concepts and tools in the field, focusing on the understanding of the values, beliefs and expressions of people with different age, gender, race, religion, etc.

■ 26 May

"Financiación de KETs en salud" (NanoMed Spain)

This conference, organized by NanoMed Spain (page 151) and Fenin and in collaboration with ACCIÓ, the Centre for the Industrial and Technological Development (CDTI) and the Spanish Platforms for Photonics and Biotechnology Markets, brought together funding experts in the R & D sector with representatives from research institutes and companies working in nanomedicine. Through panel discussions, participants heard about success stories already funded under CDTI, which finances R&D projects developed by Spanish companies and performs evaluation of calls of national R&D programmes.

■ 26-28 May and 2-4 June

Oral skills courses

PhD students and early postdocs attended the masterclass entitled "Scientifically Speaking: a Master Class in peer-to-peer presenting for scientists" to help take their presenting skills to a new level of effectiveness by developing their confidence and versatility as speakers in multidisciplinary scientific contexts.

June

■ 8 June

Stress management course

Fourteen people attended this course, open to staff at all career stages.

■ 16 June

ACER Escola de primavera

Hosted at and co-organized by IBEC, ACER's 5th Escola de Primavera (Spring School) brought together 40 communications professionals from Catalonia's research centres for a morning of talks, discussions and networking opportunities. Presentations included "Getting the attention of the international media" by journalist Michele Catanzaro and "Crisis communications" by Joan Francesc Cánovas of the UPF. The day also featured a poster session, with submissions from IRTA, ICN2, ICFO, IDIBAPS, VHIR, IPHES, IBEC, IRB and CREAF.

■ 26 June

Kids' Day

On Friday 26th June IBEC, in collaboration with IRB, celebrated its first edition of Kids' Day, when staff and researchers from the two institutes were invited to bring their children to the PCB for a morning of science activities.

Kids' Day was an opportunity for staff to show their children their workplace, and gave the 47 IBEC visitors – who were aged between 3 and 12 – the chance to be a 'little researcher' for a day via tours of the labs, games and interactive activities, including a science show by Ciència Divertida.

July

■ 3 July

IBEC Summer Day

More than 70 participants enjoyed IBEC's Summer Day on 3rd July. Attendees played team sports such as football or paddletennis, or took part in fitness activities such as zumba together, before relaxing by the pool for the afternoon with a packed lunch.

■ 15 July

Workshop on work-life balance in research

In this session, four IBEC group leaders were invited to participate as guest speakers in a

ACER's 5th Escola de Primavera for communications professionals

The IBEC-organised B·Debate on "Future Tools for Biomedical Research: *In vitro, in silico* and *in vivo* Disease Modeling"

round table session where they shared with the audience their experiences as successful role models who have managed to reach a leading position in research while, at the same time, raising their children or taking care of their family. In addition, concepts such as vertical segregation or the 'glass ceiling' effect were discussed.

September

■ 16 September

Statistics workshop

This course, aimed at aimed at early career researchers – master students, PhDs and junior postdocs – attracted 17 participants and covered areas such as data collection, hypothesis testing, statistical analysis, and the graphical display of data. The trainer was Dr. Beatriz F. Giraldo, Senior Researcher of IBEC's Biomedical Signal Processing and Interpretation group (page 78) and professor of Analysis and Statistical Computing of Biomedical Data in the Master of Biomedical Engineering in the Department of Automatic Control (ESAII) at the Technical University of Catalonia (UPC).

■ 28-29 September

ISC Meeting

Monday 28th September saw the arrival of IBEC's International Scientific Committee for their annual two-day meeting with the directorate. Among other things, the panel of experts from research and industry, who came from as far afield as the USA and Singapore, reviewed the international candidates for the group leader and tenure track positions.

■ 30 September

8th Annual IBEC Symposium

On Wednesday 30th September, IBEC's 8th Annual Symposium took place at Barcelona's AXA auditorium. On the theme of Bioengineering for Regenerative Therapies, the symposium welcomed speakers Josep Samitier and Nuria Montserrat from IBEC; Michael Schneider, Imperial College London; Manuel Salmerón-Sánchez, University of Glasgow; Giorgio Scita, University of Milan; and Ronald McKay, Lieber Institute for Brain Development, Baltimore. The programme also featured flash presentations by selected poster contributors.

This year the symposium was kindly supported by Izasa Scientific, BioLab, Merck Millipore and Fisher Scientific, and included an information session by Izasa.

October

■ 1-2 October

B·Debate on "Future

Tools for Biomedical Research"

The IBEC-organised B·Debate on "Future Tools for Biomedical Research: *In vitro, in silico* and *in vivo* Disease Modeling" took place at CosmoCaixa in October. This two-day Centre for International Scientific Debate event, an initiative of Biocat and Obra Social "la Caixa", looked at new tools and approaches for basic research and preclinical trials of new drugs, finding new solutions to replace the traditional way of evaluating drug safety – such as the use of animals – and how nanotechnology and bioinformatics are enabling the custom design of tailored treatments for individual patients and disease profiles.

Speakers at the B·Debate included IBEC director Josep Samitier; Elisabet Berggren of the European Union Reference Laboratory for Alternatives to Animal Testing (EURL-ECVAM); Steve Brown, head of the Mammalian Genetics Unit at MRC Harwell; Roger Kamm, Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering at MIT, who is also a member of IBEC's ISC, and James Kirkpatrick, Emeritus Professor of Pathology at the Johannes Gutenberg University of Mainz.

■ 7 October

Identifying skills to promote your career

In this workshop, the 11 participants had the opportunity to gain a deeper insight into the skills and competences that they have developed while and since achieving their PhD, and how these can help them succeed in their career development, in or outside academia.

Participants shared their experiences and questions, and a large number of practical exercises and case studies helped them identify and appreciate their skills.

■ 8 October

Managing harassment at work

Open to the entire IBEC community, and especially aimed at the members of the Gender and Diversity committee, the Anti-Harassment Committee and the Health and Safety Committee, this course addressed ways to identify and tools to deal with potential harassment situations.

December

■ 17 December

Christmas celebration

150 people attended IBEC's biggest, best Christmas party yet, which featured a Body Percussion session, a tombola and some surprises. In total, partygoers raised €665 for local homeless charity Arrels Fundació.

Oiane Urra presents her work in a flash presentation at the 8th annual IEBC symposium

IBEC Seminars and PhD Discussions Sessions

Throughout the year, international experts, scientists who work with our research teams on certain projects, and some of the IBEC group leaders are invited to give lectures as part of the IBEC Seminars programme. The aim of these events is to provide an overview of the state-of-the-art research in various fields and to give the audience the opportunity to discuss recent developments with the guest speakers.

In addition, the PhD Discussions Sessions are intended to encourage the participation of PhD students, providing a forum where they can present the results of their research and discuss it with fellow students and researchers. Throughout 2015, ten PhD students presented their work in these sessions. Additionally, in order to help IBEC students in their career development and provide them with additional skills, invited speakers gave lectures on 'Intellectual and Industrial Property: Turning science into business' and 'Planning for an Academic Career: A postdoc and beyond'.

■ January 16

David Caballero
IBEC, Nanobioengineering group (page 117)
The cell ratchet: interplay between protrusion activity and adhesion determines cell motion"

■ February 3

Ralph G. Andrzejak
Department of Information and Communication Technologies, Pompeu Fabra University
Application of nonlinear signal analysis to electroencephalographic recordings from epilepsy patients

■ February 12

Daniel Oliver
Asociación Española de Crowdfunding
Crowdfunding for scientific and health projects

■ February 13

Pia Cosma
Center for Genomic Regulation (CRG) / Institució Catalana de Recerca i Estudis Avançats (ICREA)
Studying Wnt signaling activity in cell reprogramming and tissue regeneration

■ February 27

Gilles Subra
Institut des Biomolécules Max Mousseron (IBBMM), Montpellier
Hybrid inorganic–biorganic peptide materials and polymers: a bottom-up approach

■ March 20

Romain Quidant
Institut de Ciències Fotòniques (ICFO) / Institució Catalana de Recerca i Estudis Avançats (ICREA)
Bioplasmonics: Designing novel optical nanotools for Biomedicine

■ April 10

Núria Montserrat
IBEC, Pluripotent stem cells and activation of endogenous tissue programs for organ regeneration group (page 98)
Dreaming of organ regeneration: new hopes for regenerative medicine

■ May 8

J. Miguel Rubi
Departament de Fisica Fonamental, University of Barcelona
Somatic exocytosis of serotonin mediated by molecular motors

■ May 22

Thomas Graf
Gene Regulation, Stem Cells and Differentiation Program, Center for Genomic Regulation (CRG) / Pompeu Fabra University, Barcelona
Mechanisms of transcription factor induced transdifferentiation and reprogramming to pluripotency

■ June 12

Alexandra P. Marques
3Bs Research Group, University of Minho, Portugal
Driving skin wound healing: stem cells and extracellular matrix role

■ June 16

Javier G. Fernández
Assistant Professor and Founder Academic Member, Singapore University of Technology and Design
Bioinspired materials

■ June 19

Matteo Palma
School of Biological and Chemical Sciences, Queen Mary University of London, U.K.
Bio-inspired self-assembly for single-molecule investigations

■ July 6

Saman K. Halgamuge
Department of Mechanical Engineering and Biomedical Engineering Program Melbourne School of Engineering, University of Melbourne, Australia
Big Data Analytics in Metagenomics

■ July 24

François St. Pierre
Department of Neuroscience, Baylor College of Medicine / Department of Electrical and Computer Engineering, Rice University
Imaging electrical activity in vivo *with ultrafast protein sensors*

■ September 17

Richard Reilly
Trinity Centre for Bioengineering, Trinity College Dublin
All a question of Timing: Sensory processing in Dystonia and Parkinson's Disease

■ September 18

Marc Martí-Renom
Genome Biology Group, Centre Nacional d'Anàlis Genòmica (CNAG) /Structural Genomics Group, Centre de Regulació Genòmica (CRG), Barcelona
Structure determination of genomes and genomic domains by satisfaction of spatial restraints

■ September 22

Albert Folch
Associate Profesor, University of Washington, Seattle
Print-and-Play Microfluidics

■ October 16

Lorenzo Albertazzi
IBEC, Nanoscopy for nanomedicine group (page 44)
Nanoscopy for Nanomedicine: looking at nanomaterials in action one molecule at a time

■ October 19

Clara Streiff
ThermoFisher Scientific
Cell Imaging Day – Molecular Probes: Seminar and demonstration

■ October 22

Nanomalaria joint unit seminar, Faculty of Medicine
Konstantinos Mitsakakis
University of Freiburg
LabDisk, a multi-purpose, multi-target diagnostic platform for patient management and surveillance at the point-of-care

■ October 23

Miquel Bosch Pita
IBEC, Nanoprobes and nanoswitches group (page 72)
The molecular mechanisms of memory persistence: imaging how single synapses learn in real time

■ November 19

Luis de Lecea
Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine
Optogenetic control of arousal

■ November 27

Chia-Fu Chou
Senior Research Fellow/Professor, Institute of Physics, Academia Sinica, Taiwan
Low-copy number biomolecular analysis with dielectrophoretic enrichment /trapping via molecular dam and plasmonic electrode nanogaps

■ December 3

Alexandre Perera i Lluna
Bioinformatics and Biomedical Signals Laboratory (B2SLab), Biomedical Research Center (CREB), Universitat Politècnica de Catalunya
Fracking (vs. Mining) Biological Knowledge from Metabolomics data

■ December 11

Roberto de la Rica
University of Strathclyde
Bioplasmonics in nanofabrication, biosensing and nanomedicine

Outreach activities in 2015

Throughout the year

Group visits

Throughout the year, 15 groups of students from high schools in Barcelona and Catalonia visited IBEC: Escola Suïssa de Barcelona on 17th February (16 participants); Escola Montlau on 26th February (19 participants); Insitut Miquel Martí i Pol on 5th March (26 participants); Institut Tremp on 19th March (20); Escola Roig Tesàlia on 16th April (20); Institut Moisés Broggi on 20th April (11); Institut Secretari Coloma on 22nd April (20); Institut Pau Claris on 5th May (25); Institut Francesc Macià on 18th May (25); Institut Torrent de les Bruixes on 21st May (17): Institut Sales de Viladecans on 4th June (32); Escola Amor de dios on 27th October (18) and 11th November (28) and Centre Escolar Joan Maragall on 24th November (20). Some of these visits were part of the ESCOLAB programme, an initiative of the City Council of Barcelona, which introduces groups high school students into the city's research laboratories to encourage scientific vocation.

In addition, a group of 50 pupils from the Pere IV school were here on 23rd-24th November for a tour and activity aimed at of primary school-age visitors; and 15 students from the University of Texas, USA came on 17th June.

Volunteer researchers for these visits came from the Nanobioengineering, Control of stem cell potency, Biomedical signal processing and interpretation, Integrative cell and tissue dynamics, Biomaterials for regenerative therapies, Bacterial infections: antimicrobial therapies, Nanoprobes and nanoswitches, Molecular and cellular neurobiotechnology and Signal and Information Processing for Sensing Systems groups.

Entrevistas de Bachillerato

An initiative at IBEC to help nurture the scientific minds of the future, the Entrevistas de Bachillerato, pairs high school students with IBEC PhD students to talk about subjects such as nanotechnology for the pupils' final baccalaureate work. Four such one-to-one encounters took place throughout 2015, with IBEC's young researchers from the Control of stem cell potency, Biomaterials for regenerative therapies, Bacterial infections: antimicrobial therapies groups resolving questions and doubts and sharing new ideas to help with the school projects.

Research placements for students

This scheme offers high school students the opportunity to have their research projects be assessed by a tutor and to gain hands-on experience in a laboratory. IBEC volunteers from the Nanotechnology Platform and the Molecular and cellular neurobiotechnology, Control of stem cell potency, Integrative cell and tissue dynamics, Signal and Information Processing for Sensing Systems, Biomaterials for regenerative therapies and Nanobioengineering groups looked after a

Visitors have a hands-on experience when they visit IBEC

total of 13 students in 2015.

Some of these students came to IBEC as part of the PCB's Recerca a Secundària initiative, addressed to 16-year-olds who are about to begin their research projects at school.

Participation in IBEC's outreach blog

Arnau Biosca (Nanomalaria group, page 64) and Anna Crespo (Bacterial infections: antimicrobial therapies, page 128) contributed articles or interviews to IBEC's outreach blog, http://divulga.ibecbarcelona.eu.

February

■ 24 February

CTM course for high school teachers

Nineteen secondary school teachers learnt about "Los biomateriales, nuevos materiales para terapias regenerativas" at IBEC as part of the Generalitat's Department of Education Programa de formación científica, tecnológica y matemática (CTM). The participants found out about the different materials that are currently used for implants, prosthetics and surgery, and why surface characteristics and biocompatibility are so important.

March

■ 20 March

Saló de l'Ensenyament

IBEC participated in the Espai Ciència at March's Saló de l'Ensenyament education fair alongside other CERCA centres. With the memory game "The future of medical applications: bioengineering", some of IBEC's research projects were showcased.

The Saló de l'Ensenyament is held every year in Barcelona to guide thousands of young people who are on the point of choosing a career. In the Espai Ciència, visitors can participate in workshops and activities to experience live, interactive science demonstrations. The space is an initiative organized by the Catalan Foundation for Research and Innovation (FCRI) with the collaboration of the Fira de Barcelona, where it is held.

The Espai Ciència at the Saló de l'Ensenyament

April

■ 8-11 April

Fira Recerca en Directe

The 'Live Research' fair at Barcelona's CosmoCaixa is organized by the Parc Científic de Barcelona (PCB) with the support of the Obra Social CatalunyaCaixa. It aims to present research to the general public, with researchers demonstrating and explaining their methods and goals in an accessible way. This year the Molecular and Cellular neurobiotechnology group (page 113) gave their time and expertise at the fair with an activity entitled ¿Cómo se estudian los genes?

■ 25-26 April

Festa de la Ciencia i Tecnologia (NOVUM)

IBEC participated in the Festa de la Ciencia i Tecnologia (NOVUM) with various activities. Silvia Pittolo from the Nanoprobes and Nanoswitches group was in charge of the workshop "Diseña un fármaco inteligente",

Xavier Trepat at the inauguration of this year's Joves i Ciència

while Pilar Rodriguez and Laura Casares of the Integrative cell and tissue dynamics group measured cellular forces in the workshop "¡Las células hacen fuerza!". In addition, Arnau Biosca of the Nanomalaria group participated in the space "Ask a scientist" space on World Malaria Day, which coincided with the city-wide fair.

May

■ 20 May

Pint of Science

Group leader Xavier Trepat and postdoc Laura Casares (page 132) took part in a global science outreach event taking place simultaneously in 9 countries and 50 cities all over the world.The Pint of Science festival on 18th-20th May aimed to deliver interesting, fun and relevant talks on the latest scientific research by the people who carry it out – in the pub. Xavi and Laura gave talks on "The forces that drive cancer cells" and "Cell, the force be with you", explaining the lab techniques used to measure cellular forces and making comparisons with everyday objects that can be found at the macroscale, at the packed Café de les Delícies on Rambla del Raval. Other scientists taking part in other Barcelona pubs included researchers from the UB, ICFO, CRG and several other centres. Pint of Science, which was established by a community of postgraduate and postdoctoral researchers at Imperial College in 2012, takes place annually over three days simultaneously in pubs in the UK, Ireland, France, Italy, the US, Australia, Germany and Spain.

■ 20 and 22 May

Professors i Ciència course

IBEC was one of the 13 research centres to be chosen to take part in Fundació Catalunya–La Pedrera's 2015 edition of Professors i Ciència, an excellence programme for the specialized training for secondary school science teachers. More than 200 teachers in total will receive specific training on various subjects to take back to the classroom within the participating research centres. At IBEC, Juan Crespo from the Control of stem cell potency group (page 108) ran the workshop "Bioingeniería cardíaca: una opción de futuro" for eleven teachers.

June

■ 13 June

Joves i Ciència

Xavier Trepat from the Integrative Cell and Tissue Dynamics group (page 132) was the speaker at the inauguration of this year's Joves i Ciència programme organized by the Fundació Catalunya-La Pedrera, which exposes talented and motivated young students to 'real' scientific work to encourage more of them to embark on a scientific career. More than 100 people attended.

September

■ 25 September

European Nit de la Recerca

IBEC group leader and ICREA Research Professor Pau Gorostiza (page 72) took part in the Barcelona version of European Researcher's Night on 25th September. Held at the CCCB, the Nit Europea de la Recerca Barcelona was in celebration of the Year of Light. Pau took part in a round table moderated by BIOCAT on the subject of "Humans amb més llum: re-evolució humana gràcies a les noves tecnologies basades en la llum".

European Researcher's Night is part of a Europe-wide H2020-funded project to bring researchers and the general public together to help increase the public understanding of science, and is taking place simultaneously in over 300 cities across the continent. Barcelona's edition is organised by BIOcomuniCA'T, a non-profit science and society organization founded by researchers from the IBMB and CRG.

November

■ 18 November

Setmana de la Ciència

During the 20th edition of Setmana de la Ciència (Science Week), the Catalonia-wide science festival coordinated by the Fundació Catalana per a la Recerca i la Innovació, 45 members of the public came to IBEC to visit the labs and find out about the most advanced research in the field of bioengineering. Xavier Trepat (page 132) gave a talk, and former PhD student Maria Mattotti, provided a musical interlude with a scientific theme. Attendees also had the opportunity to talk face to face with Xavier and other researchers from IBEC to learn more about how "real" science is done.

As part of Science Week, "Science Day at les Escoles" took place, an event that comprised more than one hundred lectures throughout Catalonia aimed at of 4th year, ESO and Baccalaureate students. Laura Casares of the Integrative cell and tissue dynamics group (page 132) gave a talk at the Jesuit-Sagrat Cor de Jesus school, attended by 160 students from the host school and two others in the Eixample district.

Selected media coverage

■ 19 January

El Periódico and others

"Robots del tamaño del virus, una apuesta para combatir el cáncer"

New IBEC group leader Samuel Sánchez (page 122) appeared in articles in *El Mundo* and *El Periódico*, talking about his career so far, his new appointment at IBEC and the work he will be continuing on micro- and nanomotors.

■ 10 February

El Mundo "Innovadores"

"Miniriñones de laboratorio"

New group leader Nuria Montserrat (page 98) was featured in an article in *El Mundo* discussing her ERC grant, the work she has been doing generating "mini-kidneys" from human pluripotent stem cells, and how she will continue this important line of research at IBEC.

■ 11 February

El Periódico

"La UB y la UPC aportan siempre juventud al distrito"

IBEC Director Josep Samitier was the subject of a full-page article in *El Periódico* in a series the paper ran about Barcelona notables in relation to their neighbourhoods. In the article, journalist Carme Escales accompanied Josep to some of his favourite and most formative places in Les Corts.

■ 12 February

Medical News Today

"'Fracking' found in living tissues"

Coverage of the article published in the journal *Nature Materials*, in which researchers at IBEC and the UPC describe their discovery that 'fracking' takes place in the body at a cellular level.

■ 6 March

C&I Magazine

"Drugs on Demand"

Pau Gorostiza (page 72) and his work on photoswitchable peptides featured in an article in the February edition of *C&I Magazine*, a monthly science and business magazine published by SCI.

■ 6 March

Time Out Barcelona

"I am (Dr) Robot"

The March edition of *Time Out Barcelona* (English version) featured IBEC's spin-off, Rob Surgical Systems, in an article about technology in Barcelona.

■ 12 March

TV1, "Saber vivir"

IBEC's junior group leader Nuria Montserrat (page 98) appeared on RTVE's channel 1 programme Saber Vivir, when they had an episode devoted to kidney disease and research.

>PERSONAJES ÚNICOS / NÚRIA MONTSERRAT

La nueva investigadora del IBEC tratará de avanzar en la medicina regenerativa mediante la creación de miniriñones a partir de células madre de pacientes y posibles tratamientos a sus enfermedades genéticas. Por **David Guerrero**

Miniriñones de laboratorio

The research of Nuria Montserrat and her team was featured in an article in *El Mundo* in February

■ 7 April

Diari de Terrassa

“Estudiamos las infecciones en el intestino de la bacteria *E. coli*”

Eduard Torrents (page 128) was the subject of an article in the *Diari de Terrassa* about his work earlier this year which identified a important factor in *E. coli* infection, opening the way to developing targeted drugs against the potentially deadly condition.

■ 13 April

El Periódico

“Robots del tamaño de virus”

El Periódico featured an interview with Samuel Sànchez (page 122) following the announcement last week that he has been awarded the Premio Fundación Princesa de Girona Investigación Científica 2015.

■ 13 April

La Vanguardia

“Naturaleza replicada”

A two-page article in *La Vanguardia* talked about biomimetics and how scientists are replicating processes from nature in fields such as nanotechnology, engineering, robotics, chemistry and materials science. The article mentioned the work of the Signal and information processing for sensing systems group (page 89) in mimicking the the animal olfactory system to create an artificial nose.

■ 22 April

La Vanguardia

“Fármacos estimulados con luz actúan solo sobre células enfermas”

IBEC group leader Pau Gorostiza (page 72) and his work on developing light-regulated drugs in for focused delivery and reduced side effects were presented in an article in *La Vanguardia*.

■ 23 April

La Vanguardia

“Cinco instituciones científicas de Catalunya, acreditadas como centros de excelencia”

IBEC was one of the two centres in Spain to be awarded accreditation in the Severo Ochoa Excellence programme in 2015.

■ 24 April

ABC

“Científicos españoles manipulan por vez primera ADN de un embrión para curarlo”

Coverage of the study, led by Dr. Juan Carlos Izpisúa Belmonte of California’s Salk Institute and involving IBEC junior group leader Nuria Montserrat (page 98), that used molecular “scissors” to remove mitochondrial mutations in mouse eggs.

Josep Samiiter and an *El Periódico* journalist toured some of his most notable places in Les Corts in February

■ 3 May

Ara Diumenge

“Bioenginyeria per fer realitat l’home de carn”

In the magazine *Ara*, IBEC group leader Nuria Montserrat (page 98) and artist Marcel·lí Antúnez, who creates interactive sculpture with organic materials, such as Joan l’Home de Carn, appeared in an article together talking about organ regeneration.

■ 20 May

El Periódico, La Vanguardia and others

“El físico Xavier Trepat gana el Premio Banc Sabadell de biomedicina”

IBEC group leader and ICREA research professor Xavier Trepat’s (page 132) winning of this year’s Banc Sabadell Award for Biomedical Research was all over the newspapers. *La Vanguardia* described 2015 as “el año del triplete” for IBEC for the three major milestones of this Banc Sabadell

Award, Samuel Sánchez's (page 122) winning of the Premio Fundación Princesa de Girona Investigación Científica for his advances in the field of nanotechnology, and above all the institute's being honoured with the Severo Ochoa Excellence award.

■ 7 June

El Periódico

"La investigación tiene futuro"

In *El Periódico*, there was a four-page article about Catalonia's 'champion scientists'. IBEC was the only institute with not one but two investigators presented, Xavier Trepat (page 132) and Nuria Montserrat (page 98). They were described as some of the handful of talent under 40 working to improve the health and welfare of society.

■ 16 June

La Razón Cataluña

"Científicos catalanes descubren por qué las células no se rompen"

Coverage of the *Nature Communications* paper in which IBEC researchers revealed how cells withstand breakage during the constant changes in shape and volume experienced in most biological processes.

■ 21 June

La Vanguardia

"El cerebro que vuelve"

An article about new IBEC group leader Samuel Sánchez (page 122) talked about the 'brain gain' of having the nanotechnologist return to Catalonia after several years in Japan, the USA and Germany.

■ 23 June

El Mundo "Innovadores"

"El plástico del futuro"

IBEC alumnus Javier G. Fernandez was featured in an article about new materials inspired by insects in *El Mundo Innovadores*. Javier, who invented shrilk, a compostable material inspired by the insect cuticle and made from discarded shrimp shells and proteins derived from silk, did his PhD in IBEC's Nanobioengineering group.

■ 30 June

TV2, "Lab24"

"Nanomáquinas para la salud"

The RTVE science programme Lab24 featured an interview with IBEC group leader Samuel Sánchez (page 122), who described his research on micro- and nanomotors. Josep Samitier also featured in the video explaining the work of IBEC in general and giving several examples of the groups' research areas contributing to engineering solutions for health.

■ 19 July

La Vanguardia magazine

"¿Cómo nos verán dentro de 50 años?"

What in today's world will surprise or horrify our grandchildren in 50 years time? *La Vanguardia*'s weekend Magazine raised this question with nine "prominent people from different fields" including Xavier Trepat (page 132), who predicts that in 50 years humanity will be amazed that people ever died of organ degeneration, as it will be possible to regenerate or replace organs made from patients' own cells.

■ 22 August

El Periódico de Catalunya

"Pronto seremos capaces de generar partes de órganos fuera del cuerpo"

An interview and profile of Xavier Trepat (page 132) by the CEO of Ferrer, Jordi Ramentol, appeared in *El Periódico*.

■ 12 September

El País "Buenavida"

"¿Y si todos tuviéramos un corazón de repuesto?"

An introduction by IBEC Director Josep Samitier begins a 9-page article in *El Pais* about the future of organ replacement in light of advances in 3D printing.

■ 26 September

El País "Medicina"

"La física nos podrá enseñar a detener la progresión del cáncer"

Xavier Trepat's research was the subject on science programme Lab 24 in November

Integrative Cell and Tissue Dynamics group leader and ICREA research professor Xavier Trepat (page 132) was profiled in *El País*, where he discusses how combining physics and biology can open new roads to discovering mechanisms that can help us overcome disease and regenerate organs.

■ 6 October

El Mundo "Innovadores"

"Ciencia para curar sin dolor"

New IBEC junior group leader Lorenzo Albertazzi (page 44) was profiled in *El Mundo*'s "Personajes Únicos" section this week. The article describes his research interests and plans for his group at IBEC to develop novel self-assembling nanomaterials for the treatment of cancer and infectious diseases.

■ 2 November

BTV, "Terrícoles"

IBEC Director Josep Samitier talked to Lluís Reales in a half-hour-long interview for the BTV science programme Terrícoles.

■ 17 November

El País, "Ciencia en Español"

"Submarinos microscópicos para atacar células cancerígenas"

El País published a "Ciencia en Español" video interview with Samuel Sánchez (page 122) featuring footage of his nanorobots, which can be seen whizzing through through liquid using the expulsion of oxygen bubbles as propulsion. In the interview, Samuel explains how his new appointment in IBEC will help make advances because of the connections with biologists, hospitals and clinicians.

■ 25 November

TV2, "Lab24"

"El contacto entre las células y las matemáticas fáciles"

IBEC group leader Xavier Trepat (page 132) was interviewed on science programme Lab24, explaining why it's so important that we understand cell movement and the forces that act on our cells.

■ 1 December

Muy Interesante

"La luz: ¡qué buen rollo!"

Pau Gorostiza's (page 72) work was included in a extensive article about the science of light in the magazine *Muy Interesante*.

■ 5 December

TVE2, "Fábrica de Ideas"

IBEC was one of the subjects of the La 2 programme "Fábrica de Ideas". Josep Samitier, Samuel Sánchez, Eduard Torrents and Elisabeth Engel appeared in the programme, which was devoted to innovation and new inventions.

PhD Theses

Noninvasive mechanical estimation of respiratory
INTRODUCTION
METHODOLOGY

PhD theses in 2015

The data shows the date of the defence, the name of the student, his or her group at IBEC, the title of the PhD thesis and the awarding body.

■ January 9

Riccardo Levato
Biomaterials for regenerative therapies group (page 58)
Injectable biodegradable carriers for the delivery of therapeutic agents and tissue engineering (UPC)

■ January 15

Marta Sanmartí-Espinal
Nanobioengineering group (page 117)
Study of natural nanovesicles carrying olfactory receptors for the development of biosensing platforms (UB)

■ April 21

Cristina Vergara
Molecular and cellular neurobiotechnology group (page 113)
Papel regulador de la proteína priónica celular en la enfermedad de Alzheimer y uso de gamma-péptidos como potenciales agentes terapéuticos (UB)

■ May 11

Juan Pablo Agusil
Nanobioengineering group (page 117)
Fabrication of (bio)molecular patterns with contact printing techniques (UB)

■ May 14

Teresa Galán
Nanobioengineering group (page 117)
Conducting Polymers for Nano and Micro Electrodes. Application to Biomolecule Sensing and Release (UB)

■ July 17

Carlos Ruiz
Biomechanics and mechanobiology group (until February 2015)
A computational study of intervertebral disc degeneration in relation to changes in regional tissue composition and disc nutrition (UPC)

■ July 21

Erola Pairo
Signal and information processing for sensing systems group (page 89)
Detection of transcription factor binding sites by multivariate signal processing (UB)

■ October 27

Ana Guaman
Signal and information processing for sensing systems group (page 89)
Multivariate Signal Processing for Quantitative and Qualitative analysis of Ion Mobility Spectrometry applied to Biomedical and Food Applications (UB)

■ October 27

Andrés Arcentales Viteri
Biomedical Signal Processing and Interpretation group (page 78)
Análisis de la interacción cardíaca y respiratoria en pacientes con cardiomiopatía y pacientes en proceso de extubación (UPC)

■ November 11

Rosa Letizia Zaffino
Nanobioengineering group (page 117)
Development of a nano-sensor for the direct electrical free-label detection of DNA's hybridisation and single nucleotide polymorphism (UB)

■ November 23

Lorena De Oñate
Pluripotent Stem Cells and Activation of Endogenous Tissue Programs for Organ Regeneration group (page 98)
Research on cardiac differentiation from human pluripotent stem cells: how to get beating cells in a dish (UPF)

■ December 9

Ernest Moles
Nanomalaria joint unit (page 64)
Development of polyvalent erythrocyte- and parasitized erythrocyte-targeted nanovectors as novel site-specific drug delivery approaches for Plasmodium falciparum malaria chemotherapy (UB)

■ December 14

Maria Joana Azevedo Silva Marques
Nanomalaria joint unit (page 64)
Exploration of sulfated polysaccharides as antimalarials and as targeting molecules for nanovector-mediated drug delivery to Plasmodium *-infected cells (UB)*

■ December 18

Aitor Sánchez
Biomaterials for Regenerative Therapies group (page 58)
Biomimetic hydrogels for in situ *bone tissue engineering. Nature-inspired crosslinking methods as a tool to tune scaffold physical properties (UPC)*

Cover image: Self-assembled fibers from a small peptide generating from a specific point. They form stiff big tubes and thinner flexible fibers. - Nanoscopy for Nanomedicine group (page 44)

Compiled and produced by the Communications and Outreach Unit, IBEC.
Texts by the Communications and Outreach Department and the staff and scientists of IBEC.

Picture credits: IBEC's Communications and Outreach Unit; Ricard Badia; Marc Vergés; Maria Pujol; Christine Panagiotidis; Jordi Anguera; the staff and scientists of IBEC.

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