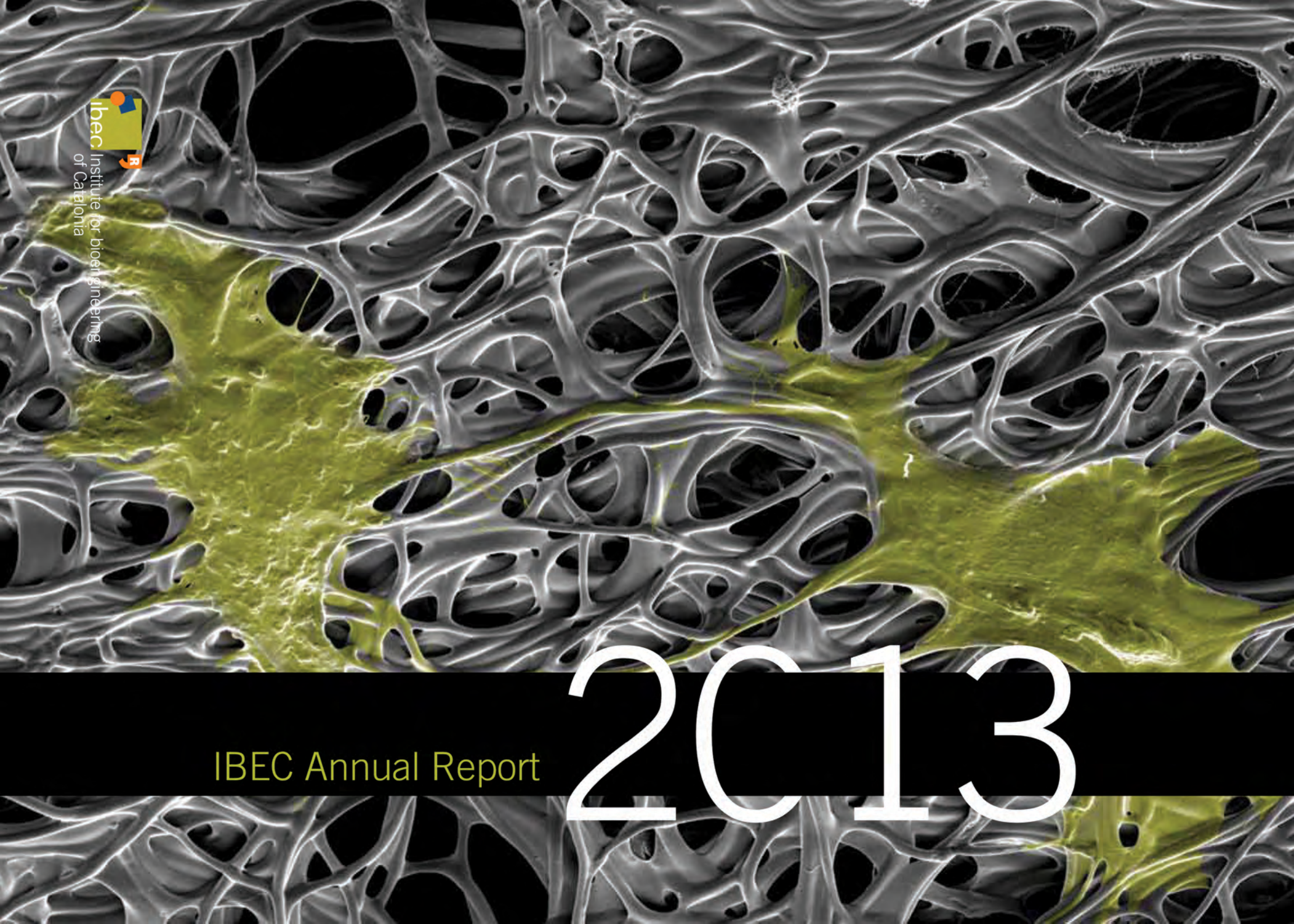
ibec Institute for bioengineering of Catalonia
IBEC Annual Report
2013

# 2013

## IBEC Annual Report

Institute for bioengineering
of Catalonia

# Introduction

**In 2013 the outstanding results obtained by our researchers, as well as the efforts, enthusiasm and involvement of our support staff, made what could have been a very difficult year into a resounding success. The continuing politicial and economic challenges faced by the whole country barely made a mark on IBEC's spirit, as scientists and staff alike stepped up with an even greater level of involvement and dedication to achieve excellent results.**

Of course, internal stability helps when facing up to external challenges, but in IBEC's case, it was all change at the top with the appointment of new Managing Director David Badia, closely followed by the departure of founding director Josep A. Planell to take on the Rectorship of the Open University of Catalonia. I hope that my own appointment soon afterwards as Director helped maintain some sense of continuity, but with this new challenge there also came new opportunities that will be addressed in the new Strategic Research Plan for 2014-2017, and we took the chance to reshuffle the support services units to better reflect their responsibilities in light of the new challenges IBEC will be facing in the future, as well as to offer an even more comprehensive and all-encompassing level of support to our researchers.

One of these units, Core Facilities (formerly Infrastructures) was profoundly affected by the year's major acquistion, the takeover of the Nanotechnology Platform from the Park Científic de Barcelona. The upheaval, the changes in working practise, the rapid move towards a new focus on service provision, and the sudden expansion required were all deftly handled with professionalism and good humour by everyone concerned.

Other changes during 2013 included the stepping down of most of the original ISC members after many years spent advising the Directorate on the research direction and institutional management of the institute. Before they went, the ISC – together with CERCA, which was simultaneously carrying out their own assessment of Catalonia's research centres – delivered a positive and encouraging evaluation of our efforts. "IBEC is now mature, and has more than fulfilled its mission", summed up the report; in a short time, it said, IBEC has achieved great success in many areas: the excellence of its research, as proven by its publications in the best scientific journals; its capacity to attract talented researchers; the quality of its management, that has helped it face acute economic problems; its robust internal organization; its international visibility and very active communication policy; its gender balance; and the strong motivation of all its staff.

I'd like to thank the departing members of the ISC for their tireless and often thankless work in advising both Josep Anton and myself as IBEC was taking its first tentative steps. These early years can be 'make-or-break' years, and thanks to the ISC's sage counsel and encouragement, we are not only still here, but also going strong, as the evaluation acknowledges.

Alongside all these changes and evaluations our scientists and administration staff have been working to their usual high standard without heed to the disruption. In 2013 we celebrated four *Nature* group papers, including a *Nature Materials* cover; 76 papers, 68% of them in the first quartile; 4 new patents; 11 PhD theses; another ERC grant in the shape of a Proof of Concept award for one group leader, who was already the holder of a Starting Grant; a fourth Tenure Track appointment; and private funding successes from sources such as RecerCaixa and La Marató de TV3 to top up our achievements in the areas of national and European competitive funding applications and the contracts and collaborations with national and international private companies. Support services activities were also boosted by competitive funding during 2013: the Communications and Outreach Unit were awarded money for an extensive outreach project by Spanish bank BBVA in the second half of the year.

The year also saw us forging ahead to build on our partnerships and collaborations both near and far, from exploring synergies with our neighbour the Institut de Biologia Molecular de Barcelona (IBMB) in February to building links with Israeli institutes on the Prime Minister of Catalonia's official visit in November. As every year, 2013 had its 'firsts': one research group and their colleagues in support services put the 'fun' back into funding with IBEC's initial – and extremely successful – venture into crowdfunding.

Of course, none of this would have been possible had it not been for the way that each and every member of IBEC pulled together and gave their utmost throughout the year. I'm proud to be the new Director of this unique and extraordinary community.

Josep Samitier
*Director of IBEC*

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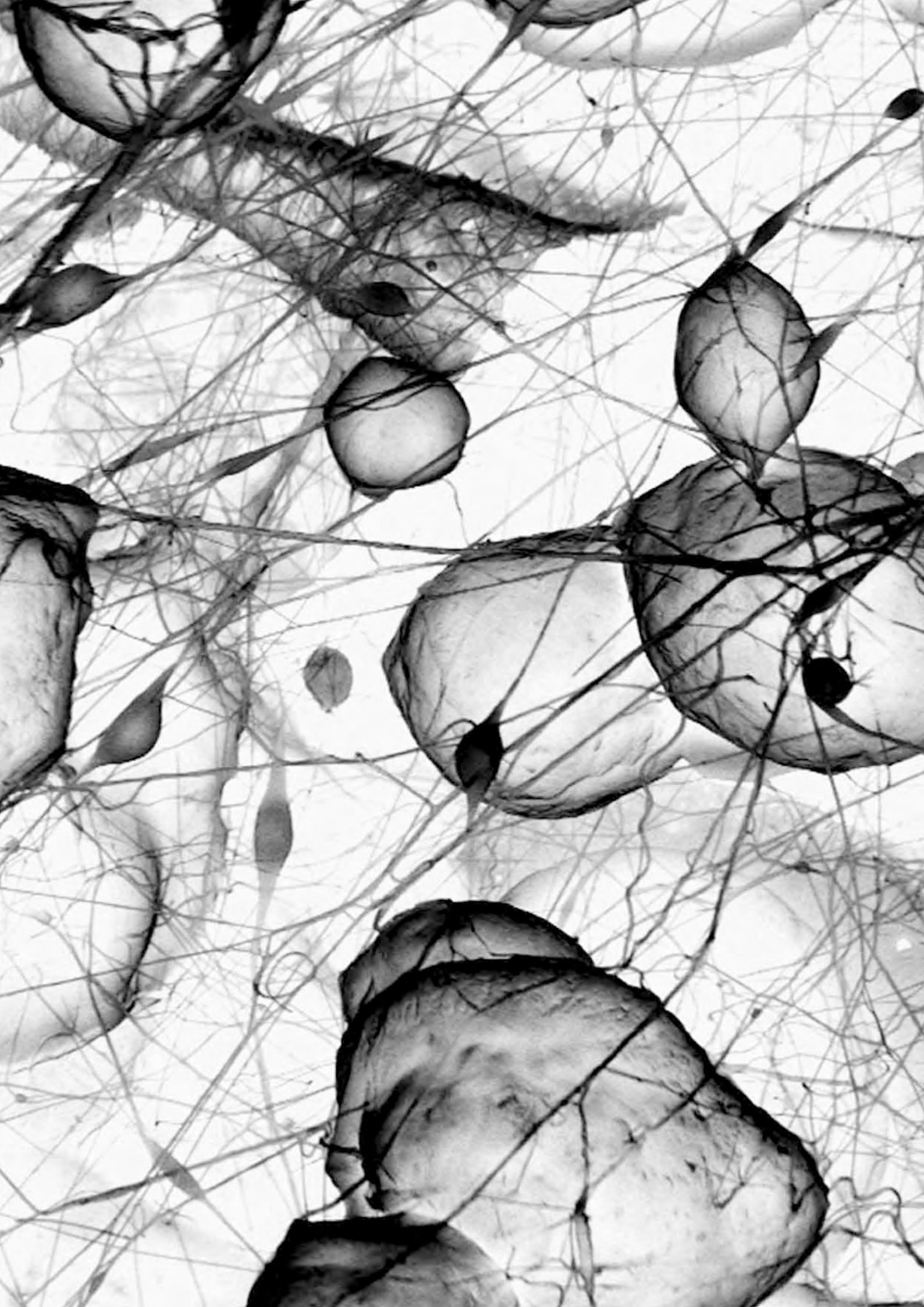
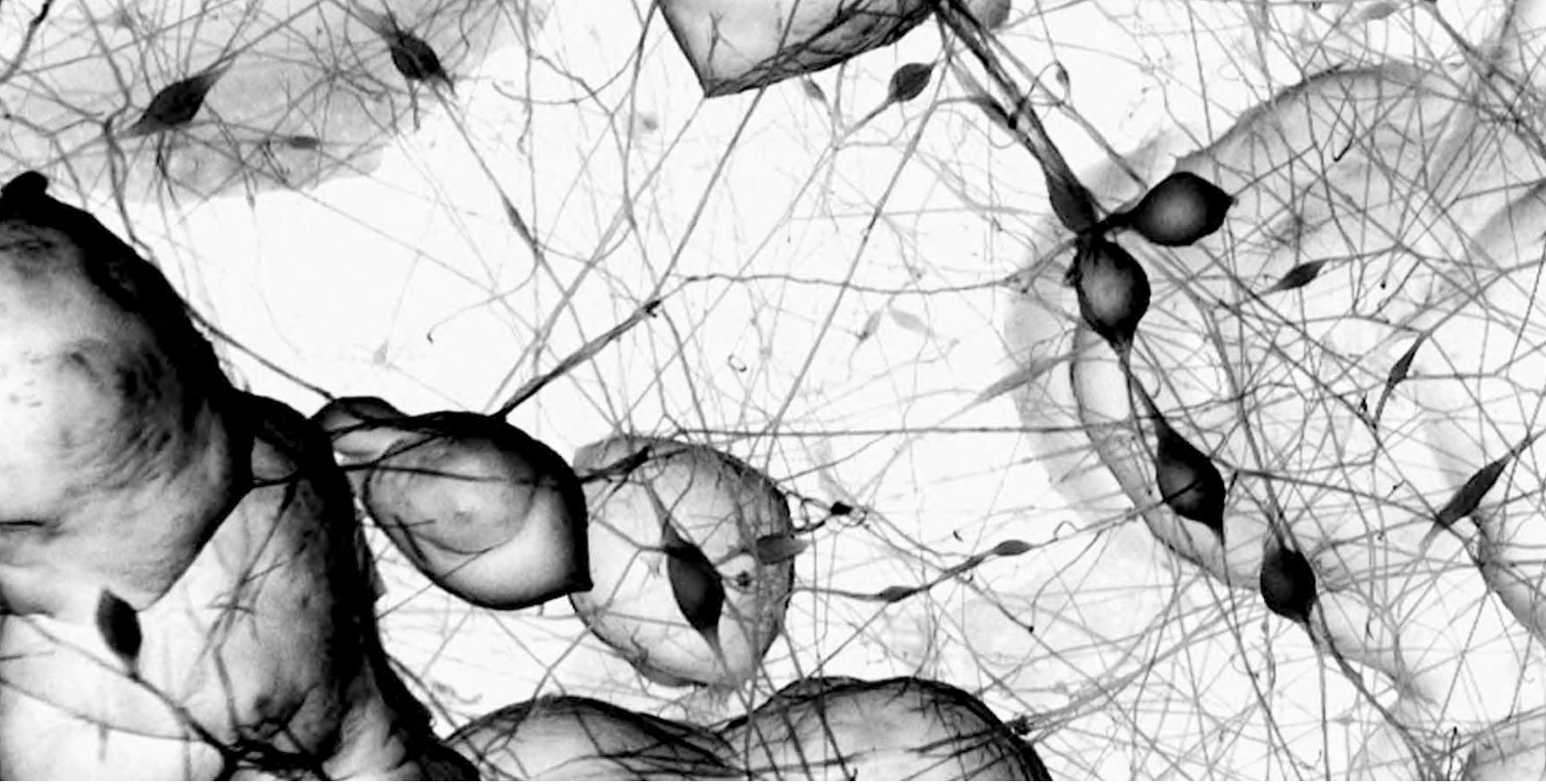




# 2013 in review

# News Highlights

## February 2013

### Change of ownership for Nanotechnology Platform

From February, the Nanotechnology Platform at the Parc Científic de Barcelona (PCB), which for many years has helped users develop innovative cutting-edge research incorporating micro- and nanotechnologies in a wide variety of fields, transferred to the ownership and management of IBEC (see pages 120-123). The acquisition of the high-tech platform was part of the institute's longer-term strategic plan to create new scientific–technical facilities in nanofabrication and bionanocharacterization. Among other equipment and services, these new facilities will incorporate the 150m$^2$ Platform, which includes a cleanroom and state-of-the-art fabrication and characterization tools.

### Researcher awarded ERC top-up grant

IBEC's Pau Gorostiza was one of the researchers selected to benefit from the European Research Council (ERC)'s top-up funding scheme 'Proof of Concept'. Worth up to €150,000 each, these grants provide funding for researchers, who are already ERC grantees, to bridge the gap between their research and marketable innovation.

Pau is one of only four researchers from Spanish institutions (3 of them in Catalonia) to be awarded this grant, from the total of 60 awardees spanning all the European member states. With his ERC Starting Grant 2007, Pau developed an innovative approach to control the activity of drugs with light in cell culture systems. The PoC grant will allow him to go a step further by testing his new methods on important pharmacological target receptors and test them *in vivo*.

### Further Pablo Motos support for IBEC research

Junior group leader Eduard Torrents was the recipient of a third "Pablo Motos" award from the Federación Española de Fibrosis Quística (FEFQ) to continue his research into identifying new antimicrobial molecules to fight the bacteria that cause complications and even death in people with cystic fibrosis.

Eduard's project was the one selected from 14 proposals, both scientific and social, to receive the national prize, which is now in its fourth year. Eduard's previous Pablo Moto awards, which he won in 2009 and 2010, helped him explore ribonucleotide reductase as a therapeutic target against bacterial pathogens in cystic fibrosis, and now he will focus on tackling a particularly problematic bacteria, *P. aeruginosa*, using new antimicrobials developed on a biofilm.

The award is made possible by Pablo Motos, TV personality and creator of the show 'El

Left: researchers using the newly-acquired Nanotechnology Platform; below, IBEC Director Josep Samitier addresses the Obra Social "la Caixa" press conference.

Hormiguero', who donates the royalties from his book 'Frases célebres de niños' to the FEFQ.

## "Nanomicrowave" cooking up something new

A new European Marie Curie Initial Training Network involving IBEC's Nanoscale Bioelectrical Characterization group is attempting to bring research into microwaves – which are used in a host of applications such as telecommunications, microwave ovens and radar – to a whole new level.

'Microwave Nanotechnology for Semiconductor and Life Sciences' or Nanomicrowave, which involves nine other partners from UK, Austria, France and Italy, makes use of recent developments in nanotechnology to explore the interaction of microwaves with matter at much smaller scales than before, namely micrometres to nanometres. Current applications of microwave technologies are based on the interaction of microwaves and matter at supra-wavelength scales: that is, bigger than centimetres.

"At these new sub-wave length scales, we expect that fascinating new physical phenomena may appear," explains Gabriel Gomila. "These will give rise to new applications of microwave technologies in many fields such as nanoelectronics, nanospintronics, nanobiology and nanomedicine." His group leads the workpackage devoted to the applications of microwave nanotechnologies to biological systems and contribute their expertise in nanoscale electrical measurements in biology to the FP7-funded project.

# March 2013

## Recercaixa funding for robotics project

IBEC Senior Researcher Joan Aranda's project 'InHANDS: robòtica interactiva per a l'assistència humana en l'entorn domèstic' was awarded funding by the RecerCaixa programme. At a ceremony at CosmoCaixa in March, Joan and the other representatives of the 25 winning research projects – which were selected from a total of 369 applications – were officially awarded the grants, which are made possible by the Obra Social "la Caixa" and the Associació Catalana d'Universitats Públiques.

Joan's project, which receives one of the largest portions of the €1.7m total, fulfilled the requirements of the programme's call under the theme of 'Disability', which looks for projects aimed at adapting the home or living environment to aid the rehabilitation or care of people with disabilities. InHANDS will use the Robotic's group's assistive kitchen to develop a system able to interprete 'visually' and in real time the gestures of a user.

# April 2013

## IBEC a "benchmark in pioneering research projects with great economic potential"

IBEC participated in an event and press conference to present the first results of the projects promoted by the five research centres included in the Obra Social "la Caixa"'s pilot scheme for funding research evaluation and technology transfer.

IBEC is one of five "benchmarks in pioneering research projects with great economic potential", according to the bank, which has allocated €2.5m over two years to promote and stimulate research in Catalonia and boost the economy. The other participating institutions are ICIQ, ICFO, IRB and CRG. IBEC's project, "Sistemes de diagnòstic i teràpia basats en la integració de noves tecnologies nano bio info i cogno" provides the Strategic Research Innovation Initiative ($SRI^2$) within which the institute's three 'flagships' – Nanomedicine, Cell Engineering and Intelligent Healthcare – are framing their interdisciplinary projects.

# May 2013

## Josep Samitier named as new Director of IBEC

At a Board of Trustees meeting, Josep Samitier was appointed as the new Director of IBEC. There were a total of nine candidates, four of them from abroad, of which three were selected for consideration by the Board.

"As Director I will maintain a continuity of IBEC's main objectives, while also reviewing and renewing our strategy to incorporate new ideas and meet present challenges," said Josep on his appointment. "This will require the solid cooperation of the whole IBEC community."

In his farewell message to staff, leaving Director Josep A. Planell described his seven years at IBEC as 'the most fulfilling of my life from a professional point of view', and conveyed his confidence in Josep Samitier's ability and dedication to help IBEC progress towards even higher achievements.

## June 2013

### Funding from BBVA for outreach project

At a ceremony in Sabadell, IBEC received its funding award for an outreach project from the Fundació Antigues Caixes Catalanes (formerly Unnim Caixa) of the BBVA.

Pilar Jiménez, representing IBEC's Communications and Outreach Unit, and Head of Finance Ana González collected the prize, which went on to fund the unit's successful proposal for a series of scientific talks on nanobiotechnology, robotics and tissue engineering to be held at libraries and civic centres in Barcelona from October to December. IBEC's project was one of the 42 chosen from nearly 250 proposals sent in this year.

### An audience of thousands

IBEC's Robotics group leader Alícia Casals represented Catalonia's scientific community when she and two doctors, a psychiatrist and a biomedical researcher read out a poem at the Concert per la Llibertat at Camp Nou on 29th June.

Alícia, along with Bonaventura Clotet (IrsiCaixa), Manel Esteller (IDIBELL), Miquel Casas (UAB) and Pere-Joan Cardona (Germans Trias i Pujol), contributed a reading of 'Ara Mateix', a poem by Catalan poet Miquel Marti i Pol, during the four-hour event. The evening featured freedom-focused songs and readings, and involved musicians, writers, actors, *castellers*, civic representatives and many others.

## July 2013

### Director of ISCIII visits IBEC

In July IBEC had a visit from Dr. Toni Andreu, the Director of the Instituto de Salud Carlos III (ISCIII), the body which coordinates the Fund for Health of Spain (FIS) for the Spanish Ministry of Economy and Knowledge. Dr. Andreu enjoyed a presentation about IBEC from Director Josep Samitier and Managing Director David Badía before visiting the labs, where group leaders Daniel Navajas, Pere Roca, Xavier Trepat, Pau Gorostiza and Ángel Raya explained some of their recent research results.

The visit came shortly after the publication of the ISCIII's new Health Research and Development Strategy, their main instrument for strengthening research and human resources in the National Health System. The Strategy, which is aligned with the EU's Horizon 2020 programme, includes nanomedicine and robotics among other research areas, so it was an ideal opportunity to discuss how IBEC can contribute.

## September 2013

### Josep A. Planell first Spanish scientist to receive European biomaterials prize

Josep A. Planell, founding director of IBEC, was presented with the European Society of Biomaterials' prestigious George Winter prize at their annual conference held in Madrid.

He was the first scientist from Spain to be awarded the prize, which recognizes researchers who have contributed significantly to the field of biomaterials through basic, experimental or clinical research. Some of the most outstanding acheivements of his illustrious career, which has lately focused on the research and development of bone cements, have included the creation of biomaterials based on porous calcium phosphate composites for bone regeneration, and the development of new angiogenic materials able to trigger new vessel formation and induce vascularisation.

In April Josep, who maintains a research position at IBEC, left the institute's directorate

after seven years to take over as Rector of the Open University of Catalonia.

## IBEC researcher in first class of d·HEALTH Barcelona

A senior researcher in IBEC's Nanobioengineering group, Mateu Pla, was one of the first class of just 12 fellows chosen for the first Design Health Barcelona (d·HEALTH Barcelona) higher education programme, which aims to bring innovation to the Catalan health sector and put the city in the first division for innovation in medical technologies. The 2013-2014 class selected for the programme, which is the flagship of Biocat's MOEBIO initiative and is inspired by Stanford University's prestigious Biodesign Fellowship, comprises 12 "brilliant young people" from the USA, Germany, Italy and Spain, who between them have 105 scientific publications and 6 patents.

# October 2013

## World experts convene for nanomedicine workshop

Experts in nanomedicine from all over the world convened to discuss the state-of-the-art of the field at the 2nd UAB Campus d'Excel·lència Internacional (CEI) Workshop on Nanomedicine in October.

IBEC director Josep Samitier addressed the audience on the subject of 'Nanomedicine in Catalonia: Present and Future' at the event, which aimed to foster dialogue and knowledge transfer between key scientists in nanotechnology on how to tackle current issues and future challenges. The day also provided a platform for groups doing basic research to connect with those involved in applied research, as well as with biotech companies interested in new patents and offering the capacity to develop applications.

## B·Debate reviews what nanotechnology can offer health

The B·Debate event 'Nanotechnologies in Health: Current Challenges and Future Prospects', organised by ICN and IBB in collaboration with IBEC, UABCEI and Nanonica, took place at Barcelona's CosmoCaixa museum. IBEC group leader Pau Gorostiza gave a talk on the control of neurotransmission with light on the first day of the three-day event, which was devoted to discussing the fundamental aspects of drug delivery, diagnostics, novel applications, and the risks related to nanotechnologies.

The B·Debate events, an initiative of Biocat and the Obra Social "la Caixa", are top-notch scientific meetings that invite experts from all over the world to get together with scientists working in Barcelona and Catalonia. They aim to create a think-tank atmosphere to promote vivid discussions, generate innovative ideas and draw powerful conclusions.

Left: Josep A. Planell bids farewell to the administration staff; Pau Gorostiza takes questions at the B·Debate 'Nanotechnologies in Health: Current Challenges and Future Prospects'.

## IBEC crowdfunding project a success

IBEC's very first venture into crowdfunding went live on the Goteo crowdfunding website in October, and after just 30 days had accumulated the requisite minimum of €8000 in funding from wellwishers.

The Dermoglass project, which involved Biomaterials for Regenerative Therapies group members Elisabeth Engel, Melba Navarro, Oscar Castaño, Miguel Angel Mateos and Soledad Pérez, was chosen to be put forward for crowdfunding under the UPC's new SUMA initiative, which identifies suitable projects and collaborates with Goteo, which promotes them online and collects the donations.

Dermoglass is a special dressing which accelerates the regeneration of the skin in hard-to-heal skin ulcers, which are a major public health problem particularly for the elderly, bedridden and wheelchair-bound. Other dermal dressings already on the market don't tackle the problem of healing in the way that the group's innovative technology does: it stimulates vascularization in the damaged tissue so that the ulcer heals more quickly. "The money we raised from crowdfunding will ensure that our dressing can proceed to preclinical testing," says Elisabeth Engel, junior group leader in the Biomaterials for Regenerative Therapies group.

# November 2013

## A helping hand for budding surgeons

A prototype developed by IBEC's Robotics group and their collaborators was presented at the European Society for Gynaecological Endoscopy's 22nd Annual Congress in Berlin.

Surgitrainer, a training platform for laparoscopic surgery – sometimes known as keyhole surgery – has been developed by Alícia Casals' group at IBEC together with researchers at the Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau and at the UPC. The training platform incorporates a number of features that improve on existing alternatives: not only does it test users' skills in keyhole surgery in conditions close to reality, it analyzes and evaluates the tests in real time without intervention or additional staff supervision. Potential applications of the equipment could be to help trainee surgeons achieve the standard accreditations they need to qualify.

Surgitrainer is currently at the fully operational prototype stage, and Alicia's group is performing tests with the collaboration of surgeons at the Hospital de la Santa Creu i Sant Pau.

## Pfizer award for IBEC/Vall d'Hebron hemophilia collaboration

A Spanish collaboration, including researchers from IBEC, was awarded the prestigious ASPIRE Europe 2013 Hemophilia Research Award from Pfizer, the world's largest research-based pharmaceutical company in November.

The project, which is led by Dr. Rafael Parra at Vall d'Hebron Hospital and also involves researchers from IBEC and the Vall d'Hebron Research Institute, is one of only five selected from submissions from 10 different European countries, and aims to develop a high-throughput platform for hemophilia A drug screening and gene correction using patient-specific cells. IBEC's Control of Stem Cell Potency group's role in the project is the development of a genuinely human model of Hemophilia A through the generation of patient-specific induced pluripotent stem cells.

## Josep Samitier accompanies president of Catalonia on Israel mission

IBEC director Josep Samitier was one of 20 scientists who accompanied President Artur Mas on his official visit to Israel in November.

The delegates, who also included researchers from CRG and ICFO, took part in the visit to forge research alliances 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 as compared to Germany which has only 22. Both countries have also attracted similar levels of funding under FP7.

The delegation visited the Israel government and four major universities in the country:

the Hebrew University of Jerusalem, Tel Aviv University, the Technion and the Weizmann Institute of Science, not only to discuss possible collaborations but also to do some 'fact-finding'. They were trying to identify why Israel, at the same size, has been so much more successful when it comes to start-ups and employment rate, and to learn about the country's effective technology transfer protocols.

The visit culminated in the signing of a colaboration agreement between Catalonia and Israel to invest in research exchange programmes and training, including as entrepreneurship, business creation and innovation programmes for postdocs.

## Marató money for tumor project

Junior group leader Pere Roca-Cusachs received funding from 2012's La Marató de TV3 for his project "Stromal stiffness in Tumor Progression".

The project, which is coordinated by Pere and also involves the group of Dr. Miguel Ángel del Pozo from the Centro Nacional de Investigaciones Cardiovasculares (CNIC, Madrid) was one of the just 42 chosen from 317 submitted to the call for research connected with cancer in February this year. The foundation announced the winning projects on 29th October after evaluation by a Scientific Advisory Committee of 257 international cancer experts.

"One of the main features of tumors is that they are stiffer than surrounding tissue, and this directly impacts their progression. Although this has been known for a long time, we don't know why or how it happens," said Pere, who leads a junior group under IBEC's Tenure Track system. "Our project aims to identify the molecular mechanisms involved, potentially revealing new targets and biomarkers for cancer therapy."

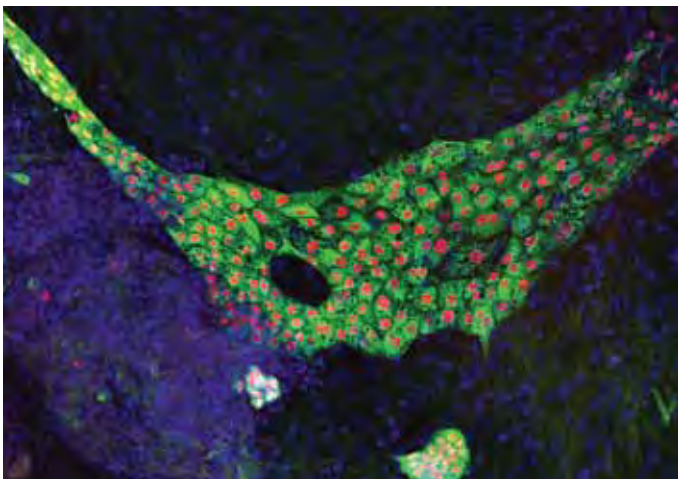
# December 2013

## IBEC scientist in launch of Barcelona Christmas lectures

Control of Stem Cell Potency group leader Ángel Raya was one of the first two speakers at a brand new series of public lectures in Barcelona.

Inspired by the BBC's prestigious Christmas Lectures in the UK, Ciència al Nadal was organised by the Institute of Evolutionary Biology (UPF-CSIC) and supported by the Fundación Botin, ICREA, the Biomedical Research Park (PRBB) and the Center of Contemporary Culture of Barcelona (CCCB).

The other speaker at the launch of the lectures, which took place on 19th December at the PRBB, was Maria V. Sanchez-Vives (ICREA/IDIBAPS).



Left: Human liver precursors grown in the laboratory at IBEC from iPS cells generated from a patient with hemophilia A. Below: postdoc Alberto Elosegui and Pere Roca-Cusachs (second and third from left) at the La Marató de TV3 ceremony.

# Scientific Highlights

## January 2013

### A step towards CNS repair

Researchers from IBEC and the University of Barcelona revealed a promising new strategy for regenerating the central nervous system in the journal *Biomaterials* in January.

Despite recent advances in understanding the mechanisms of nerve injury, tissue-engineering solutions for repairing damage in the CNS remain elusive, owing to the crucial and complex role played by the neural stem cell (NSC) niche. This zone exerts a tight control over many crucial tasks such as growth promotion and the recreation of essential biochemical and physical cues for neural cell differentiation. According to Zaida Álvarez of IBEC's Biomaterials for Regenerative Therapies group, "to develop tissue-engineering strategies to repair damage to the CNS, we need to design biomaterials that mimic the NSC niche."

In the study headed by Soledad Alcántara of the UB, the team tested types of polylactic acid (PLA) with different proportions of isomers L and D/L, a biodegradable material allowing neural cell adhesion and growth, as materials for nerve regeneration. They found that one type, PLA with a proportion of isomers of 70/30, maintained the important pools of neuronal and glial progenitor cells *in vitro*. PLA 70/30 was more amorphous, degraded faster and, crucially, released significant amounts of L-lactate, which is essential for the maintenance and differentiation of neural progenitor cells. "The aim of the research was to find a biomaterial able to sustain the population of neural stem cells and to generate new differentiated cells in order to start the development of an implant that allows brain regeneration," explains Dr Alcántara.

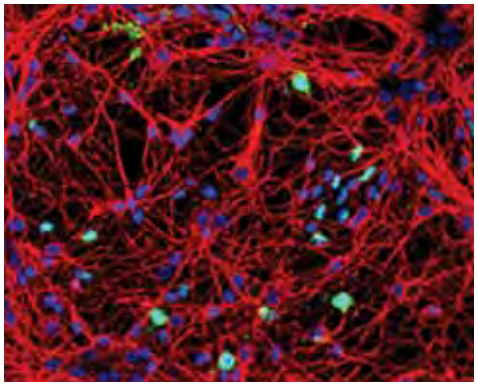
"The mechanical and surface properties of PLA70/30 make it a good substrate for neural cell adhesion, proliferation and differentiation," adds Zaida. "The physical properties of this material and the release of L-lactate when it degrades, which provides an alternative oxidative substrate for neural cells, act synergistically to modulate progenitor phenotypes."

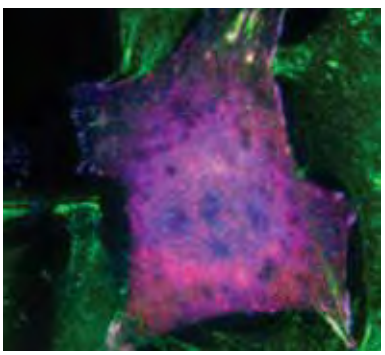
The results suggest that the introduction of 3D patterns mimicking the architecture of the embryonic NSC niches on PLA70/30-based scaffolds may be a good starting point for the design of brain-implantable devices. "These will be able to induce or activate existing neural progenitor cells to self-renew and produce new neurons, boosting the CNS regenerative response *in situ*," says Zaida. Enabling the CNS to regenerate could open doors to promising new strategies to tackle accidental damage, as well as numerous diseases like stroke and degenerative disorders such as Parkinson's.

## February 2013

### Somnoalert® presented to the world

The new technology to combat dozing off when driving developed by IBEC, UB and





Left: "A step towards CNS repair": neuronal cell cultures through a confocal microscope. The cytoskeleton is stained red, the nuclei blue and proliferative nuclei green.

Right: "Stepping up our understanding of cellular function": a cell marked with the two types of molecules, alpha-actinin (green) and talin (red). Another molecule, an integrin, appears in blue.

industry partner Ficosa was presented at 2013's GSMA World Mobile Congress in Barcelona.

The drowsiness alerter, Somnoalert®, is a smart phone application that uses inertial sensors and GPS data to detect movements that are characteristic of nodding off at the wheel, such as deviation from the driving lane, or sudden corrections. A later prototype also incorporates biomedical sensors to analyze respiration data.

The GSMA World Mobile Congress is the industry's biggest conference and is set to attract around 70,000 participants from more than 200 countries, including more than 3,000 members of the press.

## March 2013

### The 'double-whammy' that could reveal a promising strategy for Parkinson's treatments

In March an IBEC researcher and his collaborators revealed an important biological mechanism which could shed new light on how best to develop treatments for Parkinson's disease.

Ángel Raya, who heads IBEC's Control of Stem Cell Potency group, and his collaborators in Italy and the USA have been looking at an important gene, dardarin, mutations of which have been found to be the most common cause of familial Parkinson's. The normal function of dardarin or how mutations lead to the disease, however, have long been elusive.

In the paper published in *Nature Neuroscience*, the researchers revealed their discovery that dardarin is broken down by a cleaning-up process called autophagy, which enables the recycling of amino acids of degraded proteins and eliminates abnormal or damaged ones. But dardarin uses a very specific type of autophagy and does it in a rather peculiar way, so that its mutations are also able to strike out at autophagy itself and undermine its efficiency.

As if that's not bad enough, this has an effect on another crucial process that can lead to Parkinson's: the build-up of a protein called α-synuclein. Usually, α-synuclein – or α-syn – is also degraded by autophagy; but when autophagy is compromised by dardarin, α-syn is able to accumulate.

This 'double-whammy' attack inhibiting autophagy could underlie toxicity in Parkinson's disease. "In other words, two dominant features that cause Parkinson's disease converge at the same step," explains Ángel.

This new discovery – which has been made possible by the use of induced pluripotent stem cells from patients, already proving that it is applicable to humans – may help uncover specific strategies for dealing with or even preventing the neurodegenerative motor disorder. "As a result, interventions aimed at enhancing autophagy activity or at preventing its decrease may prove to be valuable, not just for the treatment of Parkinson's disease but also for other age-related disorders resulting from alterations in cellular self-regulation," says Ángel.

### Stepping up our understanding of cellular function

Also in March, an IBEC researcher and his collaborators uncovered the crucial role of two molecules in enabling cells to communicate with their environment.

You might not think that cells have much in common with cars, but it turns out that they use a similar 'gear' mechanism to transmit the forces to accomplish important functions such as cell migration, moving muscles or simply maintaining tissue integrity. Instead of using gears, however, cells employ molecules.

A team led by Pere Roca-Cusachs from IBEC discovered how cells use two of these molecules, talin and alpha-actinin, to connect with and transmit forces to their surroundings, "a bit like when you're driving a car on a mountain road, and a steep slope appears. To make sure that you can make it up the slope, you reduce gears, which improves force transmission from the motor to the wheels," says Pere. By using nanotechnologies able to both detect and apply forces to cells, the researchers have unveiled a crucial mechanism by which cells 'switch gears' by using one molecule or the other, regulating force transmission and their connection with their environment.

"As cellular forces are essential for crucial processes such as the development of embryos or wound healing, as well as in undesirable ones such as cancer progression, this discovery represents an important step in our understanding of cell function, with implications in both health and disease."

## May 2013

### Shedding new light on myelination and potential MS therapies

Research done at IBEC and published in *Cell Mol Life Sci* in May revealed a hopeful new lead in the quest to understand neurodegenerative diseases such as multiple sclerosis.

Ana Bribián, who carried out the study during her postdoc IBEC's Molecular and Cellular Neurobiotechnology group, and her new colleagues at Toledo's Hospital Nacional de Parapléjicos shed light on the role played by a particular enzyme in regulating the cells which are crucial to avoid MS.

Oligodendrocyte precursor cells (OPCs) in the central nervous system differentiate into oligodendrocytes, which produce myelin to protect and insulate the long nerve cells in the brain and spinal cord. MS is known to be a demyelinating disease: that is, a disease that results from the progressive breakdown of myelin in the central nervous system. When this happens, the central nervous system reacts by using proliferating adult OPCs to remyelinate. However, several factors affect the production and differentiation of these OPCs, one of them being the enzyme PDE7, which compromises their proliferation, differentation and survival.

The researchers found two new inhibitors for PDE7 which, when applied, reduced the OPCs' death rate and accelerated their maturation into oligodendrocytes which could then carry out the remyelination process.

"Our findings reveal new roles for PDE7 in regulating OPC survival and differentiation, both during brain development and adulthood," says Ana, who was at IBEC until April 2012. "This may further the understanding of myelination and help develop therapeutic remyelination strategies for MS treatment."

## June 2013

### Cells play 'tag' to determine direction of movement

Researchers at IBEC, the UB and their collaborators found that cells in our bodies, when moving collectively, carry out something similar to a game of 'tag' to coordinate their movement in a particular direction.

The scientists looked at cells in the neural crest, a very mobile embryonic structure in vertebrates that gives rise to most of the peripheral nervous system and to other cell types in the cardiovascular system, pigment cells in the skin, and some bones, cartilage, and connective tissue in the head.

They saw that, during development, these neural crest cells 'chase' other types of cells – so-called placodal cells, which give rise to the sensory organs – which dash away when approached, thus propelling the cell sheet in a certain direction.

"The effect can also be likened to a donkey and carrot effect, with the neural crest cells – the donkey – chasing but never quite reaching the carrot, the placodal cells," explains Xavier Trepat, who heads IBEC's Integrative Cell and Tissue Dynamics group. "The chasing occurs when a signaling protein, Sdf1, is present, while the 'run' effect is triggered by a different protein, N-Cadherin."

The researchers' findings shed new light on collective cell migration, a critical process in development and wound healing, but which is also inherent to the development of diseases such as cancer. Understanding more about how and why cells move the way they do can lead to valuable insights into how and why cancers occur and spread.

### Pioneering breakthrough in drugs controlled by light

A cooperation between chemists, biotechnologists and physicists headed by Pau Gorostiza from IBEC and Ernest Giralt from the Institute for Research in Biomedicine (IRB) led to a breakthrough that will favor the development of light-regulated therapeutic molecules.

The photo-switchable molecules to control protein-protein interactions in a remote and non-invasive manner will serve as a prototype to develop photo-switchable drugs, whose effects would be limited to a given region and time, thus reducing the side effects on other regions.

The breakthrough published in the German journal of reference in chemistry *Angewandte Chemie* in June received recognition as a "Very Important Paper", a distinction that only

5% of the articles accepted achieve, and featured on the cover of the July issue.

The scientists synthesized two peptides which, on irradiation with light, change shape, thereby allowing or preventing an specific protein-protein interaction. The association of these two proteins is required for endocytosis, a process by which cells allow molecules to cross the cell membrane and enter. Laura Nevola, a postdoc in Dr. Giralt's lab, and Andrés Martín-Quirós, a PhD student at IBEC, co-authors of the study, spent four years working on the design of photo-sensitive peptides. The team was been supported by Dr. Artur Llobet's group at IDIBELL.

"Photo-sensitive peptides act like traffic lights and can be made to give a green or red light for cell endocytosis," explains Dr. Giralt. "These molecules allow us to use focalized light like a magic wand to control biological processes and to study them," adds Pau, ICREA professor and head of the Nanoprobes and Nanoswitches group at IBEC.

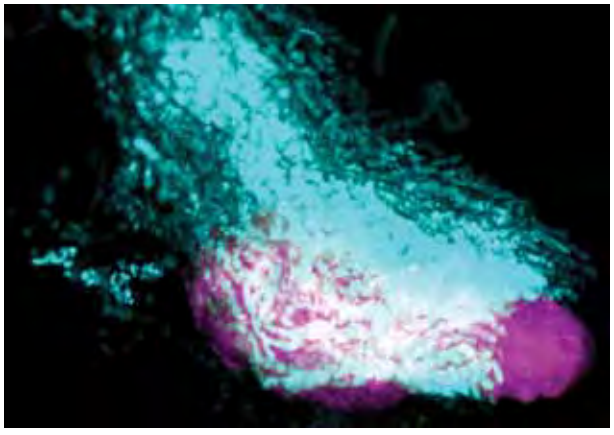
The researchers highlight the immediate applicability of these molecules to study, for example, *in vitro* endocytosis in cancer cells – where this process is uncontrolled – which would allow selective inhibition of the proliferation of these cells. Also, they would also allow the study of developmental biology – where cells require endocytosis to change shape and function, processes that are orchestrated with great spatial and temporal precision. In this context, photo-sensitive peptides will allow the manipulation of the complex development of a multicellular organism by means of light patterns.

"We are now working towards a general recipe to design photo-switchable inhibitory peptides that can be used to manipulate other protein-protein interactions inside cells by applying light," explains Pau, who came up with the idea of manipulating biological and pharmacological processes through the use of light after spending five years specializing in this field at the University of California in Berkeley. "The most immediate therapeutic applications we can expect is for diseases affecting superficial tissue such as the skin, the retina and the most external mucosal membranes."

The modification of biological processes by means of light is leading to the development of cutting-edge tools for biology and medicine and opening up new research fields, such as optopharmacology and optogenetics. The combination of drugs with external devices to control light may contribute to the development of personalized medicine in which treatments can be adapted to each patient, limiting the time given regions are treated, thus markedly reducing unwanted effects.

## Unexpected discovery about the ways cells move could boost understanding of complex diseases

Researchers at IBEC and Harvard School of Public Health found that epithelial cells—the type that form a barrier between the inside and the outside of the body, such as skin cells—move in a group, propelled by forces both from within and from nearby cells to fill any spaces they encounter. Their study, which appeared on the cover of *Nature Materials* in September, may provide scientists with crucial information about



Left: "Cells play 'tag' to determine direction of movement": trajectories of neural crest cells (blue) chasing placode tissue (purple). (© UCL).

Above: "Pioneering breakthrough in drugs controlled by light": Researchers at IRB Barcelona and IBEC design the first peptides regulated by light to modulate biological processes. @ Laura Nevola, IRB.

disease mechanisms such as the spread of cancer or the constriction of airways caused by asthma.

Using a technique called monolayer stress microscopy—which they invented themselves—they measured the forces affecting a single layer of moving epithelial cells. They examined the cells' velocity and direction as well as traction—how some cells either pull or push themselves and thus force collective movement. As they expected, the researchers found that when an obstacle was placed in the path of an advancing cell layer—in this case, a gel that provided no traction—the cells moved around it, tightly hugging the sides of the gel as they passed.

However, the researchers also found something surprising—that the cells, in addition to moving forward, continued to pull themselves collectively back toward the gel, as if yearning to fill the unfilled space. The researchers dubbed this movement "kenotaxis," from the Greek words "keno" (vacuum) and "taxis" (arrangement), because it seemed the cells were attempting to fill a vacuum.

"This new finding could help researchers better understand cell behavior—and evaluate potential drugs to influence that behavior—in a variety of complex diseases, such as cancer, asthma, cardiovascular disease, developmental abnormalities, and glaucoma," explains co-author Xavier Trepat, group leader of IBEC's Integrative Cell and Tissue Dynamics group.

## August 2013

### Engineering biomaterials at the nanoscale

IBEC researchers came up with a groundbreaking new approach to create a tough, biodegradable, bioactive and entirely new material, heralding a major milestone in the production of artificial matrices for tissue engineering.

In a letter published in *Interface* in August, the Biomaterials for Regenerative Therapies group describes a new, easy and cheap method for producing glass-coated fibrous scaffolds which not only faithfully mimic the extracellular matrix of bone, but also aim to direct stem cell fate through physical and chemical interactions.

The team coated nanostructured, electrospun polymer fibres with bioactive glass, assembling hybrid nanofibres with a strong union between the fibre and the coating – effectively creating a new material, rather than simply a composite. Previous attempts, which usually involved ceramic or glass being dispersed into a polymer matrix, which improves resilience, have always resulted in a loss of bioactivity and the collapse of the architecture. "We did it the other way around, thus avoiding the usual problems that include lack of cell adhesion and too-fast degradation," explains Nadège Sachot, first author on the paper. "Working from previously published knowledge about the different components, we have managed to coordinate dissimilar compounds with different features in one hierarchical device."

The core of the fibres is polylactic acid, a well-known biodegradable polymer, which acts as a flexible foundation and gives the coated fibers tailorable surface characteristics. They will provide the right chemical signals, topography, and mechanical properties to the cells to promote differentiation into a particular cell lineage, stimulating the formation of new tissue.

The group's new protocol has possibilities in a broad range of biomedical applications that require well-defined, hierarchically engineered biomaterials with well-defined features, such as bone, vascular, skin or nervous tissue regeneration.

### Antibiotic resistance: a 'devastating' public health issue

An IBEC paper published in *Environmental Microbiology* was just one step in the right direction to tackle a major public health issue that experts say could soon be devastating.

Microbiologists led by Antonio Juárez at IBEC and their collaborators at the University of Barcelona revealed that a particular genetic element – a plasmid – that confers multiple antibiotic resistance plays a major role in the survival of Salmonella, the cause of typhoid fever in humans. The genes of this plasmid modify several features of the pathogenic bacterium, and so could be likely targets to slow or halt the infection's soaring resistance to antibiotics.

Antibiotic resistance was recently declared 'one of the greatest threats to human health today' by the WHO. Not only have some common infections or illnesses become

resistant to the antibiotics usually used to treat them, a really pressing medical problem now is the rapid rise of 'superbugs' or multidrug-resistant bacteria, which are immune to almost all of the antibiotics that are currently available. This means that some clinical procedures like organ transplants, chemotherapy or the care of premature infants could become too dangerous to carry out, as hospitals become hotbeds for highly resistant pathogens.

"We've come to a point where we need to find ways of reversing the resistance of bacteria to antibiotics, as more and more of our drugs are rendered useless against some of the most common and threatening infections and diseases," says Antonio. "Within IBEC alone, we have teams working on several different ways to overcome bacterial resistance: either developing new drugs against new targets, or interfering with those plasmids which confer resistance against the existing antibiotics that are available."

IBEC's Bacterial Infections: Antimicrobial Therapies group, led by Eduard Torrents, explores the use of different bioengineering approaches to reveal ways to eradicate multi-drug resistant bacteria. Eduard's group follows a strategy that is complementary to that of Antonio: instead of trying to deal with the plasmids that are triggering the resistance to today's antibiotics, they are trying to develop brand new drugs against new targets. They're also using nanotechnological approaches for antibiotic delivery, to improve therapeutic efficiency and minimize unwanted side effects.

Other researchers at IBEC are also involved in the fight against antibiotic resistance. TheraEDGE, a European-funded project involving IBEC Director Josep Samitier's Nanobioengineering group, is aimed at finding solutions for the early diagnosis and effective treatment of respiratory tract infections, by eliminating diagnostic uncertainties and recommending the correct course of treatment.

## December 2013

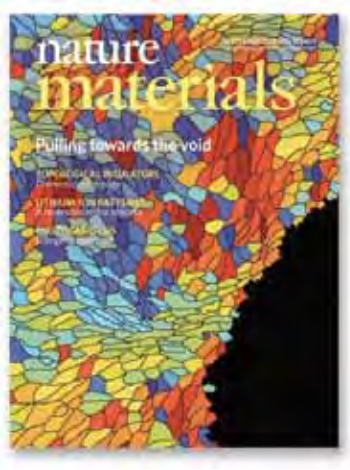
### Skin forms 'suspension bridges' for wound healing

A study on skin tissue mechanics published in *Nature Materials* demonstrated how layers of human keratinocytes (outer skin cells) form structures not unlike suspension bridges over wounds to help healing.

Scientists at IBEC and their colleagues at the Mechanobiology Institute of the National University of Singapore used microfabricated technology – miniature structures at micrometer scales – to look at how skin cells migrate to fix gaps or wounds. They showed that these regions, which have no extracellular matrix support and thus are not conducive for cell adhesion, which is essential for cell movement, are spanned by suspended multicellular "bridges" formed by layers of keratinocytes. Migrating skin cells are then able to continue to march forward as a united and homogenous group to form a protective barrier over the wound.

"These bridges are a brand new discovery. It was previously thought that this process of re-epithelialization – the restoration of skin on a wound or burn – required a 'foothold' for the cell sheets to successively migrate," explains IBEC group leader Xavier Trepat, group leader at IBEC. "Instead, it appears that the cells do something akin to slinging a rope or a bridge over the gap to then move across it."

The study was led by Lim Chwee Teck and Benoit Ladoux in Singapore.




Left: "Skin forms 'suspension bridges' for wound healing": the September edition of *Nature Materials* featuring a computer reconstruction of tissue structure around a nonadhesive region (the black area). Designed by IBEC PhD student Xavier Serra.

Right: "Engineering biomaterials at the nanoscale": A field-emission scanning electron microscope image showing the good spreading and interactions of cells (appearing as red) with a scaffold made from the PLA fibres.

# About IBEC

# 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 at the two universities which are officially associated with IBEC are listed on page 130.

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CERCA, Ministry of Economy and Knowledge, Generalitat de Catalunya

*Data correct on 31st December 2013, except: * Until 20th December 2013*

# International Scientific Committee

*Until 20th December 2013:*

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**Prof. Luigi Ambrosio** Director Institute of Composite and Biomedical Materials, University of Naples, Italy

**Mr. Léonard Aucoin** President InfoVeille Santé Ltee, Canada

**Prof. Paolo Dario** Director Polo Sant'Anna Valdera, Scuola Superiore Sant'Anna, Italy

**Prof. Jeffrey J. Fredberg** Professor of Bioengineering and Physiology Harvard School of Public Health, USA

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

**Prof. Samuel I. Stupp** Director Institute for Bionanotechnology in Medicine, Northwestern University, USA

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

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

**Prof. Bernt E. Uhlin** Professor of Molecular Biology Umeå University, Sweden

*After 20th December 2013:*

PRESIDENT **Prof. Samuel I. Stupp** Director Institute for Bionanotechnology in Medicine, Northwestern University, Evanston, IL, USA

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**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 (Administration)

In 2013 IBEC employed a staff of 31 people to carry out support activities.

**KNOWLEDGE EXCHANGE (above)**

**Head of Knowledge Exchange** Arantxa Sanz

**Project Manager** Marta Soler

**Assistant to the Director**
Pilar Ciriquián

**HUMAN RESOURCES (above)**

**Head of Human Resources**
Carol Marí

**HR Technician** Ricard Rius

**Occupational Hazards Prevention Technician**
Jordi Martínez

**Human Resources Assistant**
Gisèle Domènech

## Directorate

**Director**
Josep A. Planell (until March 2013)
Josep Samitier (from May 2013)

**Managing Director**
David Badia

**RESEARCH AFFAIRS (left)**

**Head of Research Affairs** Teresa Sanchis

**Coordinator of Project Management Office** Javier Adrián

**Project Managers** Ester Rodríguez, Juan Francisco Sangüesa (until October 2013), Guadalupe Rivero (until October 2013)

**Funding Manager** Esther Gallardo

**Research Affairs Assistant** Judith Forné

**FINANCE (right)**

**Head of Finance** Ana González

**Purchasing Technician** Mayte Muñoz

**Accounting Technician** Francisco Buenestado

**Finance Assistant** Victoria López

**Accounting Technician** Laura Casas

**IT (above)**

**IT Manager** Juli Bafaluy

**IT Technician** Francisco Contreras

**COMMUNICATIONS AND OUTREACH (below)**

**Head of Communications and Outreach** Vienna Leigh

**Coordinator of Events** Pilar Jiménez

**Coordinator of Media Relations and Branding** Àngels López

**Communications and Outreach Intern** Carolina Llorente

*For the staff list for Core Facilities, see page 122.*

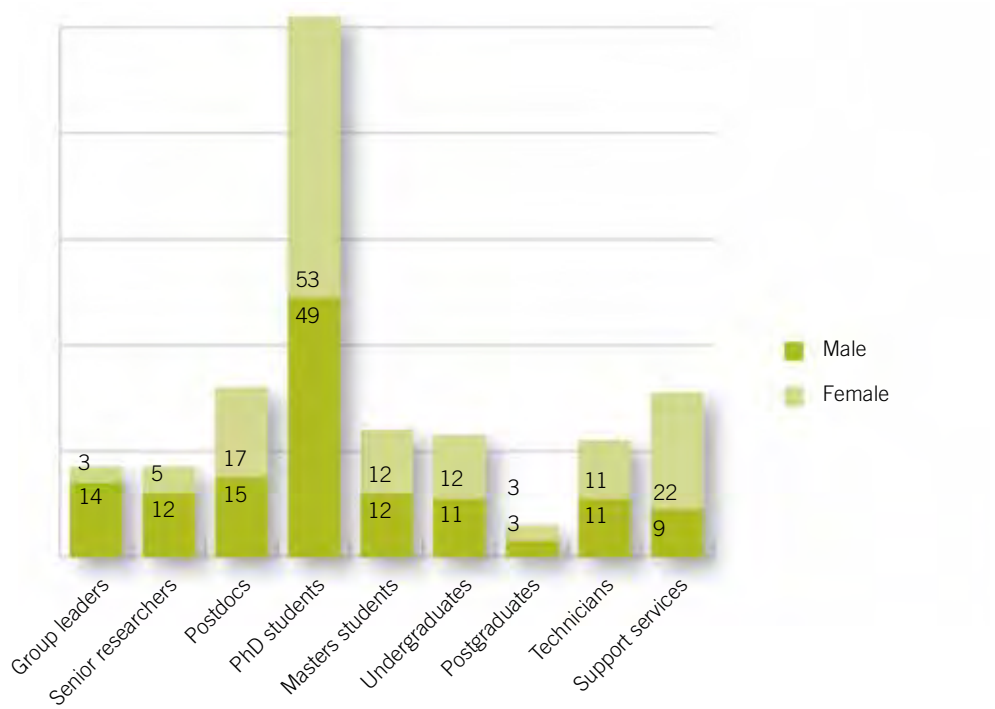
# Statistics

In 2013 IBEC's total staff, including administration staff as well as researchers, students and technicians, numbered 243. 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).

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

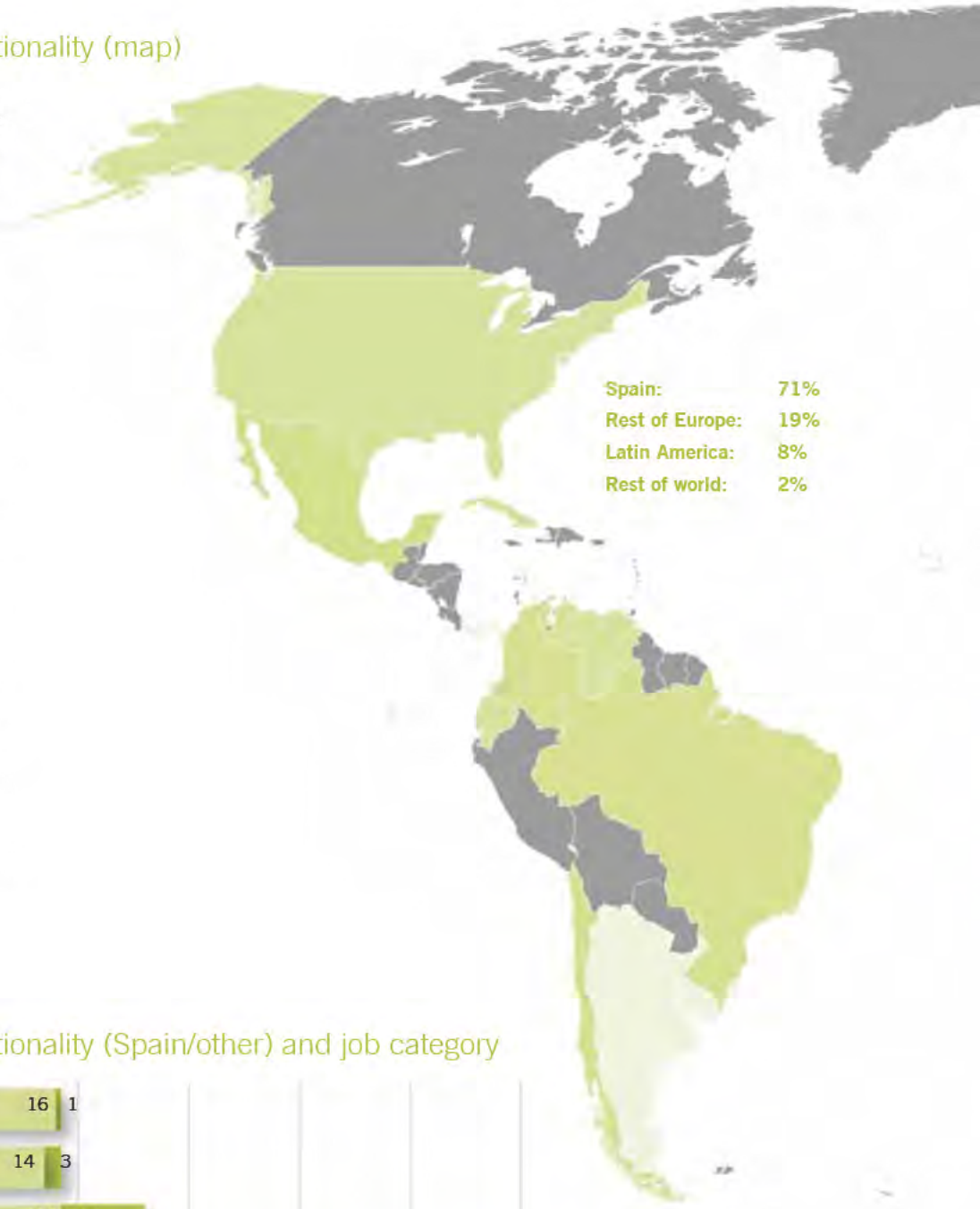

## 2. Gender of all staff


## 3. All staff by gender and job category

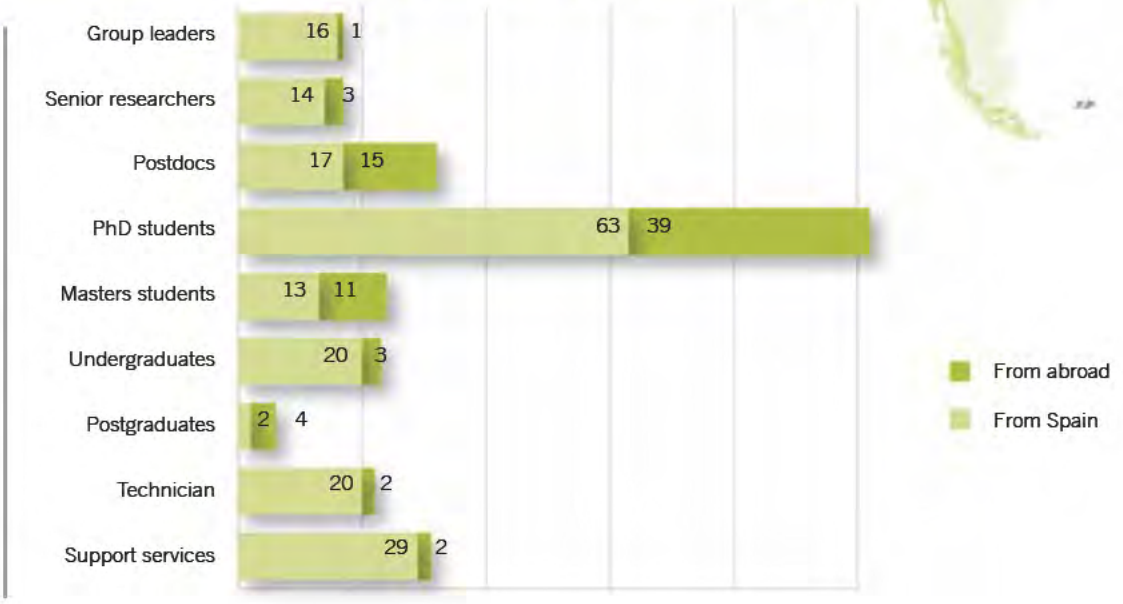


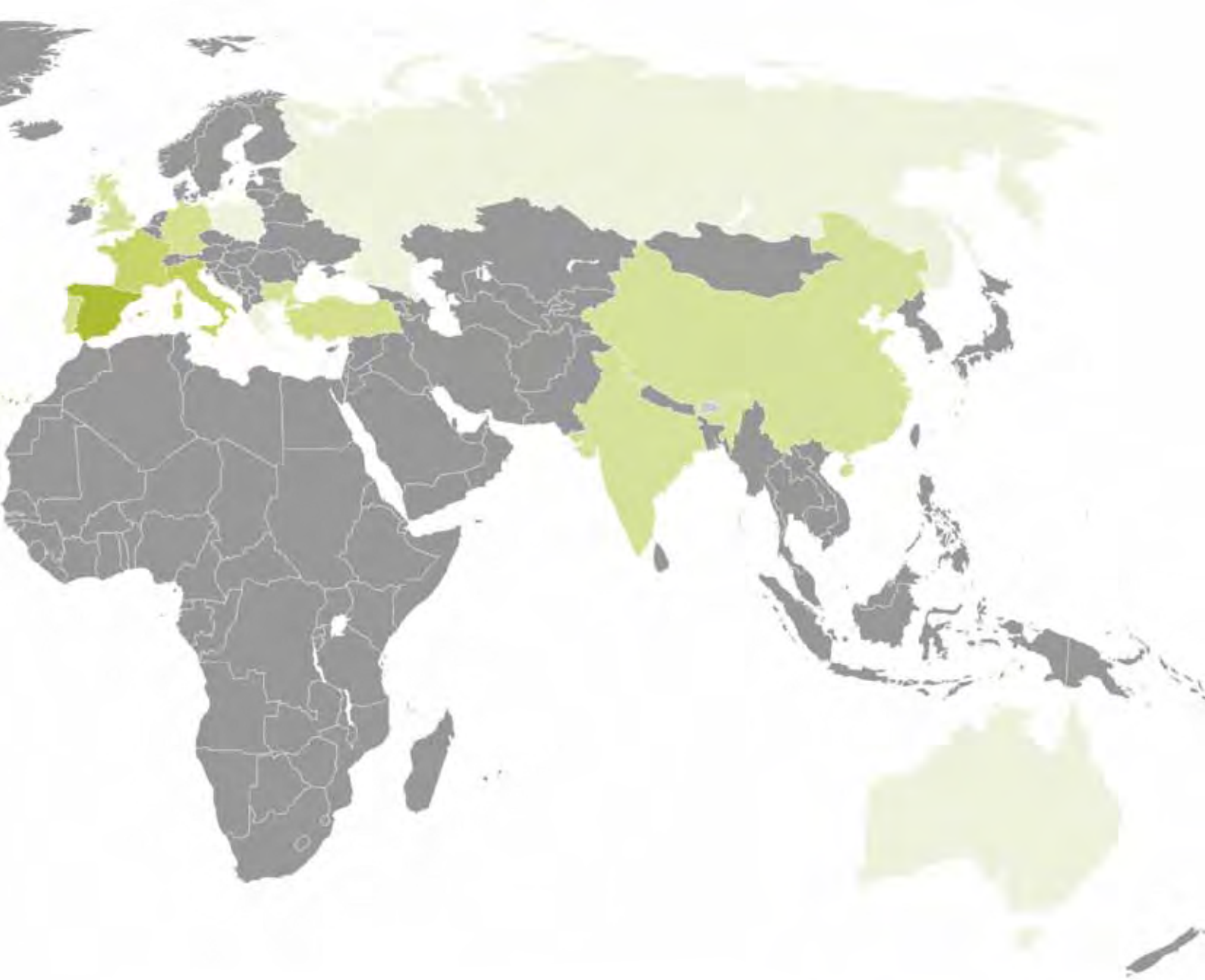
## 4. IBEC staff by nationality (map)

| | |
|---|---|
| Spain | 194 |
| Italy | 21 |
| France | 14 |
| Mexico | 4 |
| Germany | 3 |
| Portugal | 3 |
| Turkey | 3 |
| Brazil | 3 |
| Chile | 3 |
| Colombia | 3 |
| United Kingdom | 2 |
| Bulgaria | 2 |
| Cuba | 2 |
| Ecuador | 2 |
| USA | 2 |
| India | 2 |
| Venezuela | 2 |
| China | 2 |
| Argentina | 1 |
| Panama | 1 |
| Poland | 1 |
| Uruguay | 1 |
| Australia | 1 |
| Greece | 1 |
| Russia | 1 |

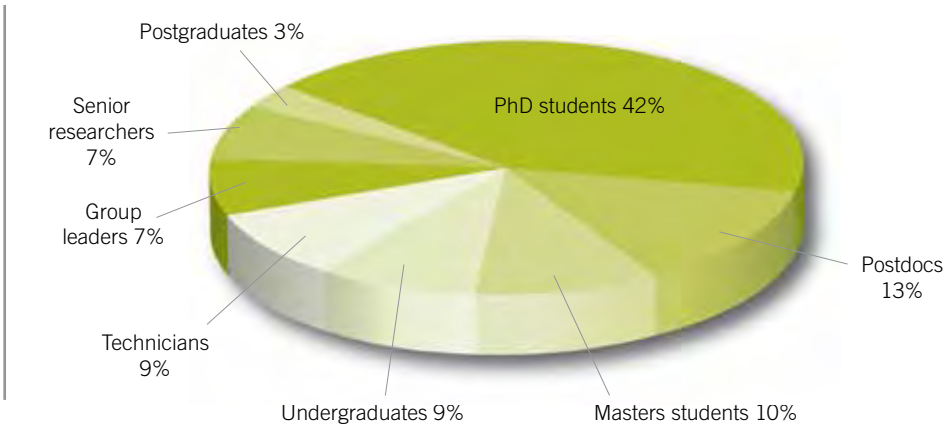



## 5. IBEC staff by nationality (Spain/other) and job category





## 6. IBEC researchers and technicians by job category



## 7. Mobility

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

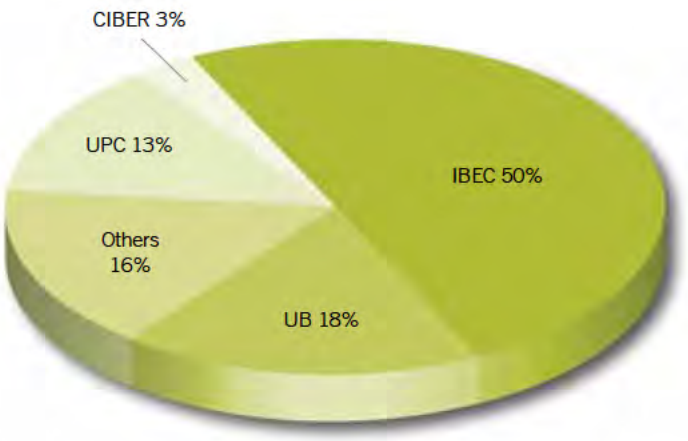
**33%** went to other centres in Spain

**63%** went to labs in the rest of Europe

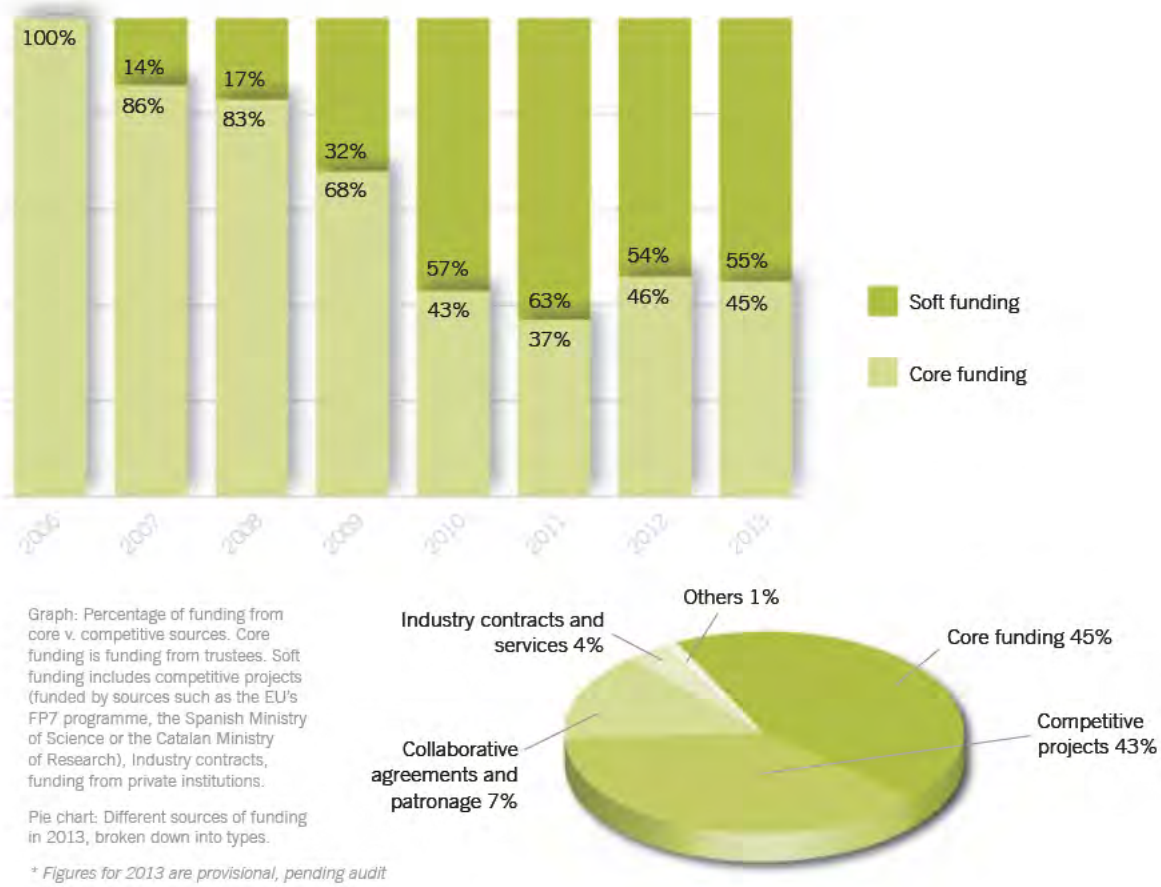
**4%** went to other parts of the world

**12%** of research staff had stays in labs outside IBEC in 2013

## 8. IBEC staff by contracting institution



## 9. Funding sources in 2013*

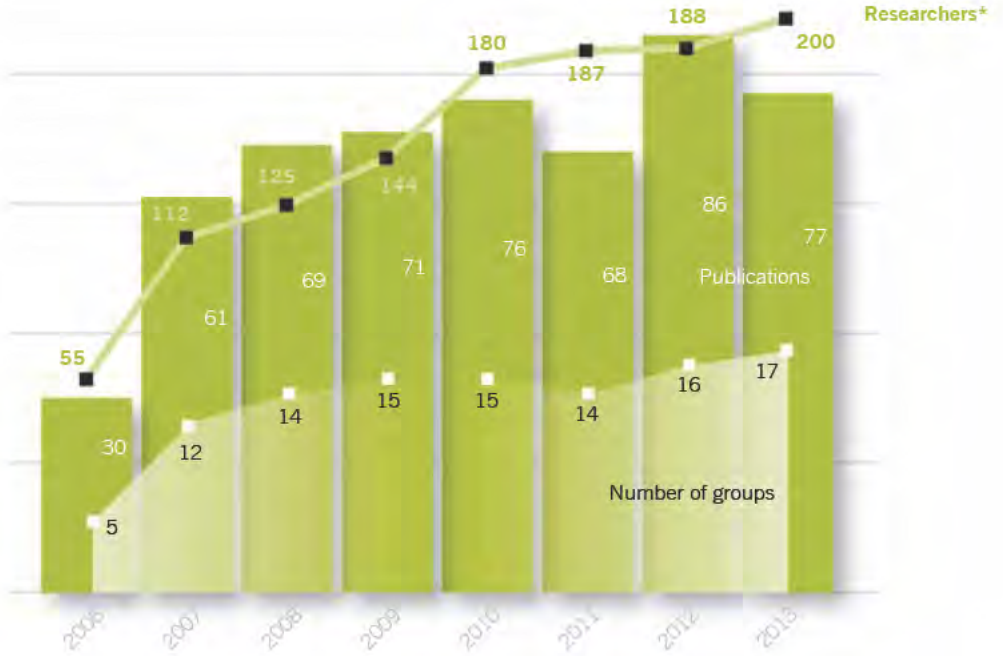



Graph: Percentage of funding from core v. competitive sources. Core funding is funding from trustees. Soft funding includes competitive projects (funded by sources such as the EU's FP7 programme, the Spanish Ministry of Science or the Catalan Ministry of Research), Industry contracts, funding from private institutions.

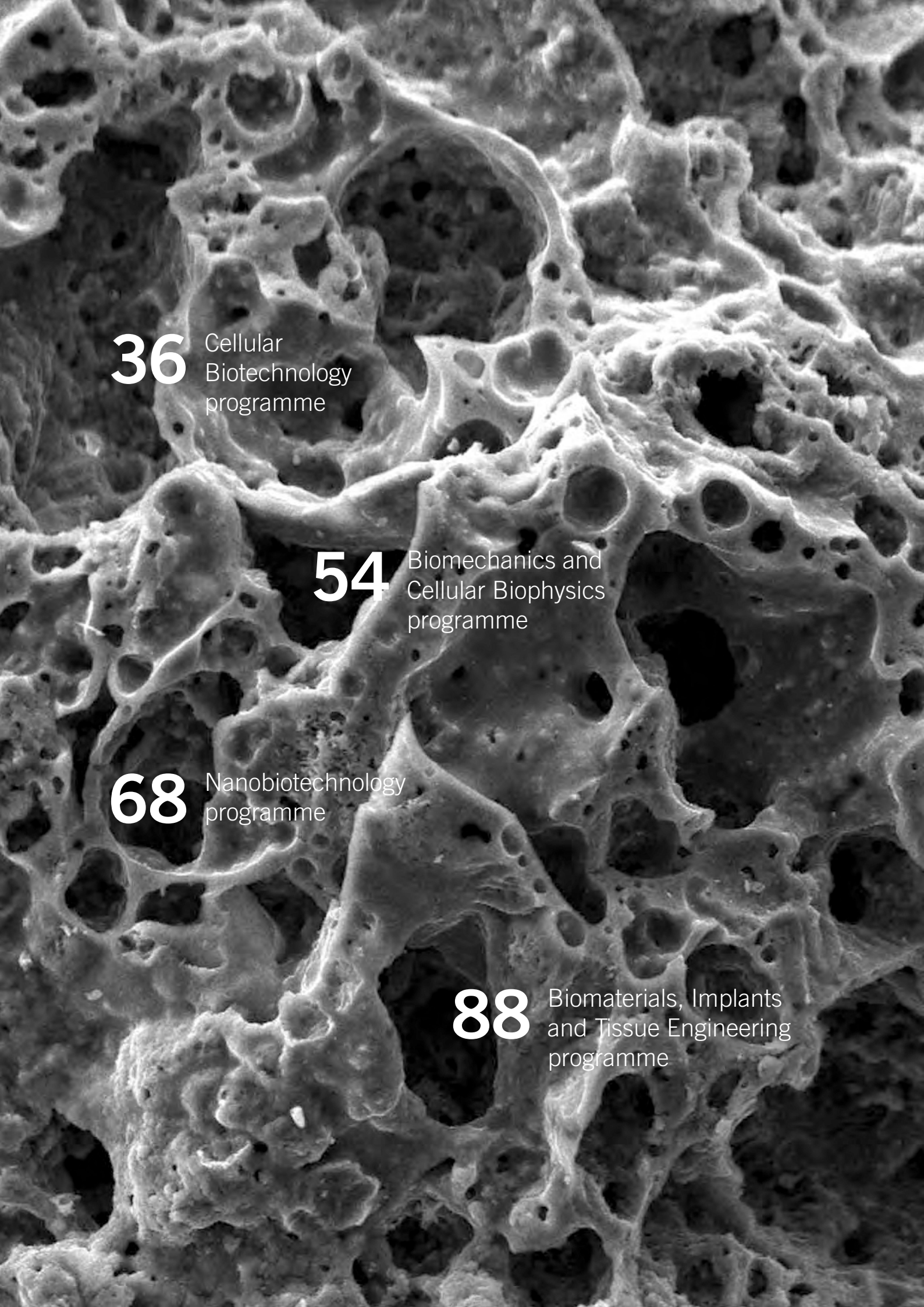
Pie chart: Different sources of funding in 2013, broken down into types.

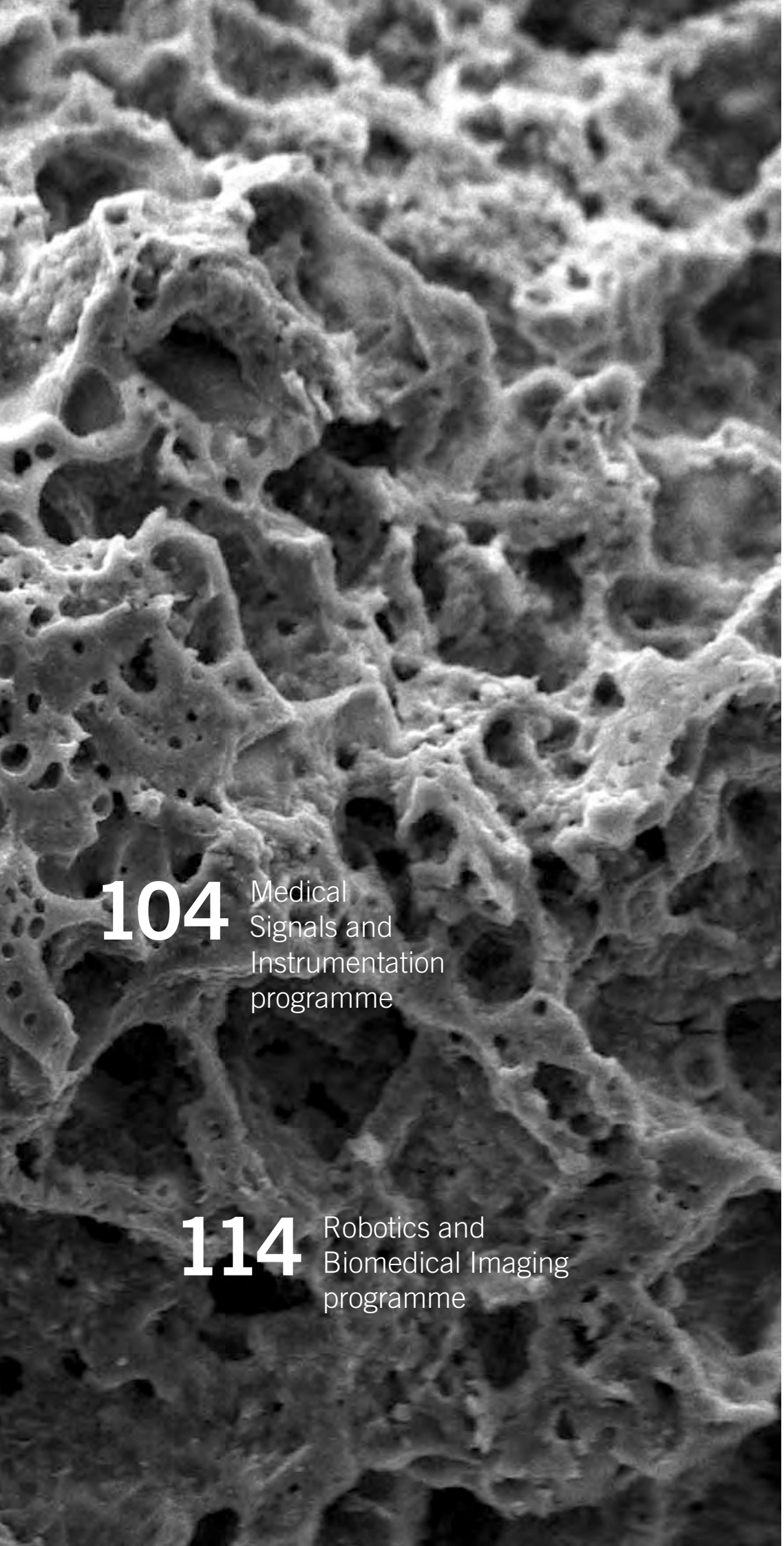
** Figures for 2013 are provisional, pending audit*

## 10. 2006-2013: Evolution of IBEC (groups, publications, researchers)




** PhD, postdoc, senior researcher, group leader and senior technician career stages; not including under- or postgraduates, masters students or lab technicians*





# Research

# Cellular Biotechnology programme

Unravelling the role played by proteins in allowing virulent bacteria to adapt to the host environment and cause disease; understanding the processes of development and neurodegeneration of the central nervous system; understanding the mechanisms that govern the potency of cells, with the aim of generating functional heart muscle cells for transplantation; using different bioengineering approaches to eradicate drug-resistant bacteria

## Microbial Biotechnology and Host-Pathogen Interaction

Prof. Dr. Antonio Juárez

## Molecular and Cellular Neurobiotechnology

Prof. Dr. José Antonio Del Río

## Control of Stem Cell Potency

Prof. Dr. Ángel Raya

## Bacterial Infections: Antimicrobial Therapies

Dr. Eduard Torrents

# Microbial Biotechnology and Host-pathogen Interaction

**Group leader:** Antonio Juárez

**Postdoctoral researcher:** Manuela Dietrich, Mário Hüttener

**PhD students:** Francesca Staffieri

**Undergraduate students:** Íñigo Cucurull, Anjelica Ibrahim, Da Li, Alejandro Prieto

**Technician:** Mª Carmen Jaramillo

## 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**

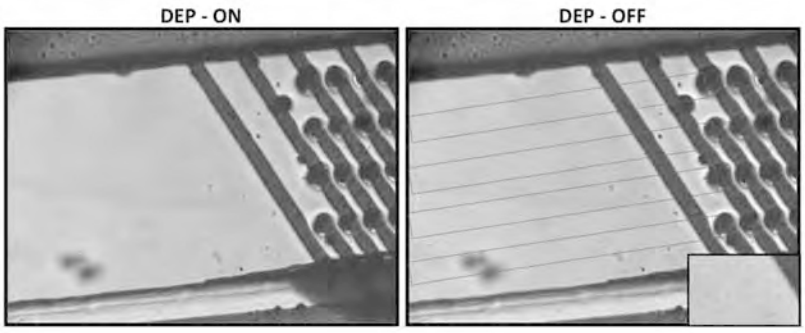
A main concern with bacterial infections is the selection of isolates that are resistant to several antimicrobial drugs. The transmission of the ability of bacterial cells of simultaneously resist several antimicrobial drugs is accomplished, in many instances, by plasmids. These genetic elements can 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.

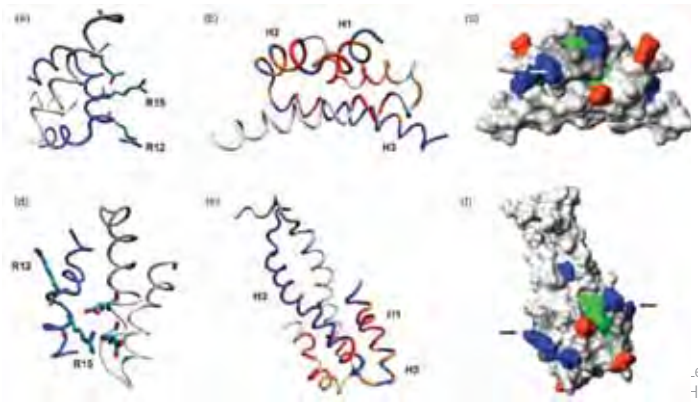
**3. Application of nanotools of bacterial biotechnology**

*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 76), 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.

Trapping of *Escherichia coli* cells in a dielectrophoresis chip.





Left: Hha perturbing H-NS structure


Left: Salmonella R27 plasmid

## Publications


- Jaramillo, M. C., Martínez-Duarte, R., Hüttener, M., Renaud, P., Torrents, E. & Juárez, A. (2013). Increasing PCR sensitivity by removal of polymerase inhibitors in environmental samples by using dielectrophoresis. *Biosensors and Bioelectronics*, 43 (1), 297-303.
- Otero, J., Baños, R., González, L., Torrents, E., Juárez, A. & Puig-Vidal, M. (2013). Quartz tuning fork studies on the surface properties of *Pseudomonas aeruginosa* during early stages of biofilm formation. *Colloids and Surfaces B: Biointerfaces*, 102, 117-123.


## Research projects

- **INTERMODS** Interconexiones de módulos plasmídicos y los genomas de bacterias patógenas (2008-2013).
PI: **Antonio Juárez** (managed by UB)
*MINECO, Consejo Superior de Investigaciones Científicas (CSIC)*

- **MEJORAVE1** Mejora sanitaria y de productos cármicos de ave.
PI: **Antonio Juárez**
*Industrial project with Mevet, S.A / CZ Veterinaria, S.A.*

- **REGENTERO** Proteínas restringidas a la familia *Enterobacteriaceae*: implicación en la transferencia génica horizontal y virulencia.
PI: **Antonio Juárez**
*MINECO*

- Grup de recerca consolidat (2009-2014).
PI: **Antonio Juárez**
*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 (2009 SGR 66)*

## 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 76)

**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

**Prof. Josep Samitier** IBEC (page 70)

**Dr. Eduard Torrents** IBEC (page 50)

## 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


- Cendra, M. M., Juárez, A., Madrid, C. & Torrents, E. (2013). H-NS is a novel transcriptional modulator of the ribonucleotide reductase genes in *escherichia coli*. *Journal of Bacteriology*, 195 (18), 4255-4263.
- Aznar, S., Paytubi, S. & Juárez, A. (2013). The Hha protein facilitates incorporation of horizontally acquired DNA in enteric bacteria. *Microbiology*, 159 (3), 545-554.


**Conference papers:**


- Paytubia, S., Dietrich, M., Queiroz, M. H. & Juárez, A. (2013). Role of plasmid- and chromosomally encoded Hha proteins in modulation of gene expression in *E. coli* O157:H7. In International Society for Plasmid Biology Meeting, Santander, Spain, "*Plasmid*", 70 (1), 52-60, Elsevier.
- Gilbert, M., Juárez, A., Madrid, C. & Balsalobre, C. (2013). New insights in the role of HtdA in the regulation of R27 conjugation. In International Society for Plasmid Biology Meeting, Santander, Spain, "*Plasmid*", 70 (1), 61/68, Elsevier.

# Molecular and Cellular Neurobiotechnology

**Group leader:** José Antonio Del Río

**Postdoctoral researcher:** Herena Eixarch, Rosalina Gavín, Vanessa Gil, Ariadna Pérez

**PhD students:** Patricia Carulla, Agata Mata, Sara Nocentini, Diego Reginensi, Óscar Seira, Cristina Vergara

**Masters student:** Andreu Matamoros

**Undergraduate students:** Ariadna Iserte, Miriam Segura

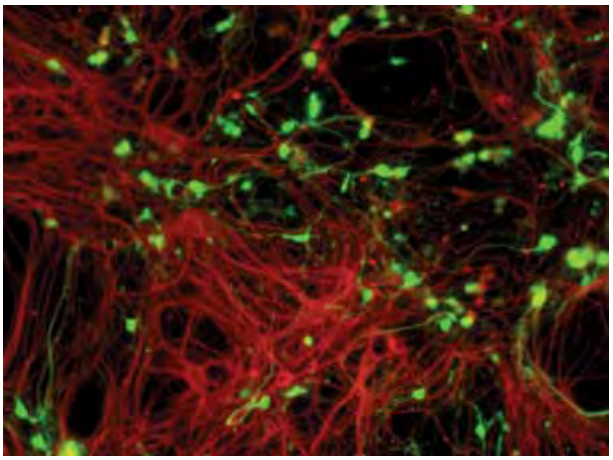
During 2013, the group has developed several studies aimed at understanding some processes of development and neurodegeneration of the central nervous system (CNS).

**Role of $PrP^c$ in the nervous system**

We have demonstrated, in collaboration with other groups, the role of the cellular prion protein ($PrP^C$) in neural stem cell proliferation and differentiation, in particular hippocampal neuronal progenitos and during the last year neuroblastoma cells using -omics techniques. We determined the $PrP^C$ -dependent gene expression signature in N2a cells and its implication in the most overrepresented functions: cell cycle, cell growth and proliferation, and maintenance of cell shape. $PrP^C$ over-expression enhances cell proliferation and cell cycle re-entrance after serum stimulation, while $PrP^C$ silencing slows down cell cycle progression. These effects are due in part to the modulation of epidermal growth factor receptor (EGFR) by $PrP^C$ in the plasma membrane, where the two proteins interact in a multimeric complex. We also described how $PrP^C$ over-expression modulates filopodia formation by Rho GTPase regulation mainly in an AKT-Cdc42-N-WASP-dependent pathway (Llorens *et al.*, 2013a). This data has been reviewed in Llorens *et al.*, 2013b. In addition, we investigated whether β-amyloid accumulation may affect prion infectivity and, conversely, whether different amounts of $PrP^C$ may affect β-amyloid accumulation. For this purpose, we used the APPswe/PS1dE9 mouse line, a common model of Alzheimer's disease, crossed with mice that either overexpress (Tga20) or that lack prion protein (knock-out) to generate mice that express varying amounts of prion protein and deposit β-amyloid. On these mouse lines, we investigated the influence of each protein on the evolution of both diseases. Our results indicated that although the presence of APP/PS1 and β-amyloid accumulation had no effect on prion infectivity, the accumulation of β-amyloid deposits was dependent on PrP(c), whereby increasing levels of prion protein were accompanied by a significant increase in β-amyloid aggregation associated with aging (Ordóñez-Gutierrez *et al.*, 2013). Lastly, we determined that central domain (CD) peptide of the $PrP^C$ is neurotoxic. In our studies we used biochemical, Transmission Electron Microscopy and Atomic Force Microscopy experiments to demonstrate that the CD peptide is able to activate caspase-3 and disrupt the cell membrane, leading to neuronal death (Vilches *et al.*, 2013).

**Regenerative neuroscience**

Moreover, in collaboration with SSSA in Italy we reported a system based on modified olfactory ensheathing cells (OECs) carrying magnetic nanoparticles as a proof of concept experiment enabling specific studies aimed at exploring the potential of OECs in the treatment of spinal cord injuries. Our studies have confirmed that magnetized OECs survive well without exhibiting stress-associated cellular responses, and that their migration can be modulated by magnetic fields. Altogether, these findings indicate the therapeutic potential of magnetized OECs for CNS injuries (Riggio *et al.*, 2013).

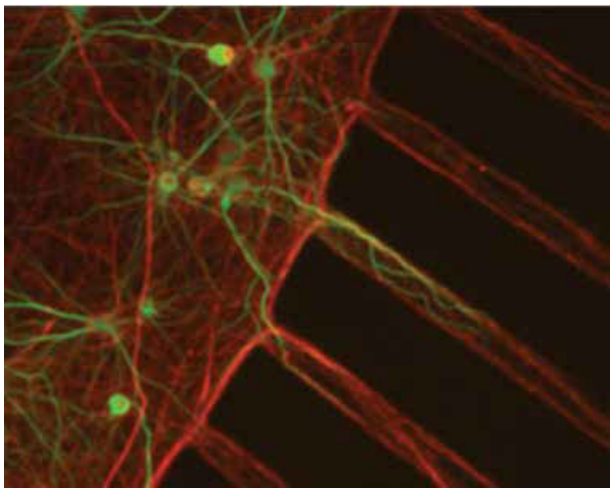


Example of fluorescence microscopy picture showing one example of cultured motorneurons (red) and glial cells (green) in microfluidic lab on a chip devices after 15 days in culture.

Finally, group members have collaborated on the study that identificates Ack1 as a novel regulator of neurotrophin-mediated events in primary neurons and in PC12 cells (La Torre *et al.*, 2013); the function of isoMIRs as functional variants of particular miRNAs. These isoMIRs may contribute to the overall effect as quantitative and qualitative fine-tuners of gene expression (Llorens *et al.*, 2013c). In addition, from our studies we propose that the use of global genomic miRNA cross-validation derived from high throughput technologies can be used to generate more reliable datasets inferring more robust networks of co-regulated predicted miRNA target genes (Llorens *et al.*, 2013d). Furthermore, we also collaborate to determine that the endogenous phosphodyesterase 7 is involved in multiple sclerosis (Bribian *et al.*, 2013; reviewed in De Castro *et al.*, 2013)

**Current experiments**

Current experiments are directed to develop chemo optogenetic non-invasive bioessays to analyze neuronal migration during brain development. In this collaboration with Ángel Raya's group (page 46) and Pau Gorostiza's group (page 60) we have generated transgenic mice with the expression of switchable fluorochromes under specific promoters to label particular neural populations. In particular the migration of pioneer neurons, Cajal-Retzius cells, is already being analyzed using these transgenic mice.



Fluorescence microscopy picture showing one example of cultured hippocampal neurons extending their neuritis inside a microchannel in a microfluidic lab on a chip device after 15 days in culture. The axon of the neurons is labeled in green and the dendrites in red.

## Publications


- Ordoñez-Gutiérrez, L., Torres, J. M., Gavín, R., Antón, M., Arroba-Espinosa, A. I., Espinosa, J. C., Vergara, C., del Río, J. A. & Wandosell, F. (2013). Cellular prion protein modulates β-amyloid deposition in aged APP/PS1 transgenic mice. *Neurobiology of Aging*, 34 (12), 2793-2804.


## Research projects

- **PRIORITY** Protecting the Food Chain from Prions: Shaping European Priorities through Basic and Applied Research (2009-2014).
  PI: **José Antonio Del Río** (managed by UB)
  *Integrated collaborative project within the framework of EU-FP7*

- **DEVREG** 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. (2013-2016).
  PI: **José Antonio Del Río**
  *MINECO, Investigación fundamental no orientada*

- **DEMTEST** Biomarker based diagnosis of rapid progressive dementias – optimization of diagnostic protocols (2012-2014).
  PI: **José Antonio Del Río**
  *Instituto Carlos III, "Optimización de Biomarcadores y la Armonización de su uso"*

- SGR Grup de recerca consolidat (2009-2014).
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 de Catalunya (2009 SGR 366)*

- **NEUROPRION** Análisis del papel de $PrP^C$ como mediador de la hiperfosforilación de tau en enfermedades neurodegenerativas (2012-2015).
PI: **Rosalina Gavín Marín**
*Fondo de investigaciones Sanitarias de la Seguridad Social*

- **IPS-PrP** Fundación Vasca de Investigación e Innovación BIOEF (2013-2015)
Scientists in Charge, IBEC subproject: **José A. del Río** and **Ángel Raya** (page 46)
*BIO12/AL/004*

## 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

**Dr. Elisabeth Engel** (page 90), **Prof. Josep Samitier** (page 70), **Prof. Xavier Trepat** (page 64), **Prof. Ángel Raya** (page 46), IBEC

**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

## Scientific equipment and techniques

- Neural stem cell culture
- Microscopy facility (Olympus BX61 and Olympus IX71 with LCi culture system)
- 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


- La Torre, A., Del Mar Masdeu, M., Cotrufo, T., Moubarak, R. S., Del Río, J. A., Comella, J. X., Soriano, E. & Ureña, J. M. (2013). A role for the tyrosine kinase ACK1 in neurotrophin signaling and neuronal extension and branching. *Cell Death and Disease*, 4 (4), e602.
- Llorens, F., Hummel, M., Pantano, L., Pastor, X., Vivancos, A., Castillo, E., Mattlin, H., Ferrer, A., Ingham, M., Noguera, M., Kofler, R., Dohm, J. C., Pluvinet, R., Bayés, M., Himmelbauer, H., del Rio, J. A., Martí, E. & Sumoy, L. (2013). Microarray and deep sequencing cross-platform analysis of the mirRNome and isomiR variation in response to epidermal growth factor. *BMC Genomics*, 14 (1), 1-15.
- Llorens, F., Banez-Coronel, M., Pantano, L., del Rio, J., Ferrer, I., Estivill, X. & Marti, E. (2013). A highly expressed miR-101 isomiR is a functional silencing small RNA. *BMC Genomics*, 14 (1), 104.
- Llorens, F., Carulla, P., Villa, A., Torres, J. M., Fortes, P., Ferrer, I. & Del Río, J. A. (2013). $PrP^C$ regulates epidermal growth factor receptor function and cell shape dynamics in Neuro2a cells. *Journal of Neurochemistry*, 127 (1), 124-138.
- Vilches, S., Vergara, C., Nicolás, O., Sanclimens, G., Merino, S., Varón, S., Acosta, G. A., Albericio, F., Royo, M., Del Río, J. A. & Gavín, R. (2013). Neurotoxicity of prion peptides mimicking the central domain of the cellular prion protein. *PLoS ONE*, 8 (8), e70881.
- Riggio, C., Nocentini, S., Catalayud, M. P., Goya, G. F., Cuschieri, A., Raffa, V. & del Río, J. A. (2013). Generation of magnetized olfactory ensheathing cells for regenerative studies in the central and peripheral nervous tissue. *International Journal of Molecular Sciences*, 14 (6), 10852-10868.
- Llorens, F., Ansoleaga, B., Garcia-Esparcia, P., Zafar, S., Grau-Rivera, O., López-González, I., Blanco, R., Carmona, M., Yagüe, J., Nos, C., Del Río, J. A., Gelpí, E., Zerr, I. & Ferrer, I. (2013). PrP mRNa and protein expression in brain and $PrP^c$ in CSF in Creutzfeldt-Jakob disease MM1 and VV2. *Prion*, 7 (5), 383-393.

# Control of Stem Cell Potency

**Group leader:** Ángel Raya

**Postdoctoral researcher:** Adriana Rodríguez

**PhD students:** Isil Tekeli, Juan Luís Vázquez, Marcel Orpí, Carlos Calatayud, Isaac Canals, Emanuele Celauro, Juan Crespo, Claudia Di Guglielmo, Anna Garcia, Alba Mateos

**Undergraduate student:** Carlos Rioja

**Senior technicians:** Yvonne Richaud, Senda Jiménez

**Technician:** Cristina García

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.

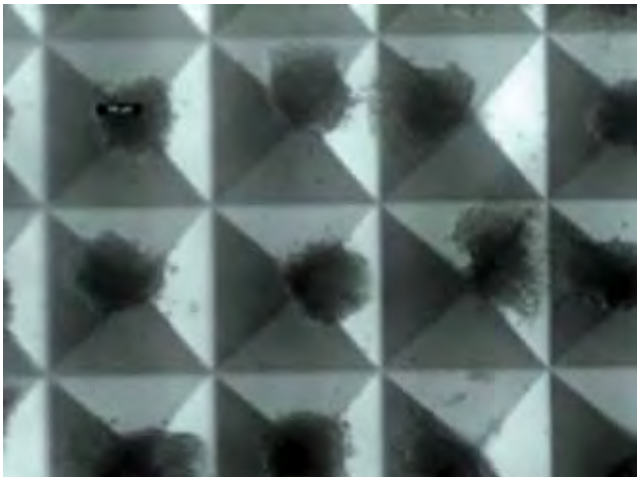
**Throughout this process, the developmental potency of individual cells, i.e. their ability to give rise to cells of a different type than their own, is progressively lost, so that somatic cells in adult individuals retain very limited potency (such as in rare adult stem cells) or show no potency at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

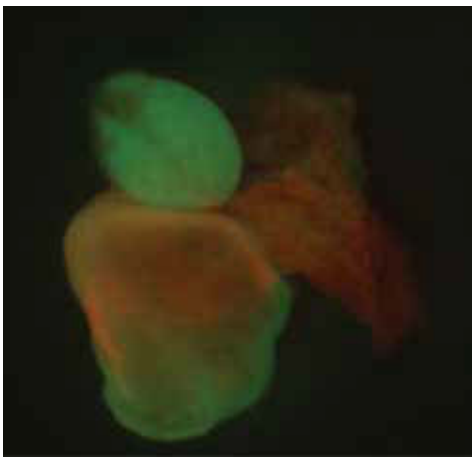
Heart-related diseases are the main cause of mortality in the world, with ischemic heart disease being the single most frequent condition accounting for the death toll. This results from the very limited ability of the mammalian heart to regenerate on its own, and underscores the pressing biomedical 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



Heart of a transgenic zebrafish showing mosaic recombination

## Publications


- Orenstein, S. J., Kuo, S.-H., Tasset, I., Arias, E., Koga, H., Fernandez-Carasa, I., Cortes, E., Honig, L. S., Dauer, W., Consiglio, A., Raya, A., Sulzer, D. & Cuervo, A. M. (2013). Interplay of LRRK2 with chaperone-mediated autophagy. *Nature Neuroscience*, 16 (4), 394-406.


## Research projects

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

- Human pluripotent stem cells and zebrafish heart regeneration as experimental tools to understand cardiac muscle cell differentiation (2009-2012)
PI: **Ángel Raya**
*MINECO, Investigación fundamental no orientada.*

- **HEMO-iPS** Use of patient-specific induced pluripotent stem cells to improve diagnosis and treatment of Hemophilia A
PI: **Ángel Raya**
*ISCIII; E-Rare JTC 2011*

- **CELLSCAFF-CART** Reparación de Cartílago Articular mediante Ingenieria de Tejidos *in situ*: modelo *in vivo* (iPSC) (2010-2013).
PI: **Ángel Raya**
*MINECO; Fomento de la cooperación científica internacional (FCCI) ACI-Promociona*

- Zebrafish heart regeneration and human pluripotent stem cells as models to understand human cardiac muscle cell differentiation
PI: **Ángel Raya**
*EMBO*

- Estudios de funcionalidad de suplementos adicionales de cultivo para mantener el estado indiferenciado de células madre humanas con pluripotencia inducida
PI: **Ángel Raya**
*Industrial contract with GRIFOLS S.A.*

## 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

**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

# Bacterial Infections: Antimicrobial Therapies

**Junior group leader:** Eduard Torrents

**PhD student:** Anna Crespo, Maria del Mar Cendra

**Masters students:** Lucas Pedraz, Aida Baelo

**Undergraduate student:** Rosa Torres

**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. Three different classes will limited sequence similarities have been described for this essential enzyme: class I (nrdAB/nrdEF) is oxygen dependent; class II (nrdJ) is indifferent to oxygen; and class III (nrdDG) is oxygen sensitive. 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 and their role in pathogenesis.

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

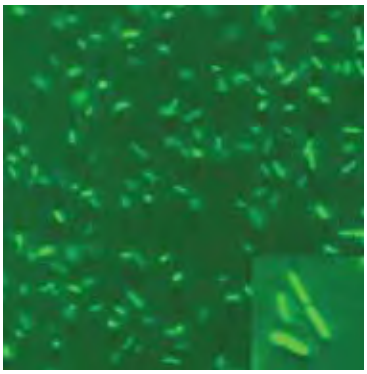
- First, to establish the molecular basis for the regulation RNR genes, their importance in virulence and biofilm formation;
- Second, the identification and screening of new molecules for the highly selective inhibition of bacterial RNR;
- Third, by using nanomedicine techniques the development of novel 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, and in particular dielectrophoresis, to study the electrical fields in bacterial cell physiology and also to concentrate bacterial pathogens and facilitate their detection, especially for the identification of bacteria which are multi-resistant to different antibiotics.

We believe this project 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.

Free living bacteria.

*Pseudomonas aeruginosa* swimming.

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



Pseudomonas aeruginosa expressing green fluorescent protein under the PnrdA promoter.

## Publications


- Jaramillo, M. C., Martínez-Duarte, R., Hüttener, M., Renaud, P., Torrents, E. & Juárez, A. (2013). Increasing PCR sensitivity by removal of polymerase inhibitors in environmental samples by using dielectrophoresis. *Biosensors and Bioelectronics*, 43 (1), 297-303.
- Otero, J., Baños, R., González, L., Torrents, E., Juárez, A. & Puig-Vidal, M. (2013). Quartz tuning fork studies on the surface properties of *Pseudomonas aeruginosa* during early stages of biofilm formation. *Colloids and Surfaces B: Biointerfaces*, 102, 117-123.


## Research projects

- Ribonucleotide reductasas: una nueva diana terapéutica contra organismos patógenos en enfermos de fibrosis quística.
PI: **Eduard Torrents**
*Federacion Española de Fibrosis Quística "PABLO MOTOS" 2012-2014*

- Inhibición de la síntesis del ADN bacteriano como diana contra organismos patogenos en enfermos de fibrosis quistica.
PI: **Eduard Torrents**
*Federacion Española de Fibrosis Quística "PABLO MOTOS" 2013-2015*

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

## Collaborations with other research centres

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

**Dr. Elisabeth Engel** IBEC (page 90)

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

■ Cendra, M. M., Juárez, A., Madrid, C. & Torrents, E. (2013). H-NS is a novel transcriptional modulator of the ribonucleotide reductase genes in *escherichia coli*. *Journal of Bacteriology*, 195 (18), 4255-4263.

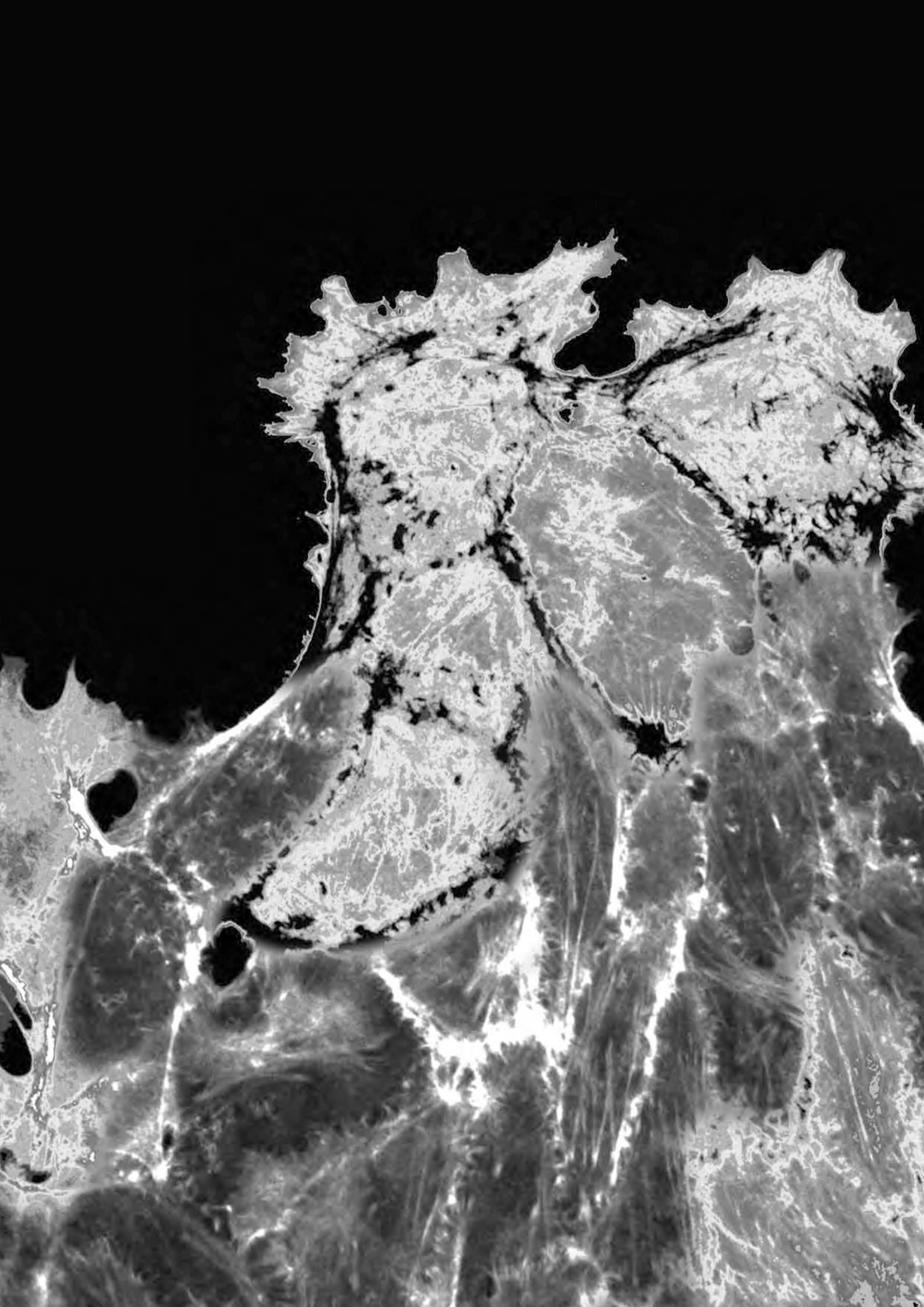
**Prof. Britt-Marie Sjöberg** Dept. Molecular Biology and Functional Genomics, Stockholm University, Sweden

**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

## Scientific equipment and techniques

- 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
- Continuous flow system model for bacterial biofilm development
- Single Channel Fiber-Optic Oxygen Meter with microsensor



# Biomechanics and Cellular Biophysics programme

Understanding cellular and respiratory biomechanics in order to improve the diagnosis and treatment of respiratory disease; developing nanoscale tools to study biological systems, such as electrochemical tunnelling microscopy and spectroscopy, and which contribute to the development of biosensors and molecular electronics devices; understanding the fundamental biophysical mechanisms underlying cell migration, which is crucial in morphogenesis, host defense and tissue healing, but also in mediating diseases such as cancer, and chronic inflammation

## Cellular and Respiratory Biomechanics

Prof. Dr. Daniel Navajas

## Nanoprobes and Nanoswitches

Prof. Dr. Pau Gorostiza and
Prof. Dr. Fausto Sanz

## Integrative Cell and Tissue Dynamics

Prof. Dr. Xavier Trepat

# Cellular and Respiratory Biomechanics

**Group leader:** Daniel Navajas

**Junior group leader:** Pere Roca-Cusachs

**Postdoctoral researchers:** Jordi Alcaraz, Alberto Elosegui

**PhD students:** Noelia Campillo, Anita Kosmalska, Tomás Luque, Esther Melo

**Masters students:** Ignasi Jorba, Roger Oria

**Undergraduate students:** Yolanda Castillo, Víctor González

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 respiratory biomechanics line, led by Prof. Daniel Navajas, studies the mechanical behaviour of the respiratory system, and how it is altered in respiratory diseases. 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.**

*Respiratory biomechanics (Daniel Navajas)*

Our goal is to gain a better understanding of cellular and respiratory biomechanics in order to improve the diagnosis and treatment of respiratory disease. Our work is organized into two interrelated areas, focusing on respiratory mechanics at both the systemic and the cellular level. We use basic and translational approaches in a multidisciplinary framework involving cooperation with clinical research groups working in the field of respiratory medicine.

At the systemic level, we study the mechanical properties of the airway and lung tissues and the changes that occur in the context of the mechanical dysfunction associated with respiratory diseases. We study the mechanics of the upper airway in sleep apnea syndrome and on mechanical ventilation in acute and chronic respiratory failure. We biofabricate engineered lungs by recellularizing lung scaffolds with stem cells.

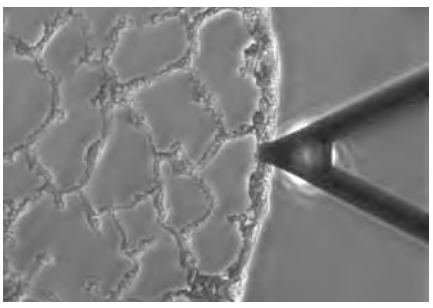
At the cellular level, we develop and apply cutting-edge nanotechnology and advanced biophysical techniques to probe the mechanical behaviour of cells and their mechanical interactions with their microenvironment. We study the mechanical properties of the cell and its response to inflammation and mechanical stresses and develop new approaches to differentiate stem cells using mechanical stimuli. We are developing a lung-on-a-chip model recreating the *in vivo* mechanical micro/nano- environment of lung cells.

*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.

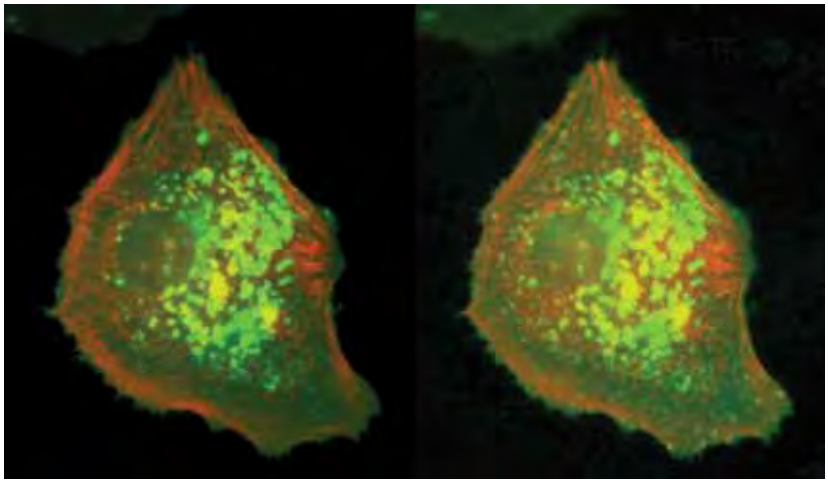
Our research aims to unravel the mechanisms that these molecules use to detect and respond

Nanomechanics of lung extracellular matrix probed with atomic force microscopy (Luque *et al. Acta Biomaterialia* 2013; 9:6852–9). Left: decellularized lung scaffold. Right: mechanical properties probed with AFM.



to forces, 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 and advanced optical microscopy. Using this approach, we have for instance 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*). We have also recently unveiled a basic micron-sized molecular structure that cells use to generate forces that probe substrate rigidity (Ghassemi *et al.*, 2012, *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.

Mouse embryonic fibroblast before and after mechanical compression. The actin cytoskeleton is shown in red, the membrane in green.



## Publications


- Roca-Cusachs, P., Sunyer, R. & Trepat, X. (2013). Mechanical guidance of cell migration: lessons from chemotaxis. *Current Opinion in Cell Biology*, 25 (5), 543-549.
- Roca-Cusachs, P., Del Rio, A., Puklin-Faucher, E., Gauthier, N. C., Biais, N. & Sheetz, M. P. (2013). Integrin-dependent force transmission to the extracellular matrix by α-actinin triggers adhesion maturation. *Proceedings of the National Academy of Sciences of the United States of America*, 110 (15), E1361-E1370.


## Research projects

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

- Fisiopatologia i Tractament de les Malalties Respiratòries (2009-2013).
PI: **A. Torres** (managed by Fundació Clínic)
*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 (2009-SGR-911)*

- **NANONET** Nanomechanics of intermediate filament networks.
Chair: E. Hol
Management Committee Member: **Daniel Navajas**
*European Commission COST Action (BMBS-BM1002)*

- **CHROMED** Clinical tRials fOr elderly patients with MultiplE Disease.
PI: Ramon Farré (UB/IDIBAPS)
*European Commission, FP7-HEALTH-2012-INNOVATION-1 Project 306093-2*

- **AFM4NanoMed&Bio** European network on applications of Atomic Force Microscopy to NanoMedicine and Life Sciences.
Management Committee Member: **Daniel Navajas**
*European Commission COST Action (BMBS-TD1002)*

- Identifying molecular mechanical pathways in cells (2012-2015).
PI: **Pere Roca-Cusachs**
*Proyectos de investigación fundamental no orientada, Ministerio de economía y competitividad (BFU2011-23111)*

- Mechanical pathways in cells: from molecular mechanisms to cell function (2012-2015).
PI: **Pere Roca-Cusachs**
Coordinator: **Daniel Navajas**
*Career Integration Grants (CIG) Marie Curie Action within the framework of EU-FP7 (MecPath 303848)*

- Stromal stiffness in tumor progression (2014-2016).
PI: **Pere Roca-Cusachs**
*Fundació la Marató de TV3*

## 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

**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


- Farré, R., Navajas, D. & Montserrat, J. M. (2013). Is there an optimal nasal pressure for treating obstructive sleep apnea-and if so, what is it? *Sleep*, 36 (4), 463-464.
- Luque, T., Melo, E., Garreta, E., Cortiella, J., Nichols, J., Farré, R. & Navajas, D. (2013). Local micromechanical properties of decellularized lung scaffolds measured with atomic force microscopy. *Acta Biomaterialia*, 9 (6), 6852-6859.
- Marí-Buyé, N., Luque, T., Navajas, D. & Semino, C. E. (2013). Development of a three-dimensional bone-like construct in a soft self-assembling peptide matrix. *Tissue Engineering - Part A*, 19 (7-8), 870-881.
- Isetta, V., Lopez-Agustina, C., Lopez-Bernal, E., Amat, M., Vila, M., Valls, C., Navajas, D. & Farre, R. (2013). Cost-effectiveness of a new internet-based monitoring tool for neonatal post-discharge home care. *Journal of Medical Internet Research*, 15 (2), e38.
- Puig, F., Fuster, G., Adda, M., Blanch, L., Farre, R., Navajas, D. & Artigas, A. (2013). Barrier-protective effects of activated protein C in human alveolar epithelial cells. *PLoS ONE*, 8 (2), e56965.
- Torres, M., Montserrat, J. M., Pavía, J., Dalmases, M., Ros, D., Fernandez, Y., Barbé, F., Navajas, D. & Farré, R. (2013). Chronic intermittent hypoxia preserves bone density in a mouse model of sleep apnea. *Respiratory Physiology and Neurobiology*, 189 (3), 646-648.
- Peñuelas, O., Melo, E., Sánchez, C., Sánchez, I., Quinn, K., Ferruelo, A., Pérez-Vizcaíno, F., Esteban, A., Navajas, D., Nin, N., Lorente, J. A. & Farré, R. (2013). Antioxidant effect of human adult adipose-derived stromal stem cells in alveolar epithelial cells undergoing stretch. *Respiratory Physiology and Neurobiology*, 188 (1), 1-8.
- Almendros, I., Montserrat, J. M., Torres, M., Dalmases, M., Cabañas, M. L., Campos-Rodríguez, F., Navajas, D. & Farré, R. (2013). Intermittent hypoxia increases melanoma metastasis to the lung in a mouse model of sleep apnea. *Respiratory Physiology and Neurobiology*, 186 (3), 303-307.

# Nanoprobes and Nanoswitches

**Group leaders:** Pau Gorostiza and Fausto Sanz

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

**Postdoctoral researchers:** Nadim Darwish, Kay Eckelt, Ana Trapero

**PhD students:** Antonio Bautista, Albert Cortijos, Fernanda Da Silva, Mercè Izquierdo, Montserrat López, Andrés Martín Quirós, Helena Masanas, Anna Palacios, Silvia Pittolo, Marta Pozuelo, Veronica Sarasso

**Masters students:** Aida Garrido, Berta Gumí, Maria del Carmen Torres Martín-Mora, Iro Tsintzou, Simone Vitiello

**Undergraduate students:** Mattia Ferrero, Sofía Frau

**Senior technician:** Núria Camarero

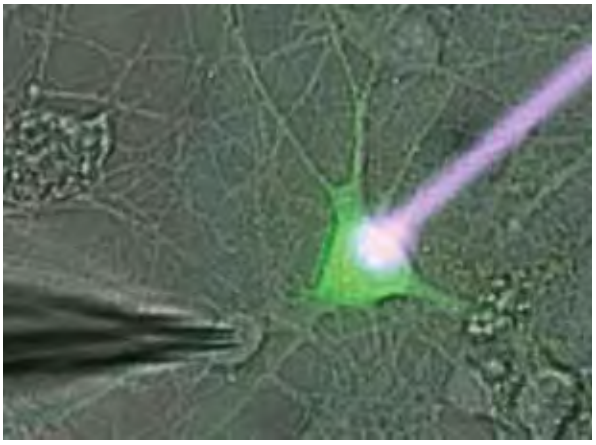
**Technician:** Ariadna Pérez

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, we have recently published a method to measure directly the distance decay constant that characterizes the rate of electron transfer (ET) in redox proteins, and we have reported single protein junctions consisting of azurin bridged between a gold substrate and the probe of an electrochemical tunneling microscope, which constitute a proof-of-principle of a single redox protein field-effect transistor.**

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 are specifically interested in the processes of neurotransmitter secretion by exocytosis and membrane recycling by endocytosis, which are the fundamental phenomena that occur at the synaptic terminal and that participate in the communication between neurons. We have recently set up a method to control neurotransmitter exocytosis with light at the presynaptic compartment by activating a calcium-permeable, light-gated glutamate receptor (LiGluR) in cultured cells. Presynaptic expression of LiGluR in hippocampal neurons enables direct and reversible control of neurotransmission with light, and has allowed for the first time the modulation of the firing rate of the postsynaptic neuron with the wavelength of illumination.



Representation of the invasive manipulation of neuronal activity by means of a conventional glass electrode in contact with the neuron on the left, and noninvasively by means of a focalized light beam over the green neuron on the right (Photomontage: Mercè Izquierdo).

## Publications


- Nevola, L., Martín-Quirós, A., Eckelt, K., Camarero, N., Tosi, S., Llobet, A., Giralt, E. & Gorostiza, P. (2013). Light-regulated stapled peptides to inhibit protein-protein interactions involved in clathrin-mediated endocytosis. *Angewandte Chemie*, 52 (30), 7704-7708.
- Hines, T., Díez-Pérez, I., Nakamura, H., Shimazaki, T., Asai, Y. & Tao, N. (2013). Controlling formation of single-molecule junctions by electrochemical reduction of diazonium terminal groups. *JACS*, 135 (9), 3319-3322.
- Punet, X., Mauchauffé, R., Giannotti, M. I., Rodríguez-Cabello, J. C., Sanz, F., *et al* (2013). Enhanced cell-material interactions through the biofunctionalization of polymeric surfaces with engineered peptides. *Biomacromolecules*, 14 (8), 2690-2702.
- Perez Madrigal, M. M., Giannotti, M. I., Oncins, G., Franco, L., Armelin, E., *et al* (2013). Bioactive nanomembranes of semiconductor polythiophene and thermoplastic polyurethane: thermal, nanostructural and nanomechanical properties. *Polymer Chemistry*, 4 (3), 568-583.
- Lima, L. M. C., Giannotti, M. I., Redondo-Morata, L., Vale, M.


## Filed patents

- **Glutamate Receptor Photomodulators** (Filing date 8th October 2013)
*Inventors: Amadeo Llebaria Soldevilla, Jesús Giraldo Arjonilla, Xavier Rovira Algans, Xavier Gómez Santacana, Silvia Pittiolo,* ***Pau Gorostiza Langa****, Cyril Goudet, Xavier Rovira Algans, Jean Philippe Pin.*
Ref. number: EP13382374.0

## Research projects

- **THERALIGHT** Therapeutic Applications of Light-Regulated Drugs (2013-2014).
PI: **Pau Gorostiza** (coordinator)
*ERC Proof of Concept Grant (ERC-PoC) within the framework of EU-FP7*

- **OPTICALBULLET** Neurosecretion by Remote Control of Exocytosis and Endocytosis with Light (2008-2013).
PI: **Pau Gorostiza** (coordinator)
*ERC Starting Independent Researcher Grant (ERC-StG) within the framework of EU-FP7*

- Bioelectrochemistry and Nanotechnologies (2009-SGR-277).
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 (2009-2013)*

- **FOCUS** Single Molecule Activation and Computing (2011-2013).
PI: **Pau Gorostiza** (Coordinator: Vincent Torre)
*European Commission Future and Emerging Technologies proactive 7: Molecular Scale Devices and Systems FP7-ICT-2009 8.7 (270483)*

- Optogenetic pacemaking to rewire neural circuits (2012-2014).
PI: **Pau Gorostiza** (Coordinator: Artur Llobet)
*Fundació Marató de TV3, Grants for Research in Neurodegenerative Diseases*

- **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)*

- SGR Grup de recerca consolidat (2009-2014).
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 (2009 SGR 277)*

## Collaborations with other research centres

**Prof. Amadeu Llebaria** Institut de Química Avançada de Catalunya (IQAC-CSIC), Barcelona, Spain

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

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

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

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

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

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

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

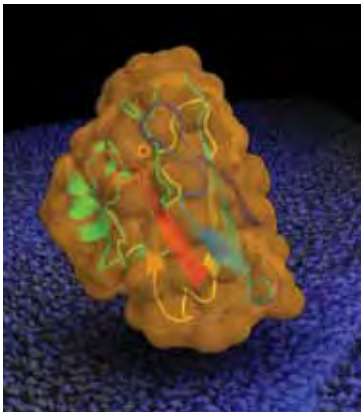
**Prof. Carles Solsona** Pathology and Experimental Therapeutics Dept, Universitat de Barcelona, Spain

**Prof. Francisco Ciruela** ICREA / Universitat de Barcelona, Spain

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

## 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



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*).


L. C., Marques, E. F. & Sanz, F. (2013). Morphological and nanomechanical behavior of supported lipid bilayers on addition of cationic surfactants. *Langmuir*, 29 (30), 9352-9361.

- Izquierdo-Serra, M., Trauner, D., Llobet, A. & Gorostiza, P. (2013). Optical control of calcium-regulated exocytosis. *Biochimica et Biophysica Acta*, 1830 (3), 2853-2860.
- Palacios-Padrós, A., Caballero-Briones, F., Díez-Pérez, I. & Sanz, F. (2013). Tin passivation in alkaline media: Formation of SnO microcrystals as hydroxyl etching product. *Electrochimica Acta*, 111, 837-845.
- Aragonès, A. C., Palacios-Padrós, A., Caballero-Briones, F. & Sanz, F. (2013). Study and improvement of aluminium doped ZnO thin films: Limits and advantages. *Electrochimica Acta*, 109, 117-124.
- Hoyo, J., Guaus, E., Oncins, G., Torrent-Burgués, J. and Sanz, F. (2013). Incorporation of Ubiquinone in supported lipid bilayers on ITO. *Journal of Physical Chemistry B*, 117 (25), 7498-7506.
- Raster, P., Späth, A., Bultakova, S., Gorostiza, P., König, B. and Bregestovski, P. (2013). New GABA amides activating GABAA-receptors. *Beilstein Journal of Organic Chemistry*, 9, 406-410.
- Stocchi, A., Lauke, B., Giannotti, M. I., Vázquez, A. & Bernal, C. (2013). Tensile response and fracture and failure behavior of jute fabrics-flyash-vinylester hybrid composites. *Fibers and Polymers*, 14 (2), 285-291.
- Izquierdo-Serra, M., Trauner, D., Llobet, A. & Gorostiza, P. (2013). Optical modulation of neurotransmission using calcium photocurrents through the ion channel LiGluR. *Frontiers in Molecular Neuroscience*, 6 (Article 3), 1-6.
- Redondo-Morata, L., Giannotti, M. I. & Sanz, F. (2013). AFM-based force-clamp indentation: Force-clamp monitors the lipid bilayer failure kinetics. *Imaging & Microscopy*, 15 (4), 25-27.

**Conference paper:**

- Guo, S., Artés, J. M. & Díez-Pérez, I. (2013). Electrochemically-gated single-molecule electrical devices. In 63rd Annual Meeting of the International Society of Electrochemistry, Prague, Czech Republic, "*Electrochimica Acta*", 110, 741-753, Elsevier.

# Integrative Cell and Tissue Dynamics

**Group leader:** Xavier Trepat

**Postdoctoral researchers:** Elsa Bazellières, Vito Conte, Anna Labernadie, Raimon Sunyer, Romaric Vincent, Dobryna Zalvidea

**PhD students:** Sandra Baker, Agustí Brugués, Laura Casares, Simón García, Pilar Rodríguez, Xavier Serra, Marina Uroz

**Masters student:** Carlos Pérez

**Technician:** Maria Bintanel

## 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.**

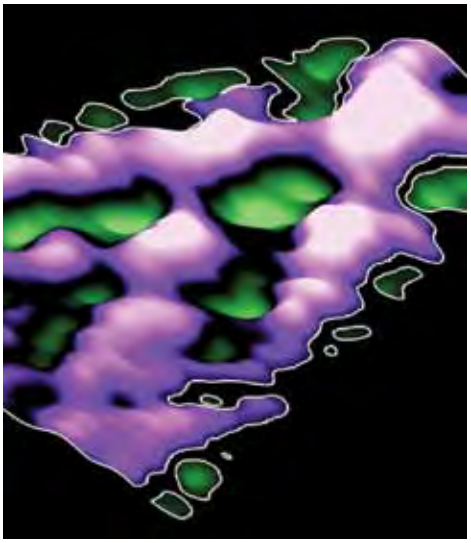
*Making cellular forces visible*

To study cell and tissue dynamics we develop new technologies to measure cellular velocities and physical forces at the cell-cell and cell-matrix interface. Using these techniques we unveiled a new mechanism of cellular guidance by intercellular physical forces we called plithotaxis. Our new tools also led to the discovery of an unanticipated mechanical 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. In collaboration with different laboratories worldwide, our technologies have contributed to the discovery of physical interactions between different cell types during neural crest development, to the identification of a new mechanism by which cells respond to free space, and to the finding that "suspended bridges" enable collective migration of skin cells during wound healing.

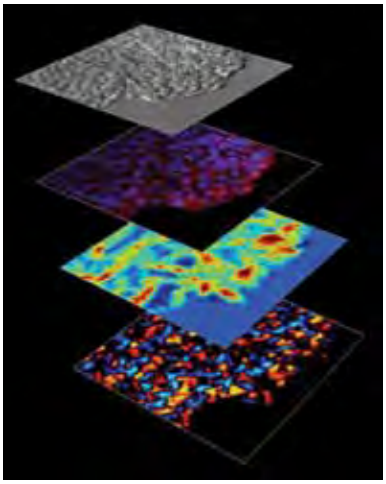
*Cytoskeletal fragility*

With every beat of the heart, inflation of the lung or peristalsis of the gut, cell types of diverse function are subjected to substantial mechanical forces. How cells sense and respond to such forces underlies fundamental biological functions including differentiation, proliferation, polarization, locomotion, invasion, gene expression and pattern formation. We identified a new class of universal cellular responses to mechanical forces we termed 'cytoskeletal fluidization' (Trepat *et al.*, 2007, *Nature*). The existence of this response class implies that the cytoskeleton of the living cell should no longer be regarded as a robust and stable scaffold but as a fragile one that is able to fluidize and quickly reorganize to adapt to its active mechanical environment. Our current research focuses on better understanding the functional implications of cytoskeletal fluidization and elucidating the underlying physical mechanisms.

Waves of cellular deformation propagate across expanding tissues.



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



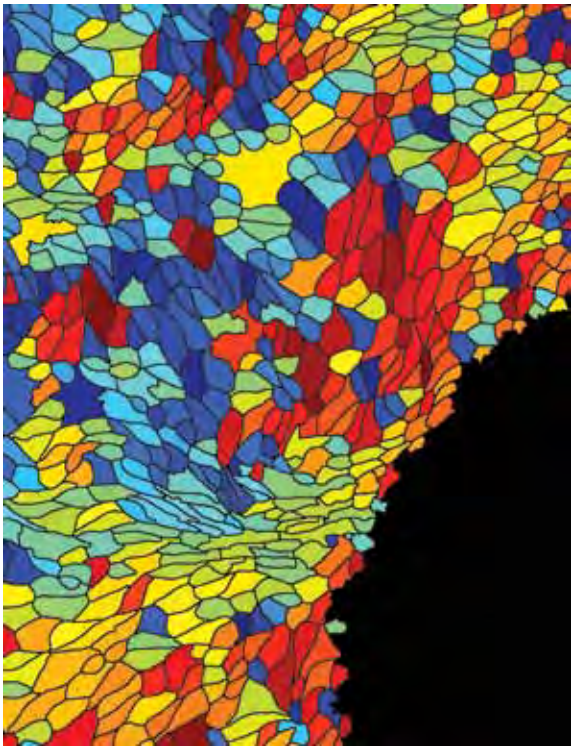


Image segmentation of epithelial cells surrounding an empty space.

## Publications


- Kim, J. H., Serra-Picamal, X., Tambe, D. T., Zhou, E. H., Park, C. Y., Sadati, M., Park, J.-A., Krishnan, R., Gweon, B., Millet, E., Butler, J. P., Trepat, X. & Fredberg, J. J. (2013). Propulsion and navigation within the advancing monolayer sheet. *Nature Materials*, 12 (9), 856-863.
- Theveneau, E., Steventon, B., Scarpa, E., Garcia, S., Trepat, X., Streit, A. & Mayor, R. (2013). Chase-and-run between adjacent cell populations promotes directional collective migration. *Nature Cell Biology*, 15 (7), 763-772.


## Filed patents

- **Monolayer stress microscopy** (Filing date 13th April 2013)
*Inventors: James P. Butler, Jeffrey J. Fredberg, Dhananjay T. Tambe,* ***Xavier Trepat****.*
Ref. number: PCT/US2012/033450

## Research projects

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

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

- 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)
*National Institutes of Health, USA*

## Collaborations with other research centres

**Julien Colombelli** Institute for Research in Biomedicine (IRB), Barcelona, Spain

**Eduard Batlle** IRB, Barcelona, Spain

**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


- Roca-Cusachs, P., Sunyer, R. & Trepat, X. (2013). Mechanical guidance of cell migration: lessons from chemotaxis. *Current Opinion in Cell Biology*, 25 (5), 543-549.
- Tambe, D. T., Croutelle, U., Trepat, X., Park, C. Y., Kim, J. H., Millet, E., Butler, J. P. & Fredberg, J. J. (2013). Monolayer stress microscopy: Limitations, artifacts, and accuracy of recovered intercellular stresses. *PLoS ONE*, 8 (2), e55172.
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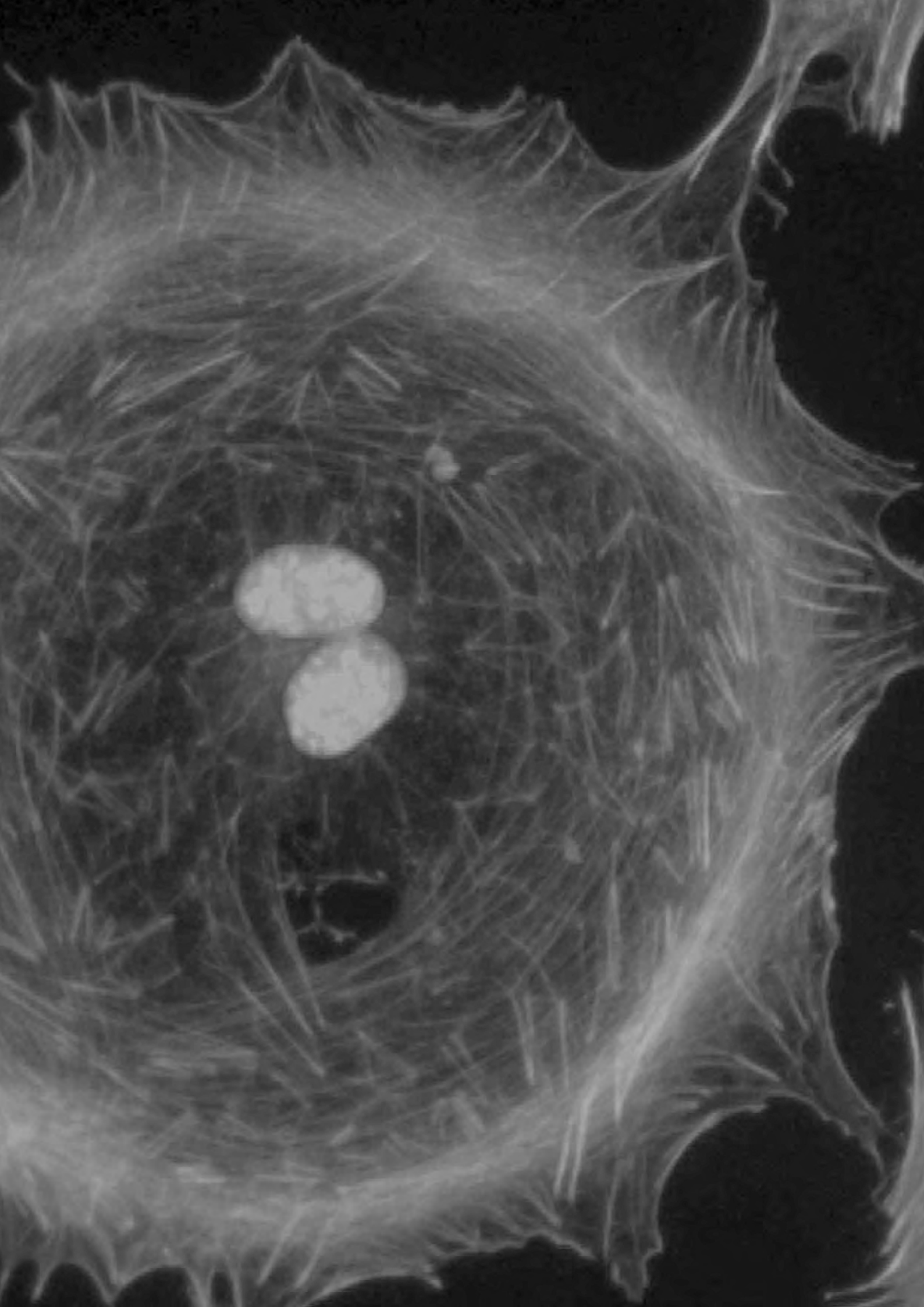


# Nanobiotechnology programme

Applying nanotechnology to improve bio/non-bio interactions for the development of new biomedical systems and devices, mainly for diagnostic purposes; developing ways, using atomic force microscopy, to measure the electrical properties of biological samples (biomembranes, single viruses or single bacteria) at the nanoscale, to develop label-free biological characterization methods and electronic biosensors; developing diagnostic and therapeutic systems for infectious diseases; demonstrating the feasibility of nanovectors as antimalarial drugs or carriers of drugs

## Nanobioengineering

Prof. Dr. Josep Samitier

## Nanoscale Bioelectrical Characterization

Dr. Gabriel Gomila

## Nanomalaria (joint group IBEC/CRESIB)

Dr. Xavier Fernández-Busquets

## Biomimetic Systems for Cell Engineering

Dr. Elena Martínez

# Nanobioengineering

**Group leader:** Josep Samitier

**Senior researchers:** Antoni Homs, Mateu Pla

**Postdoctoral researcher:** Margarita Alvira, Anna Lagunas, Mònica Mir, ZiQiu (Tommy) Tong

**PhD students:** Juan Pablo Agusil, Gizem Altay, Caterina Credi, Beatriz Del Moral, Maria Teresa Galán, Silvana Moris, Mafalda Nunes, Ana Mª Oliva, Wilmer Pardo, César Parra, Luís Rigat, Marta Sanmartí, José Luis Ávila, Bogachan Tahirbegi, Rosa Zaffino

**Masters students:** Laura González, Roberto Paoli, Érika Ramos

**Technicians:** Juan Manuel Álvarez, Miriam Funes, David Izquierdo, María de los Reyes Malavé

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) and working together in applying nanotechnology to the development of new biomedical systems and devices, mainly for diagnostic purposes.

**The main activities of the group involve the surface functionalization of materials integrated with microfluidics systems for the study of biomolecule and cell interactions to develop Organ on Chip or for the development of new biosensors that will be integrated in lab-on-a-chip devices.**

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 for clinical diagnosis and food safety applications*

- DNA sensors for cancer biomarker detection
- Antibody-based sensors for detection of pathogenic microorganisms
- Olfactory receptor-based sensors for odorant and volatile compounds detection
- Polymer nanowires-based biosensors
- Microfluidic chip for reagent handling in POC diagnosis devices
- Microfluidic chip using hydrodynamic focusing for bacteria counting and sorting

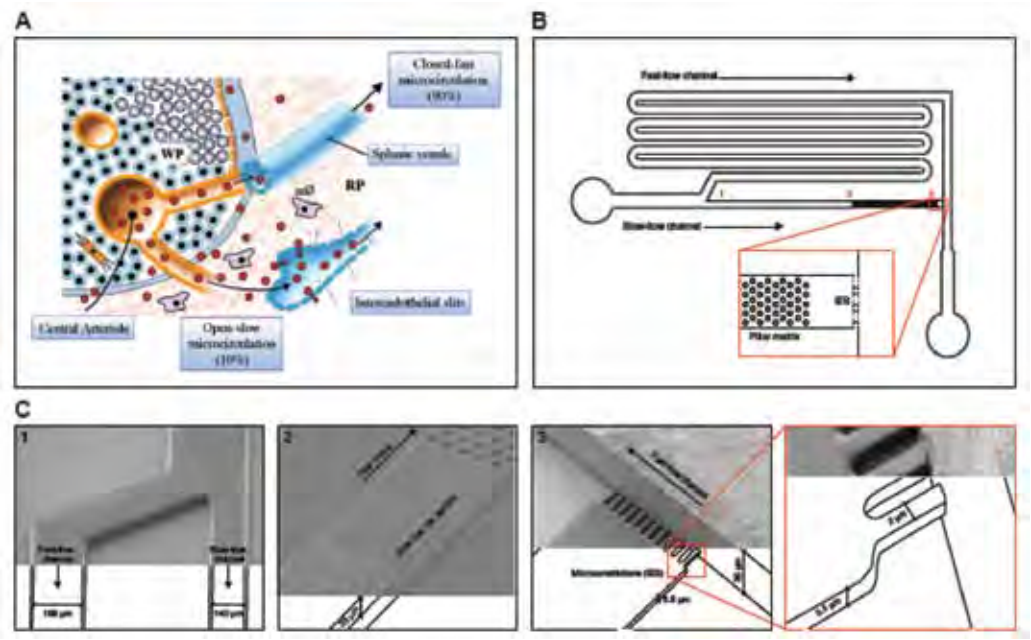
*2. Nanotechnology applied to biomolecule interaction studies and micro/nano-environments for biomedical studies and regenerative medicine applications*

- Design, production and characterization of micro/nanoenviroments with different biocompatible materials for cell behavior studies (adhesion, proliferation, differentiation)
- Design, production and characterization of scaffolds with a topography and chemical composition controlled at the nanoscale for ocular and cardiac tissue regenerative therapies based on stem cells
- Magnetic nanoparticles-biomolecules interactions and their applications

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

- Microfluidic chip for blood/plasma filtering
- Spleen-on-a-Chip development
- Engineering microfluidic platforms for neurobiological studies

Spleen organ physiology on a chip.



## Research projects

- **BOND** Bioelectronic Olfactory Neuron Device (2009-2013).
  Coordinator: **Josep Samitier** (for the UB)
  Technical Manager: **Gabriel Gomila** (page 76)
  *Collaborative project (NMP) within the framework of EU-FP7*

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

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

- **LABINACHIP** Nuevos métodos para la fabricación de dispositivos microfluídicos (2010-2013).
  PI: **Josep Samitier**
  *Centro para el Desarrollo Tecnológico Industria (CDTI), Industria de la Ciencia*

- Development of innovative tools for Ochratoxin A risk assesment (2011-2013).
  PI: **Beatriz Prieto** (coordinator)
  *Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR), Comunitat de Treball dels Prineus (CTP)*

- Diagnóstico y pronóstico de cáncer de próstata mediante nanobiosensores híbridos multianalito (2011-2013).
  PI: **Josep Samitier, Elena Martinez** (coordinator) (page 84)
  *MINECO, Instituto de Salud Carlos III. Subprograma de Proyectos de investigación en salud (FIS)*

- **CARDIO-STEM** Terapias regenerativas con células madre para el fallo cardíaco (2009-2014).
  PI: **Josep Samitier**
  *MINECO, ACI-E Medicina Regenerativa*

- Desarrollo de Tecnologías en Bionanomedicina para diagnóstico y terapia
  PI: **Josep Samitier**
  *Industrial project with Fundación Marcelino Botín*

- Desarrollo de una nueva tecnología lab-on-a-chip para la detección y cuantificación de secuencias de ADN/ARN (biomarcadores).
  PI: **Josep Samitier**
  *Industrial project with GENOMICA S.A.U.*

- Suport al desenvolupament i integració de sistemes de "point-of-care" pel diagnòstic mèdic de malalties respiratòries (dins del projecte TheraEDGE).
  PI: **Josep Samitier**
  *Industrial project with BIOKIT, S.A.*

- 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)*

## 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

## Publications


- Lagunas, A., Comelles, J., Oberhansl, S., Hortigüela, V., Martínez, E. & Samitier, J. (2013). Continuous bone morphogenetic protein-2 gradients for concentration effect studies on C2C12 osteogenic fate. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 9 (5), 694-701.

- Tahirbegi, I. B., Mir, M. & Samitier, J. (2013). Real-time monitoring of ischemia inside stomach. *Biosensors and Bioelectronics*, 40 (1), 323-328.

- Barreiros dos Santos, M., Agusil, J. P., Prieto-Simón, B., Sporer, C., Teixeira, V. & Samitier, J. (2013). Highly sensitive detection of pathogen *Escherichia coli* O157: H7 by electrochemical impedance spectroscopy. *Biosensors and Bioelectronics*, 45 (1), 174-180.

- Novo, S., Penon, O., Barrios, L., Nogués, C., Santaló, J., Durán, S., Gómez-Matínez, R., Samitier, J., Plaza, J. A., Pérez-García, L. & Ibáñez, E. (2013). Direct embryo tagging and identification system by attachment of biofunctionalized polysilicon barcodes to the zona pellucida of mouse embryos. *Human Reproduction*, 28 (6), 1519-1527.

- Caballero, D., Fumagalli, L., Teixidor, F., Samitier, J. & Errachid, A. (2013). Directing polypyrrole growth by chemical micropatterns: A study of high-throughput well-ordered arrays of conductive 3D microrings. *Sensors and Actuators B: Chemical*, 177, 1003-1009.

- Prats-Alfonso, E., Oberhansl, S., Lagunas, A., Martínez, E., Samitier, J. & Albericio, F. (2013). Effective and versatile strategy for the total solid-phase synthesis of alkanethiols for biological applications. *European Journal of Organic Chemistry*, 2013 (7), 1233-1239.

- Rodriguez-Segui, S. A., Ortuno, M. J., Ventura, F., Martinez, E. & Samitier, J. (2013). Simplified microenvironments and reduced cell culture size influence the cell differentiation outcome in cellular microarrays. *Journal of Materials Science: Materials in Medicine*, 24 (1), 189-198.

**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

**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.**

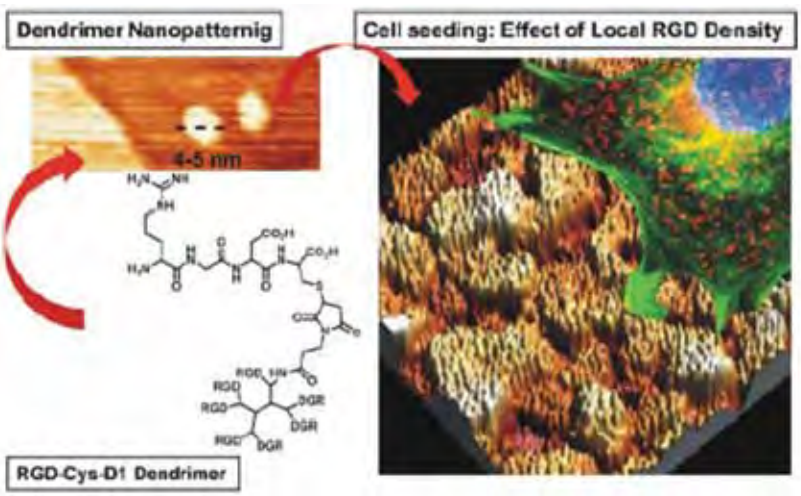
**Enantia S.L.**

**Microfluidic ChipShop GmbH**

# Scientific equipment and techniques

- Nanofabrication and nanomanipulation
  - Automatized microcontact printing system (custom-made)
  - Dip-Pen Nanolithography system (DPN)
  - Nanoplotter NPM
  - Nanotechnology Platform (PCB): equipment for hot embossing lithography, polymer processing and photolithography, chemical wet etching, e-beam evaporation
- Characterization
  - Surface Plasmon Resonance (SPR)
  - Quartz crystal microbalance (QCM)
  - Optical Waveguide Lightmode Spectroscope (OWLS)
  - Atomic Force Microscope (AFM)
  - 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
- Microfluidics
  - High precision syringe pumps
  - Peristaltic pumps

Surface functionalization using dendrimers for studies of cell adhesion with non-uniform RGD density clusters. (*Nano Research* 2014).



# Nanoscale Bioelectrical Characterization

**Group leader:** Gabriel Gomila

**Senior researcher:** Laura Fumagalli

**Postdoctoral researcher:** Jordi Otero

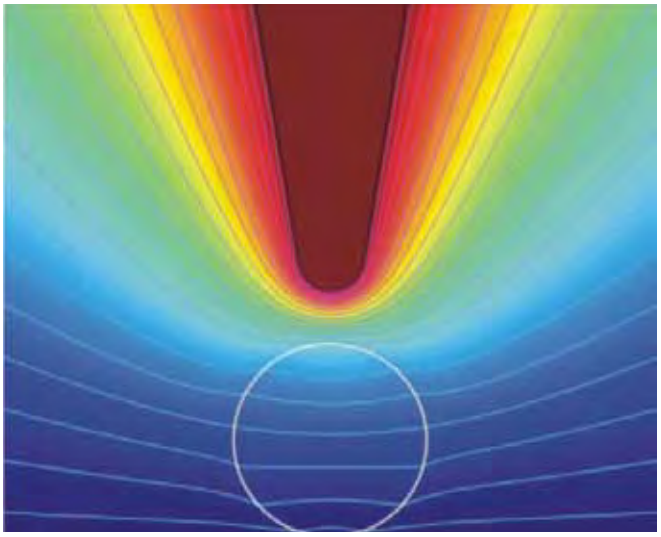
**PhD students:** Maria Chiara Biagi, Marc Van der Hofstadt

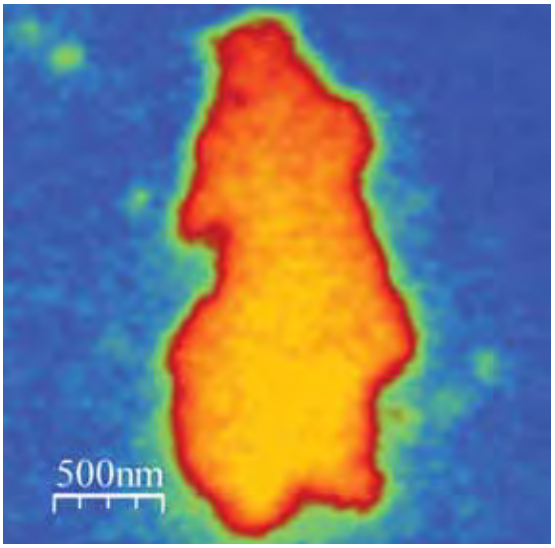
The main goal of our research group is to develop new experimental setups based on atomic force microscopy and theoretical frameworks enabling the measurement of the electrical properties of biological samples at the nanoscale (for example, biomembranes, single viruses or single bacteria).

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

During 2013 we demonstrated for the first time the possibility to measure with high accuracy the electric polarization properties (dielectric constant) of biomembranes in liquid environment revealing a direct contribution coming from membrane hydration effects. Moreover, we have deepened our theoretical understanding of quantitative electrostatic force microscopy applied to single dielectric nanoparticles and applied in liquid media. Finally, we have completed the study of the electric polarization properties of single bacteria. In addition, we have also completed the study of the mechanical properties of natural nanovesicles containing olfactory receptors for biosensor applications.

Electrical potential distribution corresponding to the electric interaction between a biased nanometric sharp conducting tip of radius 5 nm and a polystyrene dielectric nanoparticle of radius 20 nm. The electric polarization force acting on the tip is below a picoNewton, and sensitivity depends on the size, dielectric constant and non-sphericity of the nanoparticle.






Dielectric image of a 5 nm thick DPPC lipid bilayer on a highly doped silicon substrate measured in a 1mM salt concentration aqueous solution. The image has been obtained with an applied ac voltage of 0.25 V and frequency 80 MHz and using a solid platinum tip of radius 45 nm. Quantification of the dielectric image gives a lipid bilayer relative dielectric constant of $\varepsilon_{r,DPPC}$= 3.2. This value is higher than the one obtained in dry air conditions and reveals a contribution of the hydration of the polar region of the lipid bilayer.

## Publications


- Gomila, G., Esteban-Ferrer, D. & Fumagalli, L. (2013). Quantification of the dielectric constant of single non-spherical nanoparticles from polarization forces: Eccentricity effects. *Nanotechnology*, 24 (50), 505713.
- Gramse, G., Edwards, M. A., Fumagalli, L. & Gomila, G. (2013). Theory of amplitude modulated electrostatic force microscopy for dielectric measurements in liquids at MHz frequencies. *Nanotechnology*, 24 (41), 415709.
- Gramse, G., Dols-Perez, A., Edwards, M. A., Fumagalli, L. & Gomila, G. (2013). Nanoscale measurement of the dielectric constant of supported lipid bilayers in aqueous solutions with electrostatic force microscopy. *Biophysical Journal*, 104 (6), 1257-1262.


## Research projects

- **ELECTROBACTERIA** Nanotools and nanotechniques for bioelectric studies in single bacteria cells (2011-2013).
PI: **Gabriel Gomila**
*MINECO (TEC2010-16844)*

- **AFM4NanoMed&Bio** European network on applications of Atomic Force Microscopy to NanoMedicine and Life Sciences (2010-2015).
PI: **Gabriel Gomila** (Management Committee Substitute Member)
*EU COST Action TD1002*

- **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*

## Collaborations with other research centres

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

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

**Prof. Edith Pajot-Augy** Neurobiologie de l'olfaction et la prise alimentaire, Institut National de la Recherche Agronomique, Jouy-en-Josas, France

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

**Prof. Marco Sampietro** Laboratorio di Strumentazione Analogica e Materiali Polimerici, Politecnico di Milano, Italy

**Dr. Adriana Gil** Nanotec Electronica S.L., Madrid, Spain

**Prof. Lino Reggiani** National Nanotechnology Laboratory, Universita del Salento, Lecce, Italy

**Dr. Ferry Kienberger** Agilent Technologies Austria, Linz, Austria

**Prof. Modesto Orozco** Institut de Recerca Biomèdica, Barcelona, Spain

## Scientific equipment and techniques

- Cypher Atomic Force Microscope (Asylum Research)
- 2 Cervantes Atomic Force Microscopes (Nanotec Electronica)
- Easy Scan 2 Atomic Force Microscope (Nanosurf)
- AxioImager A1m Reflection Optical Microscope (Zeiss) equipped with a AxioCam ERc5s (Zeiss)
- HF2LI digital lock-in amplifier (Zurich Instruments)
- CompactStat portable electrochemical interface and impedance analyzer (Ivium Technologies)
- 2 eLockIn204 4-phase Lock-In amplifiers (Anfatec)
- Keithley 6430 sub-femtoAmp remote sourcemeter (Keithley)


- Caballero, D., Fumagalli, L., Teixidor, F., Samitier, J. & Errachid, A. (2013). Directing polypyrrole growth by chemical micropatterns: A study of high-throughput well-ordered arrays of conductive 3D microrings. *Sensors and Actuators B: Chemical*, 177, 1003-1009.
- Dols-Perez, A., Sisquella, X., Fumagalli, L. & Gomila, G. (2013). Optical visualization of ultrathin mica flakes on semitransparent gold substrates. *Nanoscale Research Letters*, 8 (1), 1-5.

# Nanomalaria (joint group IBEC/CRESIB)

**Head of Joint Unit:** Xavier Fernàndez-Busquets

**PhD students:** Joana Azevedo, Ernest Moles

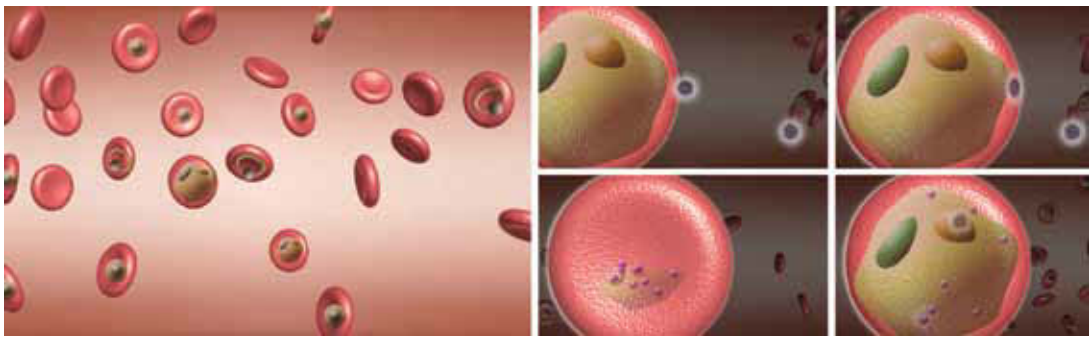
Established in 2010, the Nanomalaria Group is a Joint Unit affiliated with IBEC and the Barcelona Centre for International Health Research (CRESIB, Hospital Clínic-Universitat de Barcelona), receiving support from both, and located in the Esther Koplowitz Centre near the Hospital Clínic.

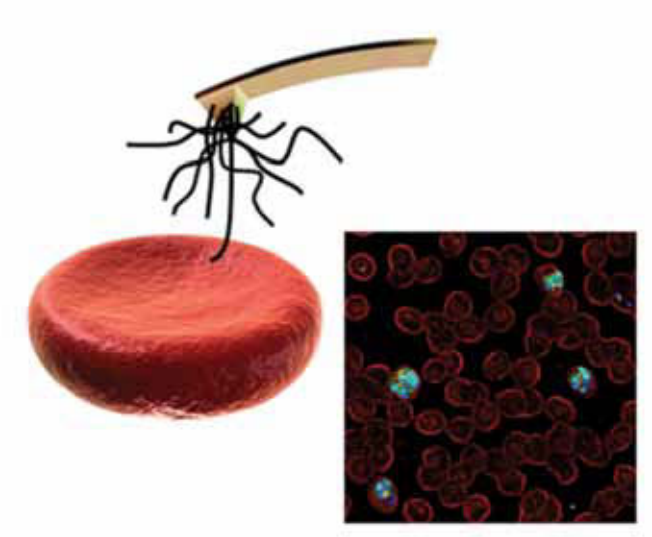
**The current activity of the Nanomalaria group is focused on the development of nanomedicine-based systems to be applied to malaria prophylaxis, diagnosis and therapy.**

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 sp*. 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 cost-related issues that might be hampering the development of nanotechnology-based medicines against malaria with the dubious argument that they are too expensive to be used in developing areas.

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) for the assembly of nanovectors capable of delivering their drug cargo with complete specificity to diseased cells. (ii) Development of DNA aptamers as cell targeting agents capable of replacing antibodies. (iii) Study of metabolic pathways present in *Plasmodium* but absent in humans, with the aim of identifying specific enzymes as therapeutic targets. (iv) Use of single-molecule force spectroscopy strategies for the biodiscovery of new antimalarial and antibiotic agents. (v) Investigation of the application of amyloid-based approaches to new malaria vaccines. (vi) Design of new methods for the targeted drug delivery to *Plasmodium* stages in the mosquito vector. (vii) Extension of our activities to new pathologies including leishmanisasis, Chagas disease, and tuberculosis.

When added to *Plasmodium*-infected blood (left panel), drug-conjugated polymers (small panels, clockwise from upper left) (i) bind and (ii) enter parasitized erythrocytes, (iii) releasing drug that (iv) eliminates the pathogen.





The adhesion of heparin to *Plasmodium*-infected red blood cells (pRBCs) has been probed by single-molecule force spectroscopy, as a pioneering approach to quantitatively evaluating heparin-pRBC interactions at the individual molecule level.

## Publications


- Valle-Delgado, J. J., Urbán, P. & Fernàndez-Busquets, X. (2013). Demonstration of specific binding of heparin to *Plasmodium falciparum*-infected vs. non-infected red blood cells by single-molecule force spectroscopy. *Nanoscale*, 5 (9), 3673-3680.
- Castangia, I., Manca, M. L., Matricardi, P., Sinico, C., Lampis, S., Fernàndez-Busquets, X., Fadda, A. M. & Manconi, M. (2013). Effect of diclofenac and glycol intercalation on structural assembly of phospholipid lamellar vesicles. *International Journal of Pharmaceutics*, 456 (1), 1-9.
- Fernàndez-Busquets, X. (2013). Heparin-functionalized nanocapsules: Enabling targeted delivery of antimalarial drugs. *Future Medicinal Chemistry*, 5 (7), 737-739.


## Filed patents

- **Heparin-Lipidic Nanoparticle Conjugates** (Filing date January 22nd, 2013).
*Inventors:* ***Xavier Fernàndez-Busquets***, ***Joana Marques*** & ***Ernest Moles***
Ref. number: EP13152187.4

## Research projects

- **NANOMALNET** Exploration of new efficient targeting molecules for nanovector-mediated antimalarial drug delivery (2012-2014).
PI: **Xavier Fernàndez-Busquets**
*Biotechnology Programme, MINECO, Spain (BIO2011-25039)*

- Group for the study of self-aggregating proteins (2009-2014).
PI: **Xavier Fernàndez-Busquets**
*Consolidated Research Group certified by the Generalitat de Catalunya, Spain (2009-SGR-760)*

## 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

**Dr. José Antonio García Salcedo** Instituto de Parasitología y Biomedicina "López-Neyra", Consejo Superior de Investigaciones Científicas (CSIC), Granada, Spain

**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. José Luis de Paz** Instituto de Investigaciones Químicas CSIC-University of Seville, 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

**Prof. Amílcar Labarta** Departament de Física Fonamental, University of Barcelona, Spain

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

## Scientific equipment and techniques

- Zeiss Primostar microscope
- Shake 'N' Stack (Thermo Hybaid) hybridization oven
- BIO-RAD electrophoresis system for agarose and polyacrylamide gels
- *Plasmodium falciparum* cell cultures


- Fernàndez-Busquets, X. (2013). Amyloid fibrils in neurodegenerative diseases: villains or heroes? *Future Medicinal Chemistry*, 5 (16), 1903-1906.

**Conference paper:**

- Pujol, A., Riera, C., Fisa, R., Molina, I., Salvador, F., Estelrich, J., Urbán, P. & Fernàndez-Busquets, X. (2013/08/01). Nanomedicine for infectious diseases: Application of quantum dots encapsulated in immunoliposomes to the study of targeted drug delivery against leishmaniasis and malaria. In 4th International Conference on Nanotechnology: Fundamentals and Applications. Ontario, Canada (2013), "*Proceedings of the 4th International Conference on Nanotechnology: Fundamentals and Applications*", 1-8, International ASET Inc.

# Biomimetic Systems for Cell Engineering

**Junior group leader:** Elena Martínez

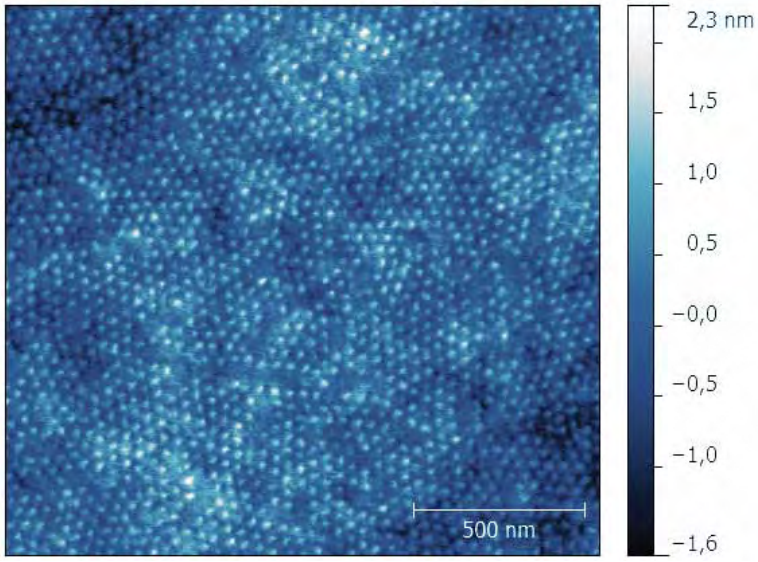
**PhD students:** Albert Garcia, Verónica Hortigüela, Maria Valls

**Undergraduate students:** Alicia Pozo, Ana Rodríguez

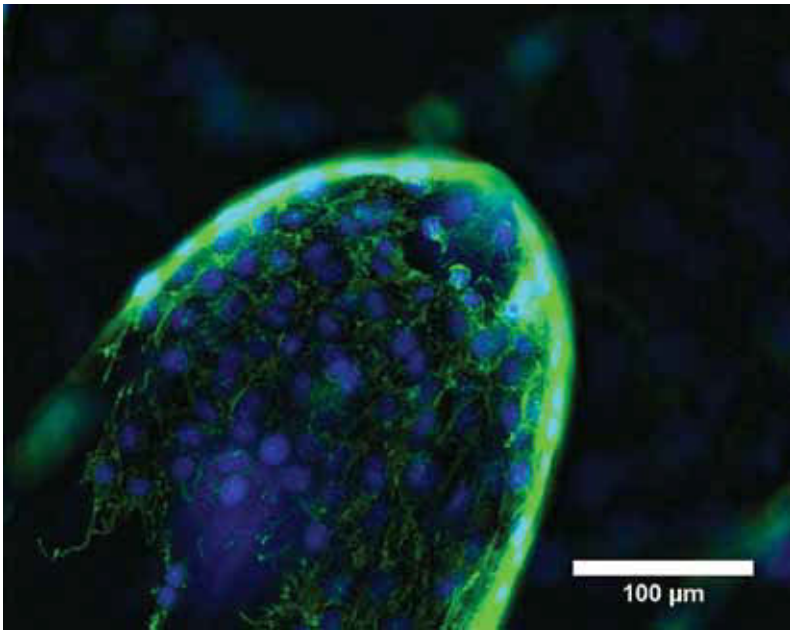
*In vitro* assay platforms involving human cells are increasingly important to study tissue development, tissue regeneration, construct models of disease or develop systems for therapeutic screening that predict the human *in vivo* context.

**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.




Atomic force microscopy picture of a thin layer of PS-b-PMMA copolymer. The two phases of the block copolymer self-assembled into an ordered nanostructure.




Mouse fibroblasts seeded on a PEG-AA micropillar functionalized with fibronectin.

## Publications


- Lagunas, A., Comelles, J., Oberhansl, S., Hortigüela, V., Martínez, E. & Samitier, J. (2013). Continuous bone morphogenetic protein-2 gradients for concentration effect studies on C2C12 osteogenic fate. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 9 (5), 694-701.
- Prats-Alfonso, E., Oberhansl, S., Lagunas, A., Martínez, E., Samitier, J. & Albericio, F. (2013). Effective and versatile strategy for the total solid-phase synthesis of alkanethiols for biological applications. *European Journal of Organic Chemistry*, 2013 (7), 1233-1239.


## Research projects

- Diagnóstico y pronóstico de cáncer de próstata mediante nanobiosensores híbridos multianalito (2011-2013).
PI: **Josep Samitier, Elena Martinez** (coordinator)
*MINECO, Instituto de Salud Carlos III. Subprograma de Proyectos de investigación en salud (FIS)*

- **CARDIO-STEM** Terapias regenerativas con células madre para el fallo cardíaco (2009-2014).
PI: **Josep Samitier**
*MINECO, ACI-E Medicina Regenerativa*

## Collaborations with other research centres

**Prof. Ángel Raya** IBEC (page 46)

**Dr. Núria Montserrat** Center of Regenerative Medicine in Barcelona (CMRB), Barcelona (Spain)

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

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

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

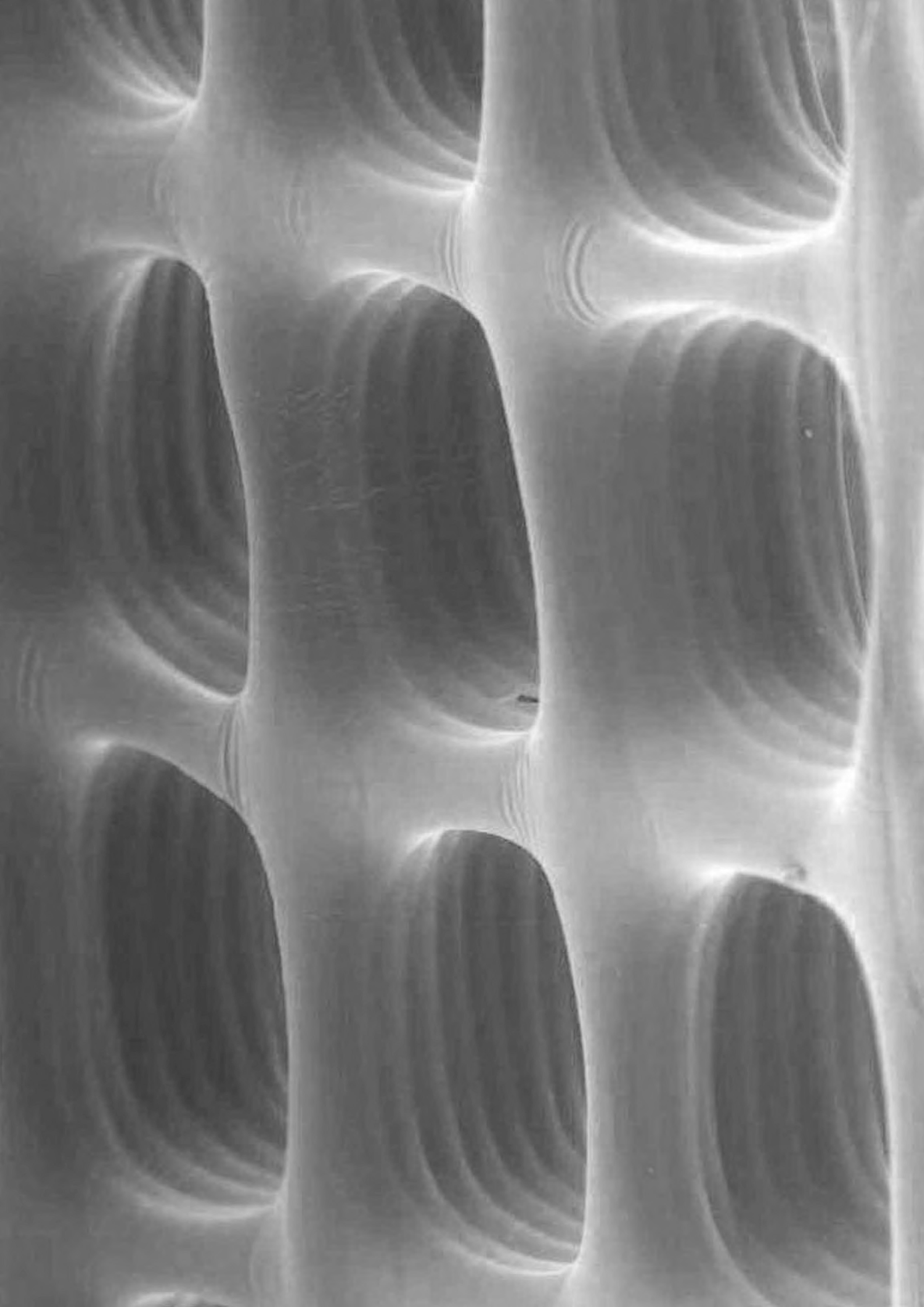
**Prof. Fernando Albericio** Institut de Recerca Biomédica (IRB), Barcelona (Spain)

**Prof. Vasco Teixeira** Universidade do Minho, Braga (Portugal)

## 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)


- Rodriguez-Segui, S. A., Ortuno, M. J., Ventura, F., Martinez, E. & Samitier, J. (2013). Simplified microenvironments and reduced cell culture size influence the cell differentiation outcome in cellular microarrays. *Journal of Materials Science: Materials in Medicine*, 24 (1), 189-198.



# Biomaterials, implants and tissue engineering programme

Development of bioactive and biodegradable materials for tissue regeneration which aid the repair and functional restoration of tissues or organs with 3D scaffolds, cells or signals; studying the interactions between tissue physics and biological processes, and how these interactions can affect the functional biomechanics of organs

## Biomaterial for Regenerative Therapies

Dr. Elisabeth Engel

## Molecular Dynamics at Cell–Biomaterial Interface

Prof. Dr. George Altankov

## Biomechanics and Mechanobiology

Dr. Jérôme Noailly

# Biomaterials for Regenerative Therapies

**Junior group leader:** Elisabeth Engel

**Research fellow:** Josep A. Planell

**Senior researchers:** Oscar Castaño, Miguel Angel Mateos, Melba Navarro

**Postdoctoral researcher:** Soledad Pérez

**PhD students:** Zaida Álvarez, Irene Cano, Riccardo Levato, Luca Liverani, Joan Martí, Claudia Navarro, Nadège Sachot, Aitor Sánchez, Tiziano Serra

**Masters students:** Tabatha Bourgois, Pauline Carreras, Ludovic Moulin, Thomas Ngue-No

**Undergraduate students:** Gerard Rubí, Pep Pau Soriano

**Technician:** Belén González

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 develop 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.**

The group masters its own techniques to produce biomaterials such as biodegradable polymers, calcium phosphate glasses and glass-ceramics, and combinations of these as composites and hybrids. Different fabrication techniques such as solvent-casting, rapid prototyping, electrospinning and micro-nano particles production allow the manufacture of 3D scaffolds with tuned geometry, inner architecture, handleability, and the requisite mechanical and surface properties for different clinical applications. For example, we have optimized surface functionalization with different biochemical cues to signal and recreate the biological environment, as well as incorporating of topographical and mechanical features. We have also explored the preparation and design of materials and scaffolds for *in vitro* and *in vivo* fundamental studies, and a further focus is the provision of useful tools to assess mechanisms that govern cell behavior in regenerative medicine.

The group also has the capacity to isolate and culture stem and precursor cells for the *in vitro* biological characterization of the developed scaffolds for tissue engineering. One of our objectives is the development of a biodegradable dressing based on the release of ions that stimulate the cellular processes involved in skin wound healing, based on the release of ions together with the appropriate mechanical settings for skin regeneration.

The group has also the knowledge to understand and coordinate interactions with soluble factors, other cells, and extracellular matrices, defining a local biochemical and mechanical microenvironment with the complex and dynamic regulations that control the fate of stem cells for therapeutical benefit. One of the most important signals is extracellular calcium, which acts as first and second messenger in biological systems, with many functions which have already been described and new ones arising constantly. The detailed knowledge of the mechanisms that govern calcium biochemistry in the healing process is required in order to enhance the efficiency of our biomaterials.

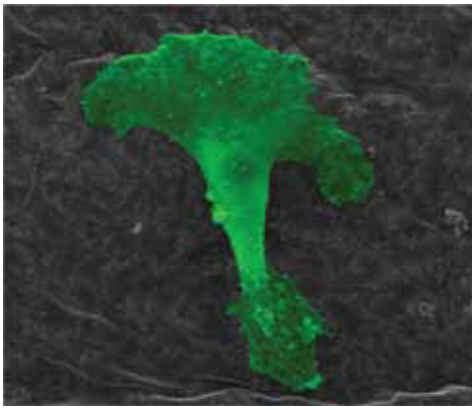
As an applied science group, one of our main goals is the transfer of know-how to industry through the creation of connections between researchers, companies and hospitals. We already have projects in place with different companies such as Ferrer, Conic Vascular and Euroimplant, as well as with hospitals such as the Hospital Terrassa, Barcelona's Vall d'Hebron University Hospital and Hospital Clínic, and the Bordeaux Hospital University Center (CHU).

In 2013, we made important progress towards the synthesis of new materials with calcium release properties and angiogenic/osteogenic potential. We fabricated biodegradable 3D scaffolds containing glass microparticles and applied them to bone tissue engineering, demonstrating a good enhancement of angiogenesis both *in vitro* and *in vivo*. Rapid prototyping (RP) scaffolds with well-defined and reproducible architectures were set as biodegradable scaffolds for studying bone regeneration. In cell therapy applications, we developed and optimized polymeric microparticles, injectable microcarriers that were tested as potential cell carriers, paying particular attention to cell adhesion, proliferation and differentiation, as well as migration. We also developed and tested nanoparticles for drug delivery purposes, as well as developing electrospun polymer fiber-based scaffolds for skin wound healing and neural regeneration. In both applications, structure and degradation products were shown to have an effect on cells.

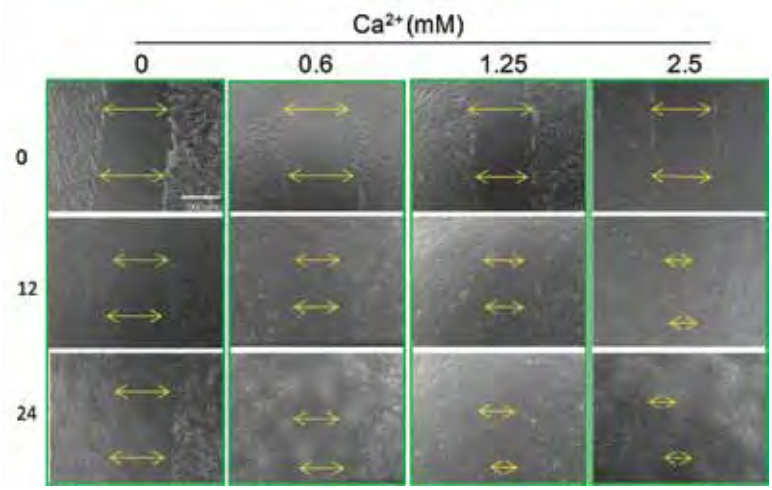
The group has also worked with Elastin-like Recombinant Polymers (ELR) promoting mineralization, and we are studying their potential application in *in situ* bone regeneration. The combination of these materials and controlled manufacturing processes, together with their biofunctionalization, has allowed us to develop of new customized biodegradable systems for different clinical applications such as ophthalmology, the nervous system, skin, tendon and bone.

In 2013 the group had a successful outcome with the crowdfunded project Dermoglass, which attracted much attention. The generosity of the donors will enable us to launch a skin regenerative dressing on the market in the medium term.

hMSC on the surface of elastin-like recombinamers hidrogel crosslinked with citric acid after 14 days in culture.



Typical polymeric mesh fabricated by rapid prototyping.




Effect of extracelular Ca2+ on dermal fibroblast migration in a wound scratch assay.

## Research projects

- **THE GRAIL** Tissue in Host Engineering Guided Regeneration of Arterial Intimal Layer.
PI: **Elisabeth Engel** (partner)
*EU - Cooperation - HEALTH*

- **nAngioFrac** Angiogenic nanostructured materials for non-consolidating bone fractures.
PI: **Elisabeth Engel** (coordinator)
*EU - EURONANOMED - PI11/03030*

- Grup de recerca consolidat (2009-2014).
PI: **Josep A. Planell**
*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 (2009 SGR 474)*

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

- Bioactive biomaterials design and development for skin regeneration based on controlled ion release signaling.
PI: **Elisabeth Engel**
*MINECO MAT2012-38793*

- Tendon Tissue Engineering: A Helping Hand for Rotator Cuff Tears (BIOTENDON)
PI: **Elisabeth Engel**
*RecerCaixa*

- Desarrollo de un nuevo producto de terapia avanzada para la regeneración y reconstrucción de la superficie ocular.
PI: **Elisabeth Engel**
*Technology transfer project with Ferrer*

- **VALOR** Development of a wound dressing for the treatment of vascular ulcers that promotes revascularization and tissue regeneration (2011-2013).
PI: **Melba Navarro**
*AGAUR – Ajuts destinats a incentivar els projectes i les activitats de valorització de recerca i de tecnología (VALOR 2010)*

## Publications


- Álvarez, Z., Mateos-Timoneda, M. A., Hyrossová, P., Castaño, O., Planell, J. A., Perales, J. C., Engel, E. & Alcántara, S. (2013). The effect of the composition of PLA films and lactate release on glial and neuronal maturation and the maintenance of the neuronal progenitor niche. *Biomaterials*, 34 (9), 2221-2233.
- Best, S., Planell, J. A., Santin, M., Voskerician, G. & Amédée, J. (2013). Editorial. *Journal of Materials Science: Materials in Medicine*, 24 (6), 1333-1334.
- Gustavsson, J., Planell, J. & Engel, E. (2013). Ion-selective electrodes to monitor osteoblast-like cellular influence on the extracellular concentration of calcium. *Journal of Tissue Engineering and Regenerative Medicine*, 7 (8), 609-620.
- López-Bosque, M. J., Tejeda-Montes, E., Cazorla, M., Linacero, J., Atienza, Y., Smith, K. H., Lladó, A., Colombelli, J., Engel, E. & Mata, A. (2013). Fabrication of hierarchical micro-nanotopographies for cell attachment studies. *Nanotechnology*, 24 (25), 255305.
- Mendes, A. C., Smith, K. H., Tejeda-Montes, E., Engel, E., Reis, R. L., Azevedo, H. S. & Mata, A. (2013). Co-assembled and microfabricated bioactive membranes. *Advanced Functional Materials*, 23 (4), 430-438.
- Punet, X., Mauchauffé, R., Giannotti, M. I., Rodríguez-Cabello, J. C., Sanz, F., Engel, E., Mateos-Timoneda, M. A. & Planell, J. A. (2013). Enhanced cell-material interactions through the biofunctionalization of polymeric surfaces with engineered peptides. *Biomacromolecules*, 14 (8), 2690-2702.
- Sachot, N., Castaño, O., Mateos-Timoneda, M. A., Engel, E. & Planell, J. A. (2013). Hierarchically engineered fibrous scaffolds for bone regeneration. *Journal of The Royal Society Interface*, 10 (88), 20130684.
- Salerno, A., Levato, R., Mateos-Timoneda, M. A., Engel, E., Netti, P. A. & Planell, J. A. (2013). Modular polylactic acid microparticle-based scaffolds prepared via microfluidic emulsion/solvent displacement

process: Fabrication, characterization, and *in vitro* mesenchymal stem cells interaction study. *Journal of Biomedical Materials Research Part A*, 101A (3), 720-732.

- Serra, T., Mateos-Timoneda, M. A., Planell, J. & Navarro, M. (2013). 3D printed PLA-based scaffolds: A versatile tool in regenerative medicine. *Organogenesis*, 9 (4), 239-244.
- Serra, T., Planell, J. A. & Navarro, M. (2013). High-resolution PLA-based composite scaffolds via 3-D printing technology. *Acta Biomaterialia*, 9 (3), 5521-5530.
- Vila, O. F., Bagó, J. R., Navarro, M., Alieva, M., Aguilar, E., Engel, E., Planell, J., Rubio, N. & Blanco, J. (2013). Calcium phosphate glass improves angiogenesis capacity of poly(lactic acid) scaffolds and stimulates differentiation of adipose tissue-derived mesenchymal stromal cells to the endothelial lineage. *Journal of Biomedical Materials Research Part A*, 101A (4), 932-941.

**Book section:**

- Pandit, A., Planell, J. A. & Navarro, M. (2013). Titanium and Nitinol (NiTi). In *Biomaterials Science. An Introduction to Materials in Medicine Classes of Materials Used in Medicine*, ed. Ratner, B., Hoffman, A., Schoen, F. & Lemons, J., 120-124, Academic Press, Oxford, UK.



## Collaborations with other research centres

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

**Dr. Izabella Rajzer** Institute of Textile Engineering and Polymer Materials, University of Bielsko-Biala, Poland

**Dr. José María Mora** Servei de cirurgia ortopédica i traumatológica, Consorci Hospital de Terrassa, Spain

**Dr. Matilde Alonso** Dept. de Física de la Materia Condensada, Universidad de Valladolid, Spain

**Dr. Mercè Alsina** Servicio de Dermatología, Hospital Clínic de Barcelona, Spain

**Dr. Soledad Alcántara** Grup de Desenvolupament Neural, IDIBELL, University of Barcelona, Spain

**Prof. Aldrik Velders** Microwave and Sustainable Organic Chemistry Department, University of Twente and Wageningen Nuclear Magnetic Resonance Centre (WNMRC), The Netherlands

**Prof. Didier Letourneur** Laboratoire de Bioingénierie Cardiovasculaire, INSERM, University Denis Diderot-Paris 7, Paris, France

Prof. Dirk Grijpma, Department of Biomaterials Science and Technology, University of Twente, Twente, the Netherlands

**Prof. Francesco Serino** Department of Vascular Surgery, Istituto Dermatologico dell'Immacolata (IDI), Rome, Italy

**Dr. Jerónimo Blanco** Institut de Ciències Cardiovasculars de Catalunya and CSIC, Barcelona, Spain

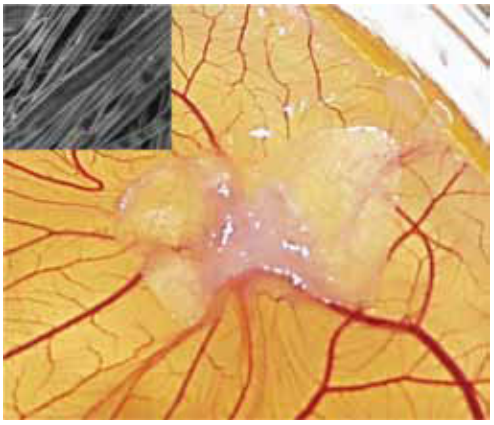
**Dr. Joelle Amedee** INSERM, University of Bordeaux Segolen, Bordeaux, France

**Dr. José Becerra Ratia** Dept. Biología Celular, Genética y Fisiología, Universidad de Málaga, Spain

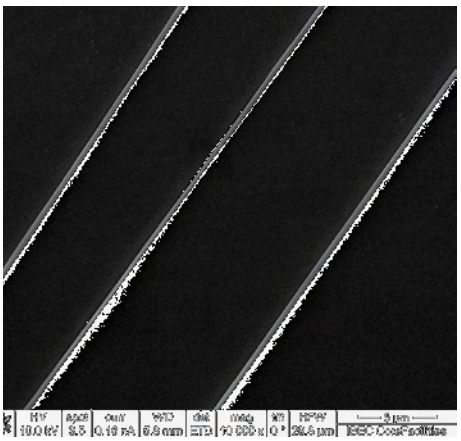
**Dr. José Carlos Rodríguez-Cabello** Dept. de Física de la Materia Condensada, Universidad de Valladolid, Spain

**Dr. Julia Buján** Dept. de Ciencias Morfológicas y Cirugía, Facultad de Medicina, Universidad de Alcalá de Henares, Spain

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



Pro-angiogenic capacity of SG5/PLA hybrid fibers in a chick chorioallantoic membrane (CAM) model. Detail of the fibers in the inset.



Parallel PLA fibers as platform for fundamental neuronal *in vitro* studies.

**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, quartz crystal microbalance, 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
- Ion selective electrodes for $Ca^{2+}$, $Na^{+}$, $K^{+}$, and pH
- ElectroForce® BioDynamic® test instrument

# Biomechanics and Mechanobiology

**Senior researcher:** Jérôme Noailly

**Postdoctoral researchers:** Andrea Malandrino, Andy Olivares

**PhD students:** Carlos Ruiz, Themis Toumanidou

**Masters students:** Leonid Sergeevich Bovkun

**Research technicians:** Gaëtan Chary, Darío Mora

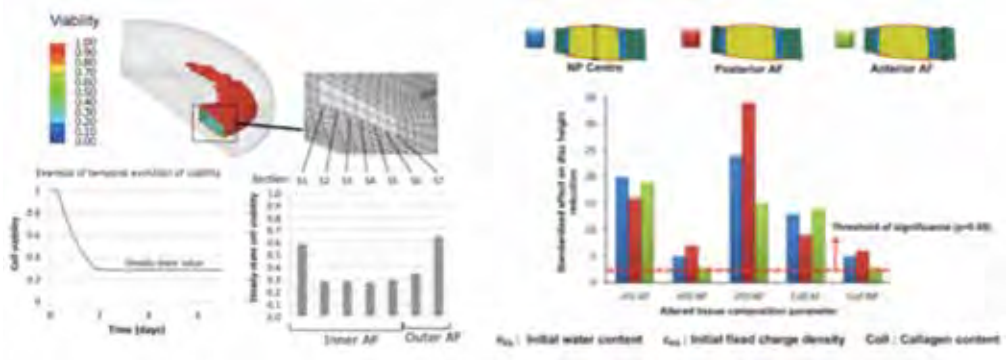
Research in the group of Biomechanics and Mechanobiology focuses mainly on (i) the interactions between tissue multiphysics and biological processes, and (ii) how these interactions can affect the functional biomechanics of organs.

**Numerical methods based mostly but not exclusively on finite element modelling are used to describe both the tissues at the organ level, and the tissue-cell interactions at the tissue and cellular levels. The numerical concepts developed are tested against *in vivo* and *in vitro* data, which allows model validations. Emphasis is given to the study of load transfer from organs to tissues and to cells, depending upon organ/tissue condition, and with or without treatment simulation. Calculations are based on mechano-regulation and/or on biophysical concepts to predict different cell environments over time.**

Most tissue and biophysical models developed so far aimed to study one of the most complex organs of the musculoskeletal system, namely the spine. Thorough knowledge about the functional biomechanics of the lumbar spine has been acquired along the time in relation to computational simulations (*J Biomech*, 40, 2414-25; *Biomech Model Mechanobiol*, 10, 203-19). In order to capture as best as possible the communications between organ and tissue biomechanics, studies of advanced tissue models have been performed, in relation to the vertebrae (*Mater Lett*, 78, 154-58), to the intervertebral discs (*J Mech Behav Biomed Mater*, 4, 124-41; *Comput Meth Biomech Biomed Engin*, 16, 923-8) and to the muscles (*J Biomech*, 45, S484). In particular, these models allowed thorough identification of the tissue parameters expected to alter cell nutrition in a deforming intervertebral disc (*PLoS Comput Biol*, 7, e1002112), leading to further relations between tissue condition and cell viability (*Poromechanics V*, 2193-2201). Care is also taken to assess the physical meaning of the tissue model parameters, and the mechanistic aspect of the simulation work is supported by both stochastic modelling and bioreactor experiments.

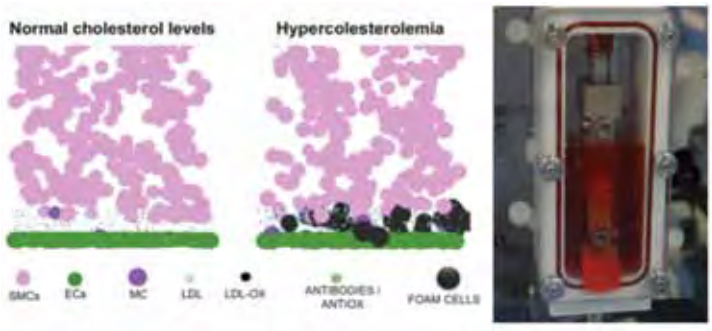
Below: Prediction of mutual interactions between strain-induced muscle activation (left) and intervertebral disc pressurization (right) during night rest simulations in a finite element model of the lower lumbar spine (L3 to L5-S1 intervertebral disc).

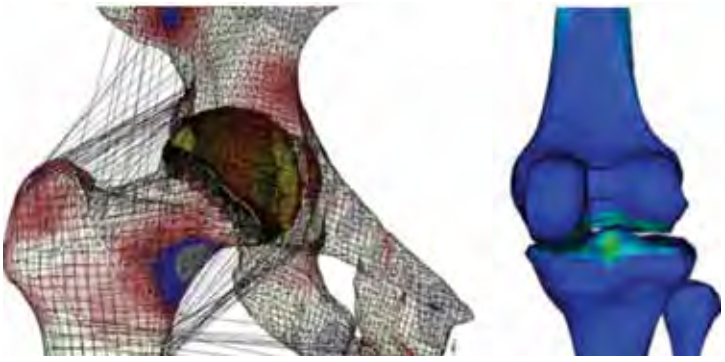
Below left: Cell viability predictions given by different mechanotransduction assumptions within a bovine intervertebral model subject to steady-state overloads. Below right: Effect of degeneration-related changes in tissue composition within the intervertebral disc on local disc height reduction along daily load.



The numerical stability of these models is also one target of the explorations performed within the group (*J Mech Behav Biomed Mater*, 26, 1-10), in order to ensure the coupling to lower scale biophysical models. Also, models have been used to for implant simulations focussed either on clinical (*J Appl Biomat Biomech*, 4, 135-42), or on design questions (*Eur Spine J*, 21, S675-87). Beyond the spine domain, both knowledge and know-how acquired are being transferred to the exploration of the cardiovascular system. Also, ongoing clinical collaborations are contributing to the adaptation of the numerical methods to study problems and treatment solutions related to the lower limbs (*J Clinbiomech,* 2014).

Left: agent-based simulations for the exploration of atheroscleroma formation as a result of complex molecular and cellular interactions. Right: dynamic culture of a cell-seeded biomaterial.



Left: Principal stress predictions in a model of the human hip joint. Right: bone stress analysis at the femorotibial junction.

## Publications

- Barreto, S., Clausen, C. H., Perrault, C. M., Fletcher, D. A. & Lacroix, D. (2013). A multi-structural single cell model of force-induced interactions of cytoskeletal components. *Biomaterials*, 34 (26), 6119-6126.

## Research projects

- **MySpine** Functional prognosis simulation of patient-specfic spinal treatment for clinical use (2011-2014)
PI: **Jérôme Noailly**
*Collaborative project within the framework of EU-FP7*

- **THE GRAIL** Tissue in Host Engineering Guided Regeneration of Arterial Intimal Layer
PI: **Elisabeth Engel** (partner)
*EU - Cooperation - HEALTH*

- Investigación de la biomecánica y mecanobiología de las fracturas de la meseta tibial mediante un modelo de elementos finitos
PI: **Jérôme Noailly**
*Clinical contract*

## Collaborations with other research centres

**Dr. Josep Maria Font / Prof. Antoni Susín** Universitat Politècnica de Catalunya BarcelonaTech (UPC), Barcelona, Spain

**Dr Ludovic Humbert** Universitat Pompeu Fabra, Galgo Medical SL, Barcelona, Spain

**Dr. Ion Carrera / Dr. Màrius Valera** Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

**Dr. Joan Carles Monllau** Hospital del Mar, Barcelona, Spain

**Dr Gianluca Vadalà** Campus Bio-Medico University of Rome, Italy

**Prof. Mauro Alini** AO Research Institute – AO Fundation, Davos, Switzerland

**Dr Benjamin Gantenbein / Dr Samantha Chan** University of Bern, Switzerland

**Prof. Stephen Fergusson** ETH Zurich, Switzerland

**Prof. Péter Pél Varga / Dr. Áron Lazáry** National Center for Spinal Disorders, Budapest, Hungary

**Prof. Christian Hellmich** Vienna University of Technology - Institute for Mechanics of Materials and Structures, Vienna, Austria

**Prof. Marie-Christine Ho Ba Tho** Compiègne University of Technology, Compiègne, France

**Prof. Hans-Joachim Wilke** Institute of Orthopaedic Research and Biomechanics, University of Ulm, Germany

**Prof. Keita Ito** Eindhoven University of Technology, Eindhoven, The Netherlands

**Prof. Damien Lacroix / Dr José Pozo / Prof. Alejandro Frangi** University of Sheffield, UK

**Dr Juan Fernando Ramírez Patiño** Universidad Nacional de Colombia, Medellín, Colombia

## Scientific equipment and techniques

- High performance computing infrastructure (48 cores, 256 GB RAM and over 11TB disc space, machine virtualization)
- Image reconstruction and finite element software
- Bose ElectroForce BioDynamic bioreactor system (orthopedic and cardiovascular configurations)
- Microfluidic chamber

Patient-specific finite element model of the musculoskeletal lumbar spine, including the lumbo-sacral joint


- Ruiz, C., Noailly, J. & Lacroix, D. (2013). Material property discontinuities in intervertebral disc porohyperelastic finite element models generate numerical instabilities due to volumetric strain variations. *Journal of the Mechanical Behavior of Biomedical Materials*, 26, 1-10.
- Malandrino, A., Noailly, J. & Lacroix, D. (2013). Regional annulus fibre orientations used as a tool for the calibration of lumbar intervertebral disc finite element models. *Computer Methods in Biomechanics and Biomedical Engineering*, 16 (9), 923-928.

**Conference paper:**

- Malandrino, A., Lacroix, D. & Noailly, J. (2013). Intervertebral disc cell death explained by metabolism-deformation couplings in a porohyperelastic finite element model. In 5th Biot Conference on Poromechanics. Vienna, Austria, "*Poromechanics V*", 2193-2201, American Society of Civil Engineers.

# Molecular Dynamics at Cell-Biomaterial Interface

**Group leader:** George Altankov

**Postdoctoral researchers:** Johan Gustavson, Tatiana Coelho

**PhD student:** Dencho Gugutkov

**Undergraduate student:** Ana Giordani

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:

*Remodeling of ECM proteins at cell-biomaterials interface*

ECM remodeling occurs in various physiological and pathological processes, 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 it proteolytic degradation is a physiological mechanism for the removal of excess ECM. Although matrix remodeling 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.

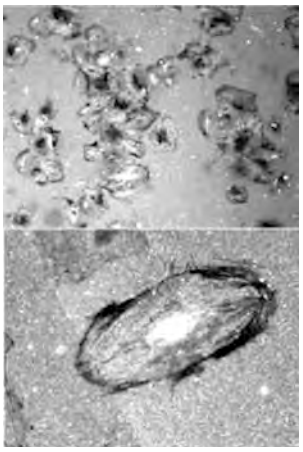
ECM organization at the biomaterial interface depends on the allowance of cells to rearrange adsorbed matrix proteins. We anticipate that materials that bind proteins loosely will support the arrangement of a provisional ECM, while stronger binding provokes its degradation.

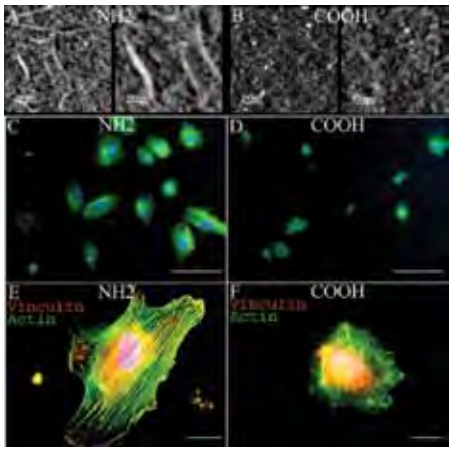
*Materials surface-driven assembly of ECM proteins at the nanoscale*

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 remodeling by engineering specific material properties. Understanding the behavior of ECM proteins on flat biomaterials interface further boosts an important bioengineering target – the biohybrid organ technologies based on two-dimensional protein layers that mimic the arrangement of the natural basement membrane.

Below left: Pericellular proteolysis of adsorbed vitronectin by HUVECs adhering for five hours on $CH_3$ chemistry.






Left: AFM images of adsorbed native collagen type IV (50 mg/ml for 30 minutes) on $NH_2$ (A) and COOH (B) functionalized surfaces, showing network-like protrusions on the $NH_2$ versus aggregated morphology on COOH. It results in a distinct difference in the efficiency of cellular interaction: endothelial cells are better spread on $NH_2$ (C, E) while rounded on COOH (D, F).

*Electrospinning of nanofibers from natural and synthetic polymers for guiding cellular behavior*

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.

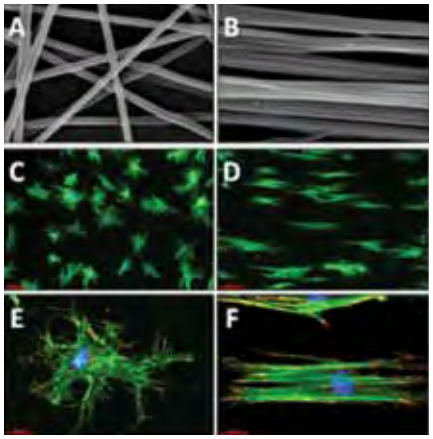
*Nanofibers-based 3D constructs to provide cells with spatially organized stimuli*

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

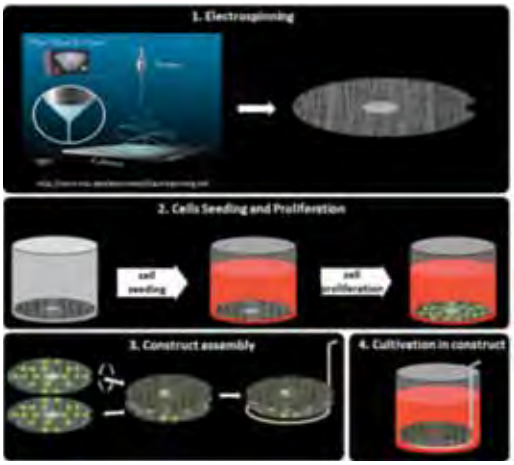
*Creating dynamic stem cell niches using stimuli-responsive biomaterials*

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.

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).




Schematic illustration of the STRUCTGEL concept.



## Research projects

- **STRUCTGEL** Nanostructured gel for cellular therapy of degenerative skeletal disorders (2012-2014).
PI: **George Altankov** (coordinator)
*EU - EuroNanoMed*

- **FIBROGELNET** Network for development of soft nanofibrous construct for cellular therapy of degenerative skeletal disorders (2013-2016).
PI: **George Altankov** (coordinator)
*EU - FP7-PEOPLE-2012-IAPP*

- **HEALINSYNERGY** Material-driven Fibronectin Fibrillogenesis to Engineer Synergistic Growth Factor Microenvironments (2012-2014).
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

**National University of la Plata**, Argentina

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

**Institute for Biophysics and 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

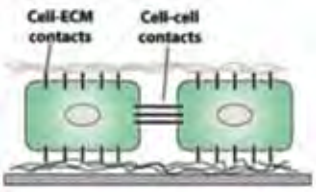
**Industrial collaborations:**

**Bio-Elpida**, France

**Genekam Biotechnology A.G**, Germany

## 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




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

## Publications


- González-García, C., Cantini, M., Moratal, D., Altankov, G. & Salmerón-Sánchez, M. (2013). Vitronectin alters fibronectin organization at the cell-material interface. *Colloids and Surfaces B: Biointerfaces*, 111, 618-625.
- Perez, R. A., Altankov, G., Jorge-Herrero, E. & Ginebra, M. P. (2013). Micro- and nanostructured hydroxyapatite-collagen microcarriers for bone tissue-engineering applications. *Journal of Tissue Engineering and Regenerative Medicine*, 7 (5), 353-361.
- Gugutkov, D., Gustavsson, J., Ginebra, M. P. & Altankov, G. (2013). Fibrinogen nanofibers for guiding endothelial cell behavior. *Biomaterials Science*, 1 (10), 1065-1073.
- Coelho, N. M., Salmeron-Sanchez, M. & Altankov, G. (2013). Fibroblasts remodeling of type IV collagen at a biomaterials interface. *Biomaterials Science*, 1 (5), 494-502.
- Llopis-Hernandez, V., Rico, P., Moratal, D., Altankov, G. & Salmeron-Sanchez, M. (2013). Role of Material-Driven Fibronectin Fibrillogenesis in Protein Remodeling. *BioResearch Open Access*, 2(5) 364-373.


ILN

# Medical Signals and Instrumentation programme

Designing and developing advanced signal processing techniques and the interpretation of biomedical signals to improve monitoring, early diagnosis, prevention and treatment of cardiac, respiratory and sleep disorders; developing biomimetic olfactory systems and signal and information processing solutions for diverse physical and chemical spectrometries, and mechanical sensors for a variety of biomedical uses

## Signal and Information Processing for Sensing Systems

Dr. Santiago Marco

## Biomedical Signal Processing and Interpretation

Prof. Dr. Raimon Jané

# Signal and Information Processing for Sensing Systems

**Group leader:** Santiago Marco

**Postdoctoral researcher:** Juan Manuel Jiménez

**Senior researcher:** Agustín Gutiérrez

**PhD students:** Ariadna Bartra, Lluís Fernández, Ana Verónica Guamán, Sergio Oller

**Undergraduate students:** Nil Franch, Sara Rica, Raquel Rodríguez, Guillem Singla

**Technicians:** Alexandre Casadevall

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 hidden information.

**In this context, artificial olfaction (AO) systems are intelligent chemical instruments for the detection of volatile compounds and smells. These systems usually combine an array of nonspecific chemical sensors with a pattern recognition system. The emphasis is not on the identification and quantification of the individual components – as is the case with analytical instruments – but rather on the overall evaluation of the odour. Moreover, AO systems tend to favour miniaturized devices capable of analyzing an odour in seconds. The focus of our research in this field is the development of signal and data processing systems inspired by the neuronal processing of the biological olfactory pathway.**

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

Our research in 2013 included the following:

**Computational olfaction**

- We have studied how redundancy and diversity play a role in the codification of odorous intensity. Results show that intensity estimation improves with not only with redundancy but also with the diversity of the dose-response curves in the olfactory receptor neurons.

**Ion Mobility Spectrometry**

- Together with the Spanish company RAMEM S.A., we have developed a Differential Mobility Analyzer for volatile organic compounds. Our group has developed the embedded software that processes the spectrometer raw signals.
- We have compared how different ionization sources play a role in the detection of biogenic amines in Ion Mobility Spectrometry.

**Artificial Olfaction**

- We have tested Bayesian chemical source localization algorithms in real environments using autonomous robots. The localization capability of the proposed algorithm improves previous proposals in the literature.
- We have proposed a methodology based on information theory to optimize the operation temperature of metal oxide chemical sensors.

Experiments using a mechanical ventilator to investigate on the influence of breathing dynamics on the response of artificial olfaction systems.

**Automotive Sensor Systems**

- In cooperation with automotive company FICOSA, we have developed algorithmic solutions to estimate driver drowsiness using vehicle sensor data available from the bus CAN. This technology has been adapted to run in a smartphone using inertial sensors, GPS and additional information introduced by the user.

Gas detector array including metal oxide sensors, electrochemical cells, photoionization sensor and an ion mobility spectrometer (Airsense Analytics GmbH).

## Publications


- Karpas, Z., Guamán, A. V., Pardo, A. & Marco, S. (2013). Comparison of the performance of three ion mobility spectrometers for measurement of biogenic amines. *Analytica Chimica Acta*, 758 (3), 122-129.
- Pomareda, V., Lopez-Vidal, S., Calvo, D., Pardo, A. & Marco, S. (2013). A novel differential mobility analyzer as VOCs detector and multivariate techniques for identification and quantification. *Analyst*, 138 (12), 3512-3521.
- Ziyatdinov, A., Diaz, E. F., Chaudry, A., Marco, S., Persaud, K. & Perera, A. (2013). A software tool for large-scale synthetic experiments based on polymeric sensor arrays. *Sensors and Actuators B: Chemical*, 177, 596-604.


## Research projects

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

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

- Intelligent signal processing for sensor systems in bioengineering (2009-2013).
PI: **Santiago Marco**
*AGAUR, Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya (2009-SGR-753)*

- **SOMNO-ALERT® P-10** Drowsiness Detection in drivers (2010-2013).
PI: **Santiago Marco**
*Industrial project with FICOSA*

- Transduccion biomimetica para olfaccion artificial (2013-2014).
PI: **Agustín Gutiérrez**
*MINECO, Europa Excelencia*

## Collaborations with other research centres

**Prof. Enrique Ruspini** European Center for Softcomputing, Mieres, Asturias, Spain

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

**Dr. Alexandre Perera and Prof. Pere Caminal** Centre de Recerca en Enginyeria Biomèdica, Universitat Politècnica de Catalunya, Barcelona, Spain

**Prof. Krishna Persaud** Chemoreception Group, University of Manchester, UK

**Dr. Zeev Karpas** Nuclear Research Institute, Israel

**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

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

**Prof. Cristina Davis** Bioinstrumentation and BioMEMS Lab, University of California in Davis, USA

## Scientific equipment and techniques

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


- Marco, S., Gutiérrez-Gálvez, A., Lansner, A., Martinez, D., Rospars, J. P., Beccherelli, R., Perera, A., Pearce, T. C., Verschure, P. F. M. J. & Persaud, K. (2013). A biomimetic approach to machine olfaction, featuring a very large-scale chemical sensor array and embedded neuro-bio-inspired computation. *Microsystem Technologies*, 1-14
- Fonollosa, J., Fernérndez, L., Huerta, R., Gutiérrez-Gálvez, A. & Marco, S. (2013). Temperature optimization of metal oxide sensor arrays using Mutual Information. In 14th International Meeting on Chemical Sensors, Nuremberg, Germany, "*Sensors and Actuators B: Chemical*", 187, 331-339, Elsevier.

**Conference papers:**

- Marco, S., Gutiérrez-Gálvez, A., Lansner, A., Martinez, D., Rospars, J. P., Beccherelli, R., Perera, A., Pearce, T., Vershure, P. & Persaud, K. (2013). Biologically inspired large scale chemical sensor arrays and embedded data processing. In Smart Sensors, Actuators, and MEMS VI, Grenoble, France, "*Proceedings of SPIE - The International Society for Optical Engineering*", 8763, 1-15, SPIE Digital Library.
- Santano-Martínez, R., Leiva-González, R., Avazbeigi, M., Gutiérrez-Gálvez, A. & Marco, S. (2013). Identification of molecular properties coding areas in rat's olfactory bulb by rank products. In BIOSIGNALS 2013, Barcelona, Spain, "*Proceedings of the International Conference on Bio-Inspired Systems and Signal Processing*", 383-387, SciTePress.
- Fernandez, L., Gutiérrez-Galvez, A. & Marco, S. (2013). Multi-way analysis of diversity and redundancy factors in large MOX gas sensor data. In 14th International Meeting on Chemical Sensors IMCS 2012, Nuremberg, Germany, "*Metal Oxide-based Sensors*", P2.07, 1279-1280, AMA Science Portal.

**Book:**

- Persaud, K.C., Marco, S. & Gutierrez-Galvez, A. (eds) (2013). *Neuromorphic Olfaction.* CRC Press, Taylor & Francis Group

# Biomedical Signal Processing and Interpretation

**Group leader:** Raimon Jané

**Senior researchers:** José Antonio Fiz, Beatriz Giraldo, Abel Torres

**Senior postdoctoral researcher:** Jordi Solà-Soler

**Postdoctoral researcher:** Leonardo Sarlabous

**PhD students:** Andrés Arcentales, Luis Estrada, Manuel Lozano, Oiane Urra

**Masters students:** Mirella López, Juan Pablo Téllez, Alejandro Calvo, Beatriz Martínez

**Technician:** Maria Puy Ruiz de Alda

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 2013**

*Obstructive Sleep Apnea and Sleep Disorders*

- An automatic non-invasive analysis method for the differentiation of obstructive and central hypopneas based solely on a single-channel nasal airflow signal (*Respiration*, 85(4), 312-318), with the Institute of Biomedical Engineering (Karlsruhe), the Klinikum Bethanien and MCC-Med, Germany.
- Assessment of the effects of anesthesia on autonomic nervous system in a rat model of Obstructive Sleep Apnea (*Computing in Cardiology* 2013, 1011-1014), with Daniel Navajas' group (page 56) and the Biophysics and Bioengineering Unit of the School of Medicine, the University of Barcelona, and the University of Zaragoza.
- New sleep transition indexes for describing altered sleep in patients with Sleep Apnea Hypopnea Syndrome (SAHS) (MEDICON 2013, 1017-1020), with the Hospital Germans Trias i Pujol, Badalona.

*Chronic Obstructive Pulmonary Disease and Asthma*

- A new method to non-invasive assessment of the diaphragm muscle efficiency (*Journal of Electromyography and Kinesiology*, 23(3), 548-557, IEEE-EMBC 2013, 3845-3848, and MEDICON 2013, 1004-1008), with the Hospital Germans Trias i Pujol, Badalona.
- Characterization of laplacian surface electromyographic signals in biceps brachii (IEEE-EMBC 2013, 535-538) and in diaphragm (MEDICON 2013, 977-980), with the Universidad Politécnica de Valencia.
- Analysis of normal and adventitious respiratory sounds for assessment of asthma (IEEE-EMBC 2013, 535-538 and MEDICON 2013, 981-984) with the Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol (IGTP) and the Hospital Germans Trias i Pujol, Badalona.

*Cardiac and cardiorespiratory diseases and ageing*

- Feature selection, based on Support Vector Machine and Wavelets, applied to predict successful weaning process of mechanical ventilation patients (*Computers in Biology and Medicine*, 43(5), 533-540, IEEE-EMBC 2013, 3849-3852 and ICCME 2013, 483-486), with Hospital de Sant Pau, Barcelona and the University of Applied Sciences, Jena, Germany.
- Analysis of heart rate and blood pressure variability in cardiomyopathy patients (Computing in Cardiology 2013, 117-120 and 22-25, and MEDICON 2013, 1021-1024) with the Hospital de Sant Pau, Barcelona, the Hospital Germans Trias i Pujol, the University of Applied Sciences, Jena, Germany and the University of Zaragoza. (Clinical trial: IIBSP-VEN-2012-168).
- Characterization of breathing pattern (IEEE-EMBC 2013, 5228-5231) and heart rate variability (*Computing in Cardiology* 2013, 991-994) in elderly patients, with Hospital de Sant Pau.

*Neurorehabilitation and Biofeedback*

- Evaluation of spatial characteristics of upper-limb movements from EMG signals for neurorehabilitation assessment (MEDICON 2013, 1795-1798) with Alicia Casals' group (page 116).

## Publications


- Morgenstern, C., Randerath, W. J., Schwaibold, M., Bolz, A. & Jané, R. (2013). Feasibility of noninvasive single-channel automated differentiation of obstructive and central hypopneas with nasal airflow. *Respiration*, 85 (4), 312-318.
- Sarlabous, L., Torres, A., Fiz, J. A., Morera, J. & Jané, R. (2013). Index for estimation of muscle force from mechanomyography based on the Lempel-Ziv algorithm. *Journal of Electromyography and Kinesiology*, 23 (3), 548-557.
- Garde, A., Voss, A., Caminal, P., Benito, S. & Giraldo, B. F. (2013). SVM-based feature selection to optimize sensitivity-specificity balance applied to weaning. *Computers in Biology and Medicine*, 43 (5), 533-540.


**Conference papers:**


- Sarlabous, L., Torres, A., Fiz, J. A. & Jané, R. (2013). Cardiac interference reduction in diaphragmatic MMG signals during a Maintained Inspiratory Pressure Test. *Conf Proc IEEE Eng Med Biol Soc. 2013*, 3845-3848, IEEE.
- Lozano, M., Fiz, J. A. & Jané, R. (2013). Estimation of instantaneous frequency from empirical mode decomposition on respiratory sounds analysis. *Conf Proc IEEE Eng Med Biol Soc. 2013*, 981-984.
- Estrada, L., Torres, A., Garcia-Casado, J., Prats-Boluda, G. & Jané, R. (2013). Characterization of laplacian surface electromyographic signals during isometric contraction in biceps brachii. *Conf Proc IEEE Eng Med Biol Soc. 2013*, 535-538, IEEE.
- Giraldo, B. F., Chaparro, J. A., Caminal, P. & Benito, S. (2013). Characterization of the respiratory pattern variability of patients with different pressure support levels. *Conf Proc IEEE Eng Med Biol Soc. 2013*, 3849-3852, IEEE.
- Giraldo, B. F., Tellez, J. P., Herrera, S. & Benito, S. (2013). Study of the oscillatory breathing pattern in elderly patients. *Conf Proc IEEE Eng Med Biol Soc. 2013*, 5228-5231, IEEE.


## Research projects

- **MIMCRID** Multimodal invasive and non-invasive biomedical signal interpretation and modelling in cardiac, respiratory and neurological disorders (2011-2013).
PI: **Raimon Jané** (Coordinator)
*MINECO*

- Respiratory sounds analysis.
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

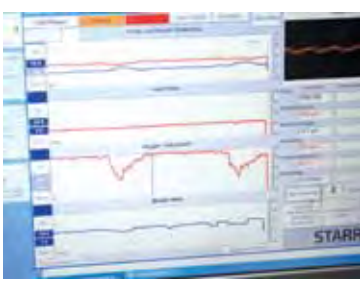
**Dr. Joaquim Gea** Servei Pneumologia, Hospital del Mar-IMIM, Barcelona

**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

Multimodal biosignal interpretation in a SAHS rat model.



Non-invasive assessment of muscle efficiency by electromyographic and mechanomyographic signal interpretation.

**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

## 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


- Jané, R., Lazaro, J., Ruiz, P., Gil, E., Navajas, D., Farre, R. & Laguna, P. (2013). Obstructive Sleep Apnea in a rat model: Effects of anesthesia on autonomic evaluation from heart rate variability measures In Computing in Cardiology Conference (CinC), Zaragoza, Spain (2013), *"CinC 2013"*, 1011-1014, IEEE.
- Giraldo, B. F., Tellez, J. P., Herrera, S. & Benito, S. (2013). Analysis of heart rate variability in elderly patients with chronic heart failure during periodic breathing. In *CinC 2013* (as above), 991-994, IEEE.
- Hernando, D., Alcaine, A., Pueyo, E., Laguna, P., Orini, M., Arcentales, A., Giraldo, B., Voss, A., Bayes-Genis, A. & Bailon, R. (2013). Influence of respiration in the very low frequency modulation of QRS slopes and heart rate variability in cardiomyopathy patients. In *CinC 2013* (as above), 117-120, IEEE.
- Arcentales, A., Voss, A., Caminal, P., Bayes-Genis, A., Domingo, M. T. & Giraldo, B. F. (2013). Characterization of patients with different ventricular ejection fractions using blood pressure signal analysis. In *CinC 2013* (as above), 795-798, IEEE.
- Gonzalez, H., Acevedo, H., Arizmendi, C. & Giraldo, B. F. (2013). Methodology for determine the moment of disconnection of patients of the mechanical ventilation using discrete wavelet transform. In 2013 ICME International Conference, Beijing, China (2013), *"Complex Medical Engineering (CME)"*, 483-486, IEEE.


KUKA

# Robotics and Biomedical Imaging programme

Design and development of intelligent robotics systems to assist people with disabilities, as well as medical personnel; development of technology for advanced processing biomedical images (acquisition, reconstruction, analysis) at the level of organs, tissues and cells or biomolecules

## Robotics

Prof. Dr. Alícia Casals

# Robotics

**Group leader:** Alícia Casals

**Senior researchers:** Joan Aranda, Manel Frigola

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

**Masters student:** Andrea Parrinello

**Undergraduate students:** Miriam Febrer, Maria Francisca Pericàs

**Research Technicians:** Emili Boronat, Roger Comas, Manuel Vinagre

Medical robotics constitutes a transdisciplinary research serving the medical field through engineering. IBEC's Robotics group's research activity is mainly application driven as new social and medical demands pose new scientific and technological problems, which become the research targets.

**The steering subjects, apart from the scientific interest that poses research challenges, are social responsibility and support for surgeons, rehabilitation and assistive staff. Designing and developing intelligent robotic strategies and control systems to assist people with disabilities, as well as medical personnel, implies the interpretation of human intention and context awareness. Thus, the goal is that the robot adapts to the user's needs and not the opposite.**

Robot control strategies for the simultaneous operation of direct muscular patient stimulation from volitional orders (neuroprosthesis) and robotic assistance (neurorobot) implies new challenges in robot control, as such control strategies should continuously adapt to the dynamic human response, to the required external assistance, and to the user physical state. 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 based on both the measured movement, with respect to the expected movement pattern corresponding to a rehabilitation exercise, and to the physiological and biological data acquired from the patient. 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, such as fatigue or the user's own attention to the therapy. In this field, the work developed has been focused on developing a control system with variable hierarchy and a status evaluator that allows the adaptation the control variables to reach the desired response and stability.

The research in surgical robots has been centered on the theoretical aspects of Human-Robot cooperation and on the process of transferring this research to industry through a spin-off, Rob Surgical Systems S.L. In addition, our previous work on analysis of behaviors and human intention has led to the study of an experimental sensorized and monitoring workstation allowing the study of surgeon behavior, with a deep evaluation of their training in manual and robotic surgery. With this aim, a specific robotic trainer has been designed, built and evaluated. This has led to the Surgitrainer system, in cooperation with the Hospital de Sant Pau, with which we are now starting a new development phase with the European Society for Gynaecological Endoscopy. The

Bitrack, the surgical robot from the IBEC-UPC spin-off, Rob Surgical Systems S L.

aim is to progressively advance in new robot surgical techniques that assist surgeons from the training phase to their performance in clinical interventions.

At present, the research team also is working within an FP7 Coordinated Action, EuRoSurge. This work not only focuses on technical aspects, but also on ethical and legal aspects that limit the commercial expansion of surgical robots.

Within this framework of human-robot interaction, an additional effort is devoted to interpret human activity and the operation context so as to be able to program robots to cooperate proactively in assisting the disabled with their daily tasks. This implies the extraction of relevant image features to recognize human posture and actions, and requires the ability to relate them to the context environment and the evolution of tasks and activities, using recognition and learning techniques.

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

## Publications

**Conference papers:**

- Casals, A. & Amat, J. (2013). Exploring improvements on the complexity-performance ratio and usability of surgical robots. In IEEE International Conference on Robotics and Automation (ICRA 2013), Karlsruhe, Germany, "*Evaluating effectiveness and acceptance of robots in surgery: user centered design and economic factors*", 1-6, Robotic SurgePedia

## Filed patents

- **Procedimiento y dispositivo para el aprendizaje y entrenamiento de operaciones de cirugía laparoscópica e intervenciones similares** (Filing date 16th October 2013)
*Inventors:* ***Alicia Casals***, ***Albert Hernansanz***, *Ramon Rovira*
Ref. number: P2832ES00

## Research projects

- **EuRoSurge** European Robotic Surgery.
PI: **Alícia Casals**
*Coordination Action FP7-ICT-2011-7*

- **HYPER** Hybrid NeuroProsthetic and NeuroRobotic Devices for Functional Compensation and Rehabilitation of Motor Disorders (2009-2014).
PI: **Alícia Casals**
*MINECO, Actividad Investigadora CONSOLIDER – INGENIO 2010*

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

■ **InHANDS** Interactive robotics for Human Assistance iN Domestic Scenarios (2013-2014).
PI: **Joan Aranda**
*RecerCaixa*

■ **ATRIO** Control para el guiado de un robot de radioterapia intraoperativa (2013-2014).
PI: **Alícia Casals**
*FIBHGM, industrial contract*

## Collaborations with other research centres

**Dr. Ramon Rovira** 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

## 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


- Vinagre, M., Aranda, J. & Casals, A. (2013). Human motion recognition from 3D pose information: Trisarea: A New Pose-based Feature. In 10th International Conference on Informatics in Control, Automation and Robotics (ICINCO 2013), Reykjavík, Iceland, "*Proceedings of ICINCO 2013"*, 2, 74-82, SCITEPRESS Digital Library.

**Book sections:**

- Giralt, X., Amigo, L., Casals, A. & Amat, J. (2013). Robotic Platform to Evaluate the Assistance and Assessment on the Rehabilitation Loop. In *Converging Clinical and Engineering Research on Neurorehabilitation*, ed. Pons, J. L., Torricelli, D. & Pajaro, M., 1, 1031-1035, Springer Berlin - Heidelberg, Germany.
- Casals, A. (2013). Adaptive control in neurorehabilitation. In *Converging Clinical and Engineering Research on Neurorehabilitation*, ed. Pons, J. L., Torricelli, D. & Pajaro, M., 1, 123-127, Springer Berlin - Heidelberg, Germany.

# Core Facilities

# 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, stae-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
- StepOnePlus Real Time PCR System – Applied Biosystems
- DNA Engine Thermal Cycler – Bio-Rad
- T100 Thermal Cycler – Bio-Rad
- ImageQuant LAS 4000 mini – GE Healthcare
- GelDoc XR+ System – Bio-Rad
- Liquid handling robot Freedom Evo – Tecan

**Head of Core Facilities**
Isabel Oliveira

**Laboratory Technicians**
Laura Gómez, Cristina Rivero, Antoni Dalmau

**Nanotechnology Platform Technicians** Raúl Pérez, Judit Linacero, Marina Cazorla, Juan Manuel Álvarez

# Nanotechnology Platform

The Nanotechnology Platform is part of the institute's long-term strategic plan to create new Core Facilities in nanofabrication and bionanocharacterization.

Currently, the platform is an accessible and versatile research facility featuring 150m$^2$ of class 10,000 cleanroom space and laboratories offering state-of-the-art equipment for the fabrication and characterization of micro- and nanodevices and structures.

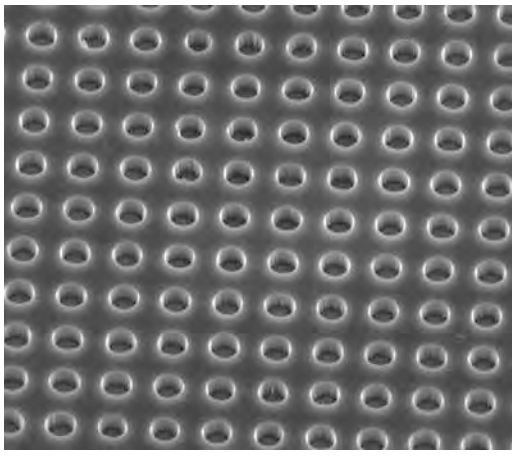
Our aim is to facilitate advanced research by providing services in the fields of nanoscience and nanotechnology for all academic and industrial researchers. Some of the many areas of application include nanobioengineering, BioMEMS, materials science, tissue engineering, optic and biomaterials.

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.

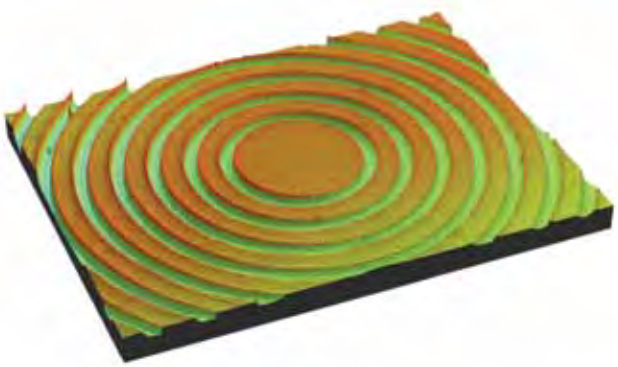
**Services**

- 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.
- Fabrication:
  - Design and development of micro- and nano-fabrication processes.
  - E-beam lithography technique, combined with other clean room fabrication techniques, for the manufacture of micro- and nano-structures.
  - Replication of micrometric and nanometric structures in thermoplastic polymers by HEL and NIL respectively.
  - Photolithography and Soft-lithography manufacture processes: Transparency and Cr masks, photoresists and SU-8, PDMS, RIE and wet-etching.
  - Thin layer deposition of metals (Au, Al, Ti, Cr, SiO2, etc.)
  - Cr Masks fabrication

SEM image of nano hole array pattern (500 nm diameter, 1 µm pitch, 500 nm depth) on silicon master fabricated using E-Beam Lithography and Reactive Ion Etching.



Interferometric photo of concentric circles (5µm width, 200nm depth) in silicon master microfabricated using Direct Write Laser Lithography and Reactive Ion Etching.

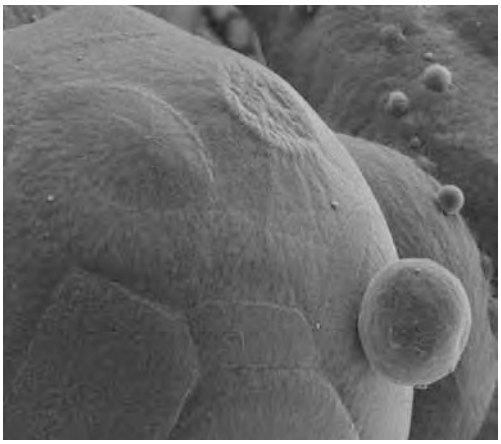


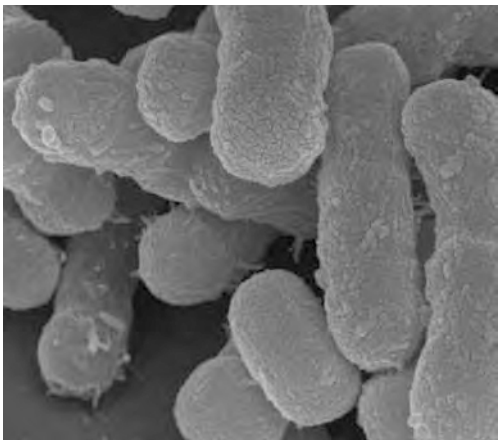
- Characterization:
  - Sample characterization using ToF-SIMS:
    - Surface microanalysis of organic and inorganic materials
    - Complete mass spectra of surfaces
    - PCA multivariate analysis for complex molecular spectra set of samples
    - Chemical mapping of elements and molecular distribution
    - Sample depth profile, implantation profiles and interface analysis.
    - 3D analysis (combines depth profiling with ion imaging).
  - SEM morphological and topographical characterization of a diverse range of samples.
  - Surface topographic analysis by using optical interferometry and mechanical profilometry.

**Equipment**

- Time-of-the-Flight Ion Mass Spectroscopy (ToF-SIMS)
- Ultra-High Resolution Field Emission Scanning Electron Microscopy (SEM)
- E-beam Lithography (EBL)
- Nanoimprint Lithography (NIL)
- Hot-Embossing Lithography (HEL)
- UV-Photolithography Mask-aligner
- Direct Write Laser Lithography
- Thermal and E-beam metal evaporator
- Reactive Ion Etching (RIE)
- Inteferometer
- Profilometer
- Chemical Bath
- Spinner
- Plasma Cleaner
- Optical microscope

SEM images of polyethylene glycol microspheres (left) and bacteria (right).





Mask aligner.

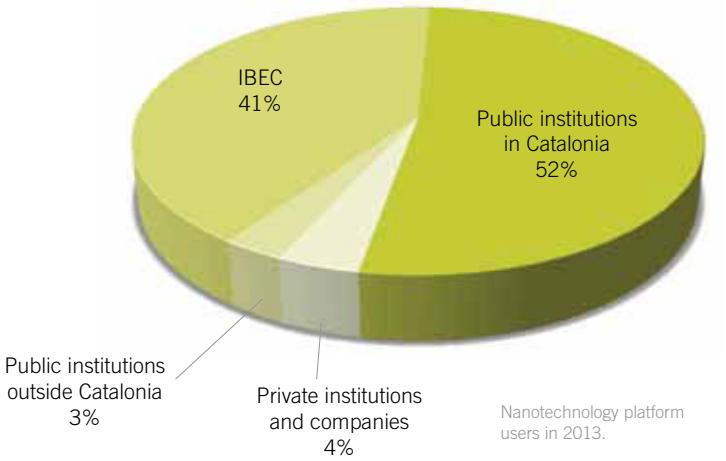
**Activities in 2013**

During its first year of operation, 53 users from seven IBEC groups, 72 users from 15 other public institutions, and five users from five private companies used the Nanotechnology Platform.

The Nanotechnology Platform staff taught in the following masters and degree courses: Master in Biomedical Engineering (University of Barcelona/Technical University of Catalonia); Master in Nanoscience and Nanotechnology (UB); Biomedical Engineering Bachelor Degree (UB).

Several dissemination activities took place during the year. A seminar, "Fundamentals of nanotechnology", was given at a workshop of the Marie Curie Initial Training Network 'Dynamol', which was hosted at IBEC in April. Together with the UB and CNM, the Nanotechnology Platform exhibited at the Transducers 2013 & Eurosensors XXVIII joint conference in Barcelona in June; and finally, the platform took part in IBEC's own seminar series in November with a talk entitled "What's on your surface? ToF-SIMS can tell you".

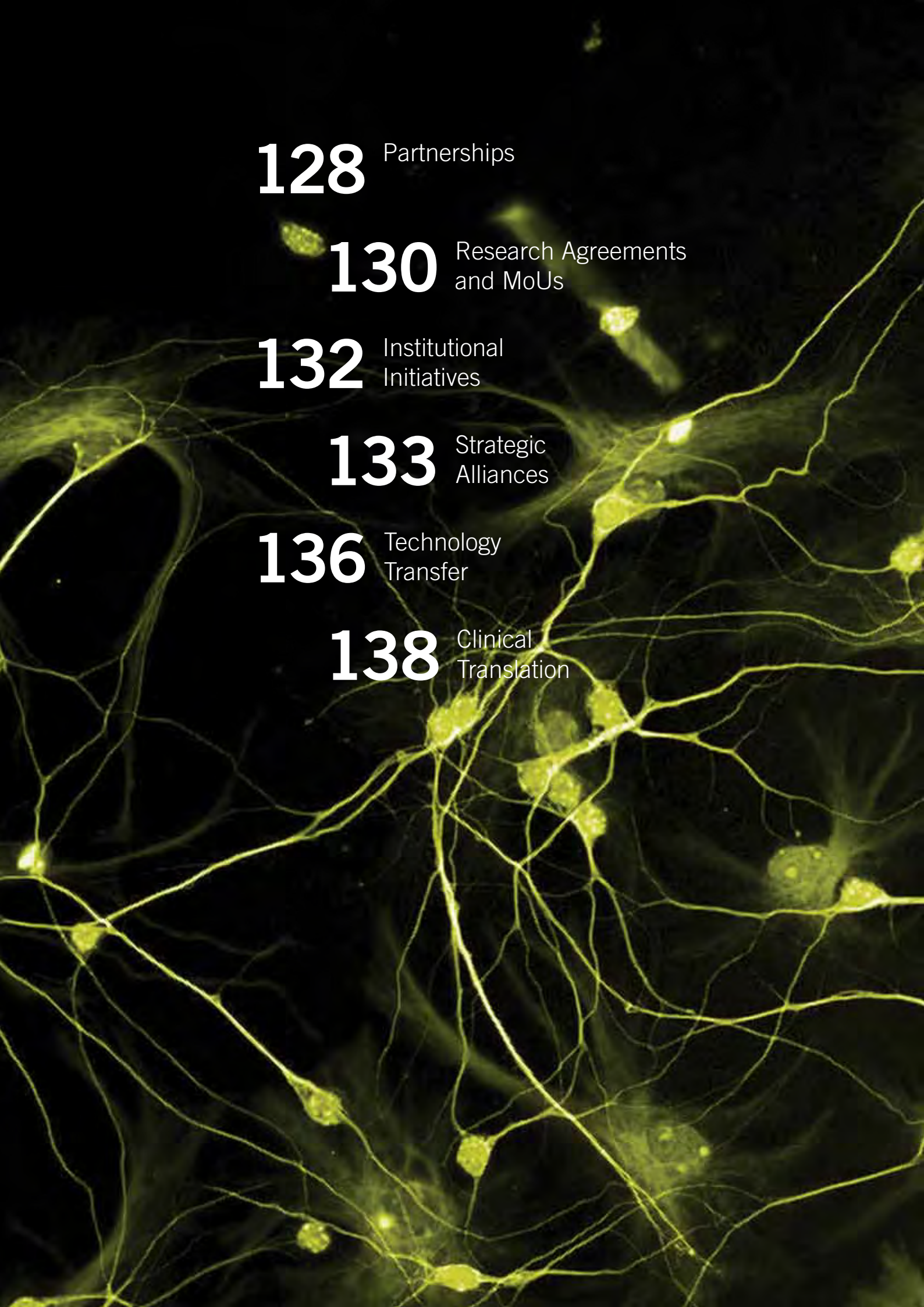
**For more information about the Nanotechnology Platform, or to register as a user, please visit www.ibecbarcelona.eu/IBEC/core-facilities.html**

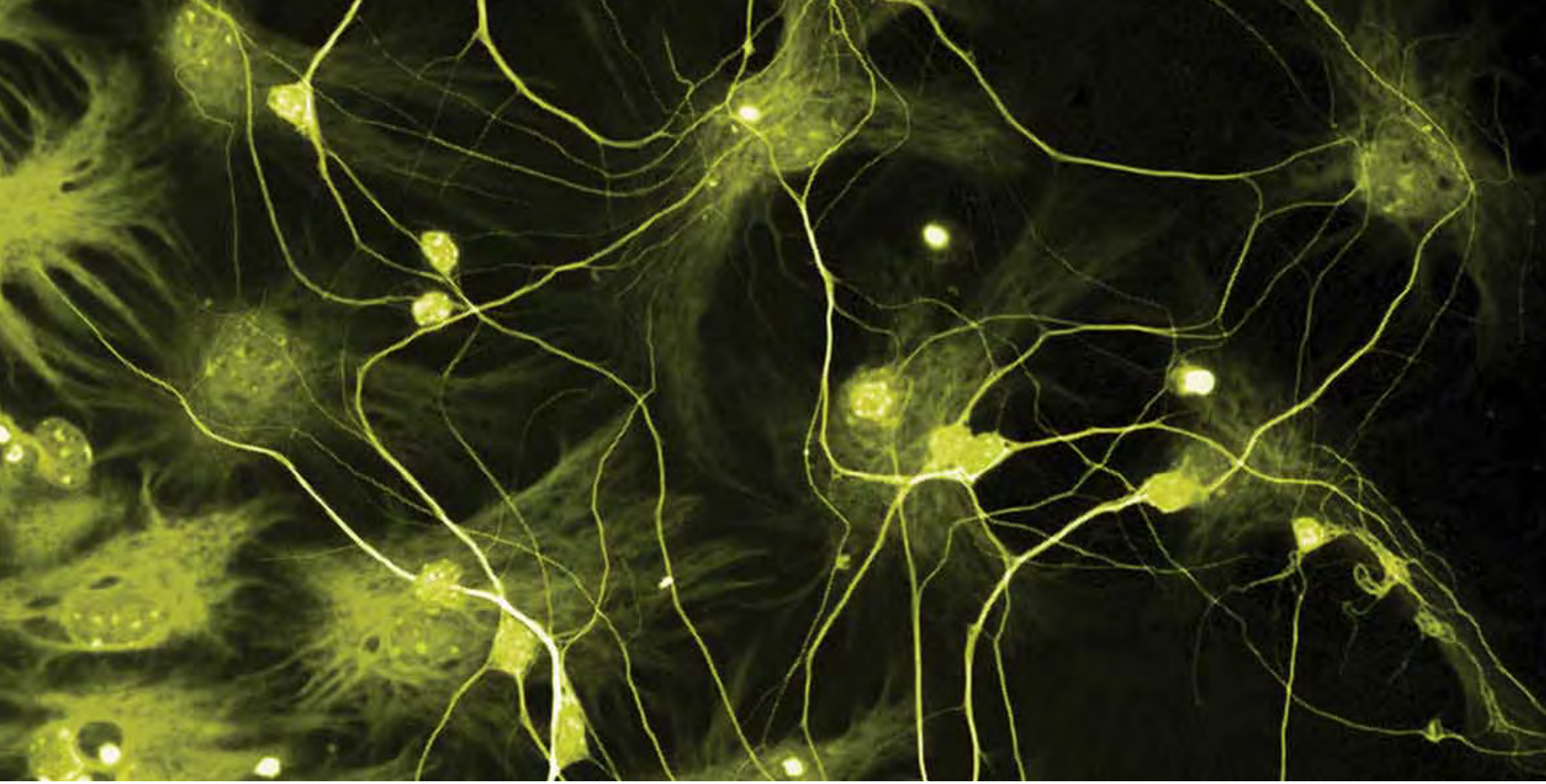



Nanotechnology platform users in 2013.

## Users

- IBEC *Various groups*
- University of Barcelona
  *Various groups*
- Technical University of Catalonia (UPC)
  *Ciència de Materials i Enginyeria Metal·lúrgica (CMEM)*
  *Centre de Recerca en Enginyeria Biomèdica (CREB)*
- Barcelona Science Park
  *CoSMo Lab*
- Fundació Institut de Recerca en Energia de Catalunya (IREC)
  *Materials avançats per l'energía*
- Instituto de Investigación Sanitaria - Fundación Jimenez Diaz
  *Laboratorio de Nefrologia Experimental y Patología Vascular*
- Institut de Recerca Biomedica (IRB)
  *Programa de Química: Farmacología Molecular*
- Institut de Microelectronica de Barcelona (CNM)
  *Integración de Sistemas*
  *Power Devices and Systems*
  *Micro and Nanosystems*
- Centre de investigación en nanociencia i nanotecnologia (CIN-2)
  *Photovoltaics Lab*
- Institut Català de Nanociència i Nanotecnologia (ICN2)
  *Phononic and photonic nanostructures group*
- Institut de Ciència de Materials de Barcelona (ICMAB)
  *Molecular nanoscience and organic materials department (Nanomol group)*
- Universidad Politécnica de Madrid
  *Centro Láser*
- Universidad de Zaragoza
  *Fisica Aplicada*
- Universidad de Valladolid
  *GIRBioforge*
- Institut Químic de Sarrià
  *Bioenginyeria d' Enginyeria de Materials*
- Infinitec Activos S.L.
- Universidad Miguel Hernandez
  *Departamento Patologia y Cirugia*
- Institut de Biologia Molecular de Barcelona (IBMB-CSIC)
  *Cell biology department*
- Fundació CTM Centre Tecnològic
  *Materials Technology Area*





# Networking

# Partnerships

While most of IBEC's funds come from the Generalitat de Catalunya, the University of Barcelona and the Technical University of Catalonia, an increasing proportion comes from national and international competitive research funding, ranging from large instruments such as the EU's Framework Programmes to independent or national foundations. Both projects and people are funded, with IBEC proud to be able to claim four group leaders with their own support from one of the most prestigious sources, ICREA, in 2013.

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 2013, four of IBEC's group leaders were ICREA research professors: Ángel Raya (Control of Stem Cell Potency group, page 46), George Altankov (Molecular Dynamics at Cell-Biomaterial Interface, page 100), Xavier Trepat (integrative Cell and Tissue Dynamics, page 64) and Pau Gorostiza (Nanoprobes and Nanoswitches, page 60).

IBEC and the Centre de Recerca en Salut International de Barcelona (CRESIB) signed an official agreement in 2010 to facilitate collaboration in certain areas of common interest. This led to the establishment of a mixed unit of personnel from both institutes to develop diagnostic and therapeutic nanomedicine-based systems to be applied to malaria (Nanomalaria group, page 80).

The agreement, which will continue as is until 2015, focused on knowledge transfer to the clinic during 2013. Towards the end of the year, the Italian CARIPLO Foundation granted a consortium formed by the University of Milano, CRESIB and IBEC with funding to perform a project to further develop nanoformulations against malaria based on poliamidoamines (PAAs). A related patent application (EP12192633.1) had been filed on 14th November 2012, and the partners agreed to continue protection procedure by following a PCT application (PCT/EP2013/073762), filed on 13th November 2013.

In addition, industrial contacts interested in heparin-conjugates have been primarily established and further collaborations are in the pipeline.

Founded in 2006, the Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN) is one of Spain's Biomedical Research Networking Centers (CIBERs). The primary aim of these consortia is to create large multidisciplinary and multi-institutional networks of research centres that will integrate basic and clinical research. CIBER-BBN, which is financed by the Instituto de Salud Carlos III, works in a number of areas including bioengineering, biomedical imaging, biomaterials, tissue engineering and nanomedicine. Research is focused on disease prevention, diagnostics systems and technologies for specific therapies, such as regenerative medicine and nanotherapies. In 2013 a strategy to merge all the CIBERs into one legal entity was begun.

IBEC works closely with CIBER-BBN, playing a role in the organisation and taking part in its research groups to help them carry out their work. The two institutions also share technical research equipment.

**Ongoing CIBER-BBN projects during 2013**

■ **BIOGELANGIO** Biomimetic extracellular matrices for angiogenic activation and anti-inflammatory activity in regenerative medicine.
PI: **Miguel Angel Mateos**

■ **Bioproterial** Biological activity of matrix proteins at the cell-material interface.
PI: **George Altankov**

■ **BIOSCAFF-EYE** Bio-engineered stem cell niches (BioSCniche) in ocular surface reconstruction for corneal blindness: from basic research to clinical trials.
PI: **Josep Samitier**

■ **CIBERES** Centro de investigación en red de enfermedades respiratorias.
PI: **Daniel Navajas**

■ **ES-CELLTHERAPY** Use of human pluripotent stem cells as vehicles for localized delivery of therapy to brain tumors.
PI: **Ángel Raya**; **Elisabeth Engel**

■ **INDI-MUSICA** Indexes obtained from computational models and multiscale-multimodal biomedical signals for the diagnosis of cardiac pathologies.
PI: **Raimon Jané**

■ **MUDIRES** Multimodal Diagnosis by Interpretation of Multiscale Signals in the Respiratory System.
PI: **Raimon Jané** (coordinator); **Daniel Navajas**

■ **NACRE** New Approaches for Cartilage Regeneration.
PI: **Ángel Raya**; **Miguel Angel Mateos**

■ **NANOFABRY** Desarrollo de nanomedicinas para terapia enzimática sustitutiva en la enfermedad de Fabry
PIs: **Fausto Sanz** (for the UB)
*Fundación Marató de TV3*

■ **NANOXEN+** *Xenopus tropicalis* as an optogenetic and photopharmacological platform.
PIs: **Fausto Sanz** (for the UB); **Pau Gorostiza**

■ **NANOMEDIAG** Nanobioanalytical platforms for improved medical diagnosis of infections caused by pathogen microorganisms.
PI: **Josep Samitier**

■ **NANO-TRANS-BRAIN** Nanocarriers for antiapoptotic drug transport across the Blood-Brain-Barrier.
PI: **Fausto Sanz** (for the UB)

■ **OLIGOCODES** Universal Diagnostic Platforms Based On Oligonucleotide Codified Nanoparticles and DNA Microarray Sensor Devices.
PI: **Josep Samitier**

■ **REWOUND** Elastic Like Recombinant polymers for wound healing applications.
PI: **Elisabeth Engel**; **Ángel Raya**

■ **SCAFFTIDE 3D** 3D scaffolds and implants functionalized and reinforced with recombinant protein polymers for regenerative medicine.
PI: **Miguel Angel Mateos**

■ **SISBIO** Biomedical Signals and Systems
PI: **Raimon Jané** (coordinator)

■ **TELTIS** Titanium-supported engineered bone tissue for orthopaedic surgery
PI: **Ángel Raya**; **Miguel Angel Mateos**

■ **ULTRASEN-4BIO** Characterization and validation of novel ultrasensitive piezoresistive all-organic sensors for multimodal biomedical signals
PI: **Raimon Jané** (coordinator)

—

One of Spain's Biomedical Research Networking Centres (CIBERs), CIBERNED is composed of 63 research groups working on basic and clinical research into neurodegenerative diseases and financed by the Instituto de Salud Carlos III.

■ Red española de investigación en enfermedades neurológicas PRY-114 (2009-2013).
PI: **Jose Antonio del Río**

■ 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**
*ISCII; Convocatoria de financiación interna para proyectos cooperativos de CIBERNED*

# Research Agreements and MoUs

IBEC pursues opportunities to collaborate on a long-term basis with other world-class national or international research institutes with an agreement or Memorandum of Understanding (MoU), with particular emphasis on clinical translation.

## Associated groups

In 2013, IBEC continued to collaborate with the University of Barcelona (UB) and the Polytechnic University of Catalonia (UPC) on joint research programmes under a succession of agreements first signed in 2006 (see page 22).

IBEC's Associated Groups at the UPC and UB, whose members may use our labs and facilities, are:

- Biomaterials, Biomechanics & Tissue Engineering (UPC)
- Biomedical Signals & Systems (UPC)
- Robotics & Vision (UPC)
- Instrumentation & Bioengineering (UPC)
- Ionizing Radiation Dosimetry (UPC)
- Graphical Computer Science (UPC)
- Bioelectronics (UB)
- Biophysics & Bioengineering (UB)
- Microbiology (UB)
- Surface Science & Nanotechnology (UB)

## Memoranda of Understanding

Memoranda of Understanding 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 2013, IBEC had MoUs in place with the following organisations:

- Fundació Clínic/Hospital Clínic, Barcelona.
- Bellvitge Institute for Biomedical Research (IDIBELL), Barcelona.
- National Institute for Materials Science (NIMS), Tsukuba, Japan.
- Institute of Tissue Regeneration Engineering (ITREN), Dankook University, Korea. In 2013, Dankook University's Bionanomedical Science Department was selected as a BK21 Plus Business Corporation under the Brain Korea 21 Plus programme of the Ministry of Education and the National Research Foundation. IBEC director Josep Samitier was elected as guest researcher in the programme, which aims to cultivate outstanding researchers in recovery medicine, as a result of IBEC and ITREN's collaboration in the exchange of researchers and professors.
- University of Warwick's Centre for Cognitive and Neural Systems, UK.
- Vall d'Hebron Research Institute (VHIR), Barcelona.
- Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol (IGTP), Badalona.

- Interstaatliche Hochschule für Technick Buchs (NTB), Switzerland.
- Barcelona Macula Foundation.
- Fundació Joan Costa Roma (JCRF), Terrassa.

During 2013, IBEC signed new Memoranda of Understanding with the following organisations:

With the departure of founding director of IBEC Josep A. Planell to take up Rectorship of the Open University of Catalonia (UOC), an agreement was drawn up to consolidate the exchange of researchers between the institutes. Through this memorandum of understanding, Prof. Planell retains a position at IBEC as Research Fellow in his former group, Biomaterials for Regenerative Therapies, and the alliance opens up further possiblities for the exchange of staff in the future.

The UOC began its activities in the academic year 1995/1996, with 200 students on officially recognized courses in Educational Psychology and Business Studies in Catalan. 200,000 people now form part of the UOC's community, and the university has increased and diversified its course offering, adding studies in Spanish and English. It has also opened two research centres specializing in the information and knowledge society, and in e-learning, becoming an international benchmark in these fields.

In 2013 IBEC signed a special agreement with the Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN, page 128), one of Spain's Biomedical Research Networking Centers (CIBERs), so that IBEC's newly acquired Nanotechnology Platform (see page 122) would be considered an integrated service platform within CIBER-BBN, thus facilitating access to all researchers within the network.

This forms part of IBEC's long-term strategic plan to foster advanced research by providing services in the fields of nanoscience and nanotechnology, offering Core Faciliites in nanofabrication and bionanocharacterization for the use of all academic and industrial researchers.

The Università degli Studi di Brescia was established in 1982 with three Schools: Medicine and Surgery, Engineering, Economics and Business. It now offers forty two schools of specialization and twenty-three doctoral courses with their administrative centre at the Università degli Studi di Brescia.

IBEC's memorandum of understanding with Brescia is specifically with the Department of Molecular and Translational Medicine, which will foster joint participation and shared development in some of the following areas, which are covered by the department: Applied Physics, Biochemistry, Clinical Biochemistry and Biology, Clinical Pathology, Food Chemistry, General Pathology, General Surgery, Genetics, Histology, Medical Genetics, Medical Statistics, Microbiology and Clinical Microbiology, Molecular Biology, Pathological Anatomy, Pharmacology and Plant Pathology and Entomology.

# 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.

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 Science and Innovation (MINECO).

In 2013, the activity of NanoMed Spain was focused on:

- The continued co-organization of the Annual Conference of the Biomedical Research Technology Platforms (Madrid, 20th-21st March 2013), together with the Spanish platforms for Innovative Medicines, Biotechnology, and Health Technology, aiming to facilitate public-private collaboration.
- The promotion and establishment of a cross-platform nanosafety group, along with the Plataforma de Seguridad Industrial (PESI), Plataforma de Materiales (MATERPLAT) and the Plataforma de Química Sostenible (SusChem). The partners are working to map the nanosafety needs of companies and to identify the services and skills that could be offered by research and technological centres in characterisation, toxicology, etc. Their results so far were presented at the major nanotechnology conference ImagineNano in April 2013, and at the Jornada Anual del Grupo Inter-Plataformas de Nanoseguridad y Nanotoxicología on 3rd December 2013.
- Approaching the food industry. After several meetings with FIAB/Food For Life España, NanoMed Spain and CIBER-BBN took part in a nanotechnology meeting at the headquarters of the Agencia Española de Seguridad Alimentaria y Nutrición (AESAN) in Madrid on 25th April to identify opportunities for joint projects. This initiative came as a result of Josep Samitier's participation in the European Food Safety Authority (EFSA), where he is the Spanish representative on the Scientific Committee for risk analysis and innovation potential of nanotechnology in food.
- In the light of the EU's new Framework Programme for Research and Innovation, HORIZON 2020 (2014-2020), preparation and defence of the Spanish position in nanomedicine was a key point on NanoMed Spain's agenda in 2013, during which a period of negotiations took place to close themes and budgets on the proposal approved by the European Parliament in 2012.

  With the European Technological Platform on Nanomedicine (ETPN), NanoMed Spain also represented the Spanish position on the proposal for a public-private partnership (PPP) in nanomedicine (see page 134).

## EC's Ro-cKETs project

Following former director Josep A. Planell's role as Sherpa in the European Commission's Key Enabling Technologies (KET) High Level Group on nanotechnology in 2012, IBEC participated as advisor in the new EC project RO-cKETs during 2013. This aims to "cross" the KETS to determine which innovative products should be manufactured by European industry in the coming decades under three or more technology enablers (such as photonics, biotechnology and nanotechnology) and how HORIZON 2020 could contribute.

IBEC's leading role is to help identify innovative products in the pharmaceutical and medical technology sectors, as well as livestock and agriculture, that may be supported by the integration of nano-bio-info-cogno techniques or methods.

# 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.

The Health UB Campus (HUBc) project, led by the University of Barcelona and with IBEC Director Josep Samitier as director, 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.

In November 2013 HUBc held their first ever International Conference on Healthy Ageing. The meeting in Barcelona examined the most significant issues in biological, medical and technological innovation on the subject healthy ageing, which is becoming a chief priority for health professionals and policy-makers. A worldwide representation of professionals with recognized expertise in the topic contributed to the two-day event.

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), which brings together public and private stakeholders to develop new innovations which can improve the quality of life of older people, whilst creating market opportunities for businesses. IBEC's 'commitments' – research activities that contributes to achieve the EIP on AHA's goals – are listed below.

- **Developing a sensor prototype along with the prototype of the central computer system to plan and monitor medicine intake.**
  *Partners: IBEC.*
- **Developing monitoring electronic devices and alerting systems (3 projects)**
  *Partners (1): IBEC, University of Barcelona (UB) and Hospital Clínic.*
  *Partners (2): IBEC, Institute of Biomedical Engineering, the Klinikum Bethanien and industrial partner MCC-Med (Germany).*

IBEC and HUBc director Josep Samitier with Inés Garcia Sanchez, Coordinator of the European Commission's European Innovation Partnership on Active and Healthy Ageing, at the first HUBc Barcelona International Conference on Healthy Ageing.

*Partners (3): IBEC, Hospital Germans Trias i Pujol and the Hospital del Mar, Barcelona.*

- **Developing decision support tools (including algorithms) and tele-monitoring devices**
  *Partners: IBEC, Hospital Germans Trias i Pujol, Hospital Clínic and industrial partner SIBEL S.A.*
- **Developing ICT based programs for remote monitoring of health status, lifestyles and adherence to medical plans for old people and chronic disease patients**
  *Partners: IBEC, University of Lund (Sweden), U. of Applied Science (Jena, Germany) and the Hospital de Sant Pau (HSP), Barcelona.*
- **Developing detection methods for biomarkers for early screening diagnostics**
  *Partners: IBEC.*
- **Developing software programme and ICT devices for feeding and food related tasks**
  *Partners: IBEC.*

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.

in 2013, along with BIOCAT and the UB, IBEC has been a leading member of a consortium which has prepared a successful proposal for the Knowledge and Innovation Communities (KICs) of the European Institute of Innovation and Technology (EIT), a body of the EU established to increase sustainable growth and competitiveness in Europe by reinforcing its innovation capacity by developing a new generation of innovators and entrepreneurs. The first three KICs, on Climate Change, Information and Communication Technologies and Sustainable Energy, were designated in December 2009.

For the new wave of KICs to be set up in 2014, the UB-IBEC-Biocat led proposal, Innolife, which has been prepared in collaboration with partners in Benelux, the UK, Germany, Spain and Scandinavia, has been selected as one of two finalists under the topic 'Healthy living and active ageing'. The final proposal will be submitted in 2014 and awarded by the end of the year.

BioNanoMed Catalunya

Fostered by IBEC and under BIOCAT's leadership, BioNanoMed Catalunya is an alliance of research centres, hospitals and companies to share know-how and resources and facilitate new developments in nanomedicine.

Among its activities in 2013, in April BioNanoMed Catalunya was a member of the Catalan delegation at Chicago's BIO International Convention, the world's largest biotechnology convention, and also fostered the organization of the B·Debate event 'Nanotechnologies in Health: Current Challenges and Future Prospects', at Barcelona's CosmoCaixa museum on 9th-11th October.

nanomedicine
EUROPEAN TECHNOLOGY PLATFORM

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 Institutional Projects Unit, to 'Roadmaps for Nanomedicine Towards 2020'. This key document in the area of nanomedicine was drawn up to advise the European Commission on future R&D investment needed to ensure successful translation of the results of research into the related sectors of medical and pharmaceutical technologies.

In 2013 IBEC collaborated with the ETPN and the NANOMED2020 project (page 132) to publish "ETPN White Paper 2013, 'Contribution of Nanomedicine to Horizon 2020'" in May 2013. This strategic document provides a set of key recommendations for the European Commission and the

EU Member States to create a favourable ecosystem for the successful deployment of Nanomedicine in Europe. It lays the groundwork to manage the efficient translation of nanotechnology from a Key Enabling Technology (KET) into new and innovative medical products.

In addition, IBEC representation attended the Annual General Assembly in Grenoble in October 2013, where a key topic was the need for the effective transfer of nano-products to the market, as reflected in the above-mentioned document. With this aim, ETPN established a Transnational Advisory Board, whose first major challenge will be the implementation of a Nanotechnology Characterization Laboratory in the EU to mirror the US National Cancer Institute.

In 2013 IBEC, in its capacity as coordinator of NanoMed Spain (page 132), represented the Spanish position on the proposal for a public-private partnership (PPP) in nanomedicine alongside the ETPN. This involved the formulation of a suitable instrument and negotiations with the European Commission. The Platform also collaborated with the ISCIII as Spanish representative on the NANOMED2020 Support Action (SA) project, "Enabling the European Nanomedicine Area until 2020", which is funded by the European Commission under the Work Programme FP7-HEALTH-2012. It will provide input to the political programme of the Commission referring to the clinical translation of nanomedicine.

VPH Institute

The Virtual Physiological Human (VPH) Institute is an international not-for-profit organisation founded in Belgium in 2011, whose mission is to ensure that emergent techniques based on theoretical modelling for patient virtualization are fully realised, universally adopted and effectively used both in research and the clinic.

As a regular member of the VPH Institute, among other 65 public and private institutions from three different continents and 15 countries, IBEC actively supports the promotion of VPH technologies towards the improvement of current healthcare through the use of personalized and integrated *in silico* medicine.

Jérôme Noailly, senior research associate in the Biomechanics and Mechanobiology group, and principal investigator of the VPH European project MySpine at IBEC, is IBEC delegate and member of the Policy Affair Working Group of the VPH Institute.

## Ongoing strategic alliances

During 2013, in addition to those listed above, IBEC continued to be a member or partner of the following organisations and initiatives:

- Associació Catalana d'Entitats de Recerca (ACER)
- CERCA Institute (the Government of Catalonia's means of supervising, supporting and facilitating the activities of Catalan research centres).
- Nanoaracat, a protocol that establishes a framework for collaboration between the regional governments of Aragon and Catalonia.

# 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 Knowledge Exchange Unit along the tech transfer and translation processes.

## Approval and implementation of Intellectual Property Policy

In May 2013 the institute's Policy on Intellectual Property was approved by the Board of Trustees, to reflect the shift in focus of the Knowledge Exchange (previously Corporate Projects) unit. The aim of the unit has moved towards knowledge transfer and innovation activities, and towards helping researchers by giving advice and support on the various options for commercialization, such as patenting or licensing, or even creating a company. They also help with negotiations over contracts or agreements, or how to put together collaborative schemes and long-term alliances. In their relations with those outside IBEC, the unit's philosophy is to promote a two-way dialogue with identified end-users and policy makers to maximize the institute's knowledge impact, both locally and globally.

The IP Policy covers how IP is managed within the institute, regarding aspects such as authorship, inventorship and ownership, as well as assignment and exploitation rights, including details on such areas as inventions co-developed with third parties. IP management and protection policies are included in the document, as well as approved rules for sharing royalties. In practice, the IP policy has been translated into a series of document models (Material Transfer and Non Disclosure Agreements, for instance) that are available to all IBEC researchers.

In June a special information session on IBEC's IP Policy and management took place (below). IBEC's legal advisors, RCD, explained the Spanish/EU legal framework that is reflected in the IP Policy, and how this affects researchers' rights and duties regarding knowledge and technology transfer and exploitation.

## ERC Proof of Concept grant for MICROGRADIENTPAGE

It was announced in December 2013 that Xavier Trepat's Integrative Cells and Tissue Dynamics group (page 64) is in line to receive up to €149k from the ERC for their project "Micro Gradient Polyacrylamide Gels for High Throughput Electrophoresis Analysis (MICROGRADIENTPAGE)" under the Proof of Concept funding scheme, which supports the transfer to market of results obtained in projects funded by previous ERC grants, in Xavier's case the 2009-2014 ERC Starting Grant for the GENESFORCEMOTION project.

The PoC grant will support the commercialization of an improved method for the preparation of miniaturized electrophoresis gels, which are widely used in the life sciences. This new technology, if it becomes a standard lab tool for the high-throughput quantification of proteins, could generate revenue from the pharmaceutical, clinical, basic research and personalized medicine markets. Studies on patentability and a commercialization plan will be performed.

## Harvard, the UB and IBEC protecting IP on Monolayer Stress Microscopy

In wound healing, tissue growth and certain cancers, the epithelial or the endothelial monolayer sheet expands. Within the expanding sheet, migration of the individual cells is strongly guided by physical forces imposed by adjacent cells. This process is called plithotaxis and was discovered using Monolayer Stress Microscopy (MSM), a technique developed by IBEC group leader Xavier Trepat (page 64) in collaboration with Prof. Fredberg's group from his time spent at Harvard (2004) and continuing afterwards when he was appointed to IBEC. MSM, which determines internal forces within and between monolayer cells based on the determined traction forces, could make possible some major steps forward in cancer diagnostics or drug screening, for example in identifying inhibitors of metastasis.

A patent (PCT/US2012/033450) for MSM belonging to Harvard, IBEC and the Fundació Bosch i Gimpera (UB) was filed during 2013.

## Surgitrainer, a training platform for laparoscopic surgery

A prototype developed by IBEC's Robotics group and their collaborators was presented at the European Society for Gynaecological Endoscopy's 22nd Annual Congress in Berlin in October 2013 (see page 12 for more details). Surgitrainer, a training platform for laparoscopic (keyhole) surgery – has been developed by Alícia Casals' group at IBEC (page 116) together with researchers at the Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau and at the UPC following an agreement signed on 20th April 2013. It is currently at the fully operational prototype stage, and Alicia's group is already performing tests with the collaboration of surgeons at the hospital. A patent application was filed by the three partners on 16th October 2013.

Obra Social "la Caixa"

IBEC's institutional project 'Sistemes de diagnòstic i teràpia basats en la integració de noves tecnologies nano bio info i cogno', supported by Fundació La Caixa, completed its second year in 2013. It provides the 'Strategic Research Innovation Initiative' (SRI$^2$) within which IBEC's three 'flagships' – Nanomedicine, Cell Engineering and Intelligent Healthcare – will frame their interdisciplinary projects. The grant from Fundació La Caixa is a pilot initiative to fund diverse types of institutional schemes.

On 12th April 2013 IBEC participated in an event and press conference to present the first results of the projects, with an audience that included Andreu Mas-Colell, Minister of Economy and Knowledge of the Generalitat de Catalunya, and Jaume Lanaspa, director general of the Fundació "la Caixa".

FUNDACIÓN BOTÍN

IBEC's collaboration with the Fundación Botín, a Spanish private institution, is in regard to the technology transfer of results obtained by the Nanobioengineering group (page 70).

# Clinical Translation

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.

## Progress of SRIs with clinical focus

Some of IBEC's interdisciplinary projects within the Strategic Research Innovation Initiative (SRI$^2$, page 137), involve a good deal of clinical collaboration. CellNanoMech (Cell mechanobiology: from nanoscale mechanisms to early diagnostic strategies) involves clinicians from Hospital Clínic and the Hospital del Mar, enabling access to tissue samples from COPD and healthy patients. MyoPatch (Bioengineering functional human myocardial tissue) involves a close collaboration with Vall d'Hebron Hospital and prompted the signing of an institutional agreement (below).

## Projects with partner Vall d'Hebron

IBEC signed an agreement with Vall d'Hebron Research Institute (VHIR) in 2012 to formalize their collaborations on innovative technologies for health, such as the ongoing collaboration of IBEC's Nanobioengineering group with the hospital's Laboratory of Translational Urological Research, to give just one example. During 2013, a project including researchers from IBEC which is led by Dr. Rafael Parra at Vall d'Hebron Hospital was one of only five winners of the prestigious ASPIRE Europe Hemophilia Research Award from Pfizer (see page 12).

## Insitutional partner Hospital Clínic

A public-private partnership between IBEC, Hospital Clínic – with which IBEC signed a collaboration agreement in 2007 – and Olympus is currently being drafted for an advanced training and research site for robotics-assisted minimal surgery validation, combining imaging and robotic surgery techniques. IBEC's research groups in these topics will be leading the technological development aspects of the site.

Existing collaborations with Hospital Clínic include the ongoing EU-funded project, Clinical tRials fOr elderly patients with MultiplE Disease (CHROMED), which involves IBEC's Cellular and Respiratory Biomechanics group (page 56) in its investigation into the applicability of an integrated solution for patients with chronic obstructive pulmonary disease (COPD).

In addition, an advisory collaboration of

Left: the Dermoglass project, IBEC's first venture into crowdfunding, began with clinical advice from Barcelona's Hospital Clínic.

Hospital Clínic – specifically with the Servicio de Dermatología – with IBEC's Biomaterials for Regenerative Therapies group (page 90) led to the team developing Dermoglass, their dressing which accelerates the regeneration of the skin in hard-to-heal skin ulcers. This was the subject of IBEC's very first venture into crowdfunding in 2013 (see page 12).

## Knowledge transfer of fractures outcome to industry and clinics

In a collaboration with Barcelona's Hospital de la Santa Creu i Sant Pau (HSCSP), the Biomechanics and Mechanobiology group (page 96) has worked on verifying a doctor's hypothesis that could explain the incidence of juvenile hip osteoarthritis. Through the use of different geometrical models, they found that cartilage is likely to be mechanically loaded more than normal, possibly favouring the early development of osteoarthritis, in young patients with slight joint retroversion.

Now, and in collaboration with the company Surgical Implants, the group is using clinical data and the geometry of fracture fixation systems provided by the Orthopaedic Surgery Service of the HSCSP, to help medical doctors anticipate the 'outcome' of external tibial plateau fractures fixations under different knee joint and load configurations. The hypothesis looks at whether the patient can put a foot on the floor safely just after surgery. This could have implications for cheaper and easier recovery, or personalised treatments.

During 2013 the group collaborated with the Knowledge Exchange Unit to manage the commercial offer, and a service contract was signed with HSCSP and Surgical Implants. Now the project is about halfway through, with promising results so far.

## Assessments for tendon regeneration

During 2013 the Biomaterials for Regenerative Therapies group (page 90) collaborated with the Servei de cirurgia ortopédica i traumatológica, Consorci Hospital de Terrassa, Spain on assessments for tendon regeneration. The aim was to develop a project to create a new biological scaffold composed of a nanofibrous polymeric scaffold with the appropriate biological signals and committed tendon cells, which will help surgeons repair rotator cuff tears in the tendons or muscles of the shoulder.

By the end of the year their project "Tendon Tissue Engineering: A Helping Hand for Rotator Cuff Tears (BIOTENDON)" had received notification of funding under the RecerCaixa programme, one of just 26 successful proposals chosen from a total of 362 applications submitted to the 2013 call.

## Respiratory success with Germans Trias i Pujol

A general framework agreement with the Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol (IGTP), as well as a Joint Research Unit coordinated by IBEC's Raimon Jané (page 110) and Miquel Àngel Gasull of IGTP, began in 2012.

During 2013, the collaboration of Raimon Jané's group and Dr. José Antonio Fiz from Germans Trias i Pujol Hospital led to 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.

Also in 2013, the Joint Research Unit developed 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.

## Ongoing framework agreements or collaborations

During 2013, in addition to those listed above, IBEC had framework agreements in place with the following hospitals or clinical partners:

- Hospital Universitari de Bellvitge;
- Consorci Sanitari Terrassa;
- Barcelona Macula Foundation;
- Corporació Sanitària Parc Taulí.

**142** Events and meetings in 2013

**146** IBEC Seminars and PhD Discussions

**148** Outreach activities in 2013

**152** Media coverage in 2013


# Events and Communications

# Events and meetings in 2013

## Throughout the year

### Institutional and scientific projects

Throughout the year, IBEC hosts meetings for the consortia of its ongoing institutional and scientific projects. In 2013 the scientific projects nAngiofrac, Fibrogelnet, IPRES, Teccare, MySpine, HYPER, V SMMART Nano, Plantoid, Theralight and SMART IMS all held meetings at IBEC.

## January

■ 10 January

### 3rd UBB-IBEC Symposium

Organised with the Biophysics and Bioengineering Unit of the University of Barcelona, the UBB-IBEC 'mini symposia' on biomechanics are organised by IBEC's Integrative Cell and Tissue Dynamics group leader Xavier Trepat (page 64), and involve the Cellular and Respiratory Biomechanics group of Daniel Navajas (page 56) as well as that of Ramon Farré at Barcelona's Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS). A fourth UBB-IBEC meeting was held on 1st July 2013.

## February

■ 12 February

### Image processing for image diagnosis and laboratory applications

Organised by National Instruments and held at IBEC, this workshop aimed to provide a basic understanding of the hardware and software components of vision applications, including image stitching, filtering and statistics; multi-channel processing; image Diagnosis innovation through parallel processing technologies; MultiCore; FPGA; GPU and more.

■ 19 February

### IBMB-IBEC Joint Workshop

About 130 researchers from IBEC and

Left: enjoying lunch al fresco at the IBMB-IBEC Joint Workshop; right, IBEC group leader Antonio Juárez speaking at the 6th IBEC Symposium on Bioengineering and Nanomedicine.

the Institut de Biologia Molecular de Barcelona (IBMB), which is also located in the Barcelona Science Park (PCB), got together for a joint workshop to identify synergies and possible areas for collaboration. The event, which was held at the Institut d'Estudis Catalans in central Barcelona, opened with a presentation about IBEC from then director Josep A. Planell and an introduction to the institute's 'flagships', Nanomedicine, Intelligent Healthcare and Cell Bioengineering. Various group leaders and facility heads from both sides presented their research and took questions and comments, and the poster sessions and refreshment breaks allowed the participants to network further.

## March

■ 14 March

### Training session in Risk Prevention

The joint health and safety service based at the Barcelona Science Park (PCB), the Servei de Prevenció Mancomunat IBEC–IRB–PCB, organised a risk prevention training session for IBEC researchers and staff in March. A second session took place in October.

## April

■ 18 April

### Dynamol Workshop: "Fundamentals of Nanotechnology"

The Marie Curie Initial Training Network Dynamol had its project meeting in Barcelona, part of which was an open workshop held at IBEC, "Fundamentals of Nanotechnology". IBEC and ICMAB collaborated with Dynamol, which conducts research on establishing powerful new approaches based on dynamic covalent chemistry (DCC) for the preparation of nanostructures, in the organization of the workshop.

Speakers at the workshop includes the Dynamol coordinator and representatives from several of its partners, including the University of Cambridge and industry partner DSM Dyneema, as well as Miguel Angel Mateos, Vienna Leigh and Isabel Oliveira from IBEC, and researchers from ICMAB.

## May

■ 8 May

### 6th IBEC Symposium on Bioengineering and Nanomedicine

The IBEC Symposium on Bioengineering and Nanomedicine is the institute's major event of the year. The 6th edition in May welcomed 230 participants, almost 40 of them coming from outside IBEC from places as far afield as Belgium and Colombia.

The symposium was opened by Gabriel Capellá, Head of Research and Innovation in the Generalitat's Department of Health, and Jordi Alberch, vice-rector of the UB, and the first keynote speaker was former IBEC director Josep A. Planell with his entertaining presentation 'Everything you wanted to know about IBEC's history that nobody told you before'. Later in the day, Josep was presented with a goodbye gift, and both Capellá and Alberch and ISC president Jean Louis Coatrieux thanked him for his dedication at the helm of the institute for the past seven years.

Other keynote speakers this year were IBEC's George Altankov, new ISC members Jocelyne Troccaz and Bernat Soria, and Albert van den Berg from the University of Twente. Themis Toumanidou of the Biomechanics and Mechanobiology group won the prize for Best Flash Presentation, and Zaida Álvarez from the Biomaterials for Regenerative Therapies group won Best Poster.

■ 8 May

### Fira d'Empreses

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.

## June

■ 13 June

### Intellectual Property workshop

A special information session organised by the Knowledge Exchange unit was held on June 13th to explain the institute's revised IP policy within the framework of Spanish law, as well the services on offer. It involved presentations by Oscar Alegre of IBEC's legal advisors RCD and head of Knowledge Exchange Arantxa Sanz.

■ 25-29 June

### 'Interrogations at the Biointerface' Advanced Summer School

The 'Interrogations at the Biointerface' Advanced Summer School, which is co-organized by IBEC, the Instituto de Engenharia Biomédica (INEB) and the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUB), both in Portugal, introduces PhD students and early postdocs to advanced experimental techniques. The third edition focused on the topic of "The inflammation/repair interface" and took place in Porto on 25th-28th June.

The course had a duration of four days, with lab sessions being held during the first day and lectures in the last three days. Lectures took place in a very informal environment, and participants are encouraged to bring questions that may contribute to the advancement of knowledge through integrative approaches.

## July

■ 3, 4, 10 and 11 July

### Training sessions in Effective Communication

Twelve staff members from administration took part in a training course organised by the Human Resources Unit, "Recursos de comunicació efectiva II (Enfoc interdependent)", to help improve their communication and teamwork skills.

## October

■ 23 October

### Cinema al PCB

In a new initiative by the PCB and its research institutes, the Auditori Antoni Caparros in Torre D bacome a cinema on 23rd October, with a free showing of *Lorenzo's Oil*. The film was preceded by an expert introduction, and there was be a discussion and questions afterwards.

The aim of 'Cinema al PCB' is to show science, technology or health-related classic movies, not only to provide some free on-site entertainment after the working day, but also to offer a friendly social and networking occasion for people at the different organisations in the PCB.

■ 24 October

### Third Spanish Chapter Meeting of the European Society of Biomechanics

IBEC organised and hosted the 3rd Spanish Chapter Meeting of the European Society of Biomechanics (ESB) in 2013. The event welcomed 60 people from research centres, hospitals and universities throughout Spain. The meeting's main aim was to put professionals and researchers in the field of biomechanics in touch, to enhance collaboration between universities, hospitals and companies, and also to encourage dissemination and promotion of studies in this field throughout Spain.

Almost half of the participants also took part in three courses the day before, which provided an overview of the techniques used for the development of a patient model form clinical data.

The papers "Explicit simulation of muscle activation in combination with intervertebral disc swelling reproduces *in vivo* intradiscal pressures in a L3-S1 lumbo-sacral spine model" presented by IBEC's Themis Toumanidou in the Science category and "The role of both micro/nano-topography and Na+ ion to enhance osseointegration"

presented by Marc Fernández Yagüe in the Technology Transfer and Clinics category, were awarded for their excellence, content and presentation.

During the meeting, the election of the Chapter's executive committee also took place, whose candidates were Sebastian Idelsohn, Javier Martínez Reina and IBEC's Jérôme Noailly.

## November

■ 14-15 November

### 1st Barcelona International Conference on Healthy Ageing

In his capacity of Director of HUBc, the Health Campus of Barcelona University, IBEC Director Josep Samitier presided over their first ever International Conference on Healthy Ageing, held in Barcelona in November.

The HUBc 'Campus of Excellence' organized the meeting to examine the most significant issues in biological, medical and technological innovation on the subject healthy ageing, which is becoming a chief priority for health professionals and policy-makers. A worldwide representation of professionals with recognized expertise in the topic contributed to the two-day meeting.

■ 14 November

### SAMSUNG meeting

IBEC coordinated a one-day event in which managers from the headquarters in Korea of multinational conglomerate Samsung met with the Directors, Heads of Unit and researchers from IBEC and some of its partner institutes to get to know more about their research, as well as identifying synergies and technology transfer opportunities.

■ 12, 14, 19 and 21 November

### Writing Successful Research Papers

In November the Human Resources unit offered a complementary skills training session to postdocs and senior researchers on the subject of Writing Successful Research Papers and Proposals. Eight researchers benefitted from the intensive course, which aimed to help them achieve a clear, concise and coherent writing style.

## December

■ 13 December

### Christmas celebration

Bodypercussionists Santi Serratosa and Mariona Castells provided the interactive entertainment at the 2013 IBEC Christmas celebration, which was attended by most of IBEC's staff and researchers.

Below left: IBEC staff and researchers enjoyed some 'bodypercussion' activity at the 2013 Christmas celebration.

Below: the 3rd Spanish Chapter Meeting of the European Society of Biomechanics (ESB) in October.

# 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 2013, 12 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, three invited speakers gave lectures on various topics.

■ 7 January

**David Juncker**
McGill University, Montreal, Canada
*Self-powered capillary microfluidics and nanocontact printing: From immunoassays to digital nanodot gradients for cell chemotaxis studies*

■ 15 February

**Ivan Montoliu Roura**
Nestlé Research Center, Lausanne
*Crossroads in data analysis: a Metabolomics perspective*

■ 22 February

**PhD Discussions Complementary Skill Session: Itziar De Lecuona**
Associate Professor, Dept. of Public Health, School of Medicine/Bioethics and Law Observatory, University of Barcelona
*Why does biomedicine needs bioethics? The case of regenerative biomedicine in research and healthcare*

■ 1 March

**Jordi Garcia Ojalvo**
Universitat Pompeu Fabra
*Self-organization of bacterial populations: from gene regulation to mechanical patterning*

■ 8 March

**Antoni Bayes-Genis**
Hospital Universitari Germans Trias i Pujol/ Professor Titular, UAB
*Cardiac tissue engineering: fact or fantasy?*

■ 15 March

**Juan Antonio Hueto Madrid**
Servei de Cirurgia Oral i Maxil.lofacial, Hospital General Universitari Vall d'Hebrón
*Technology in Oral and Maxillofacial Surgery*

■ 22 March

**Miguel Esteban**
South China Institute of Stem Cell & Regenerative Medicine, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences
*The role of histone deacetylases in somatic cell reprogramming*

■ 5 April

**Johan de Rooij**
Hubrecht Institute, The Netherlands
*Mechanotransduction at the cadherin-actomyosin interface*

■ 12 April

**Nieves Casañ Pastor**
ICMAB, CSIC Bellaterra
*Electroactive materials for electrodes in the neural system*

■ 15 April

**Kyung A. Kang**
Professor and Graduate Program Director; University of Louisville, Kentucky, USA
*Metal Nanoparticles for Disease Diagnosis and Treatment; Primo Vascular System and Its Potential Implication in Future Health Care*

■ 26 April

**PhD Discussions Complementary Skill Session: Sebastian Grinschpun**
Freelance science communicator
*Communicating science: why and how*

■ 15 May

**Liang Tang**
University of Texas, San Antonio, USA

*Innovative Applications of Nanotechnology in Biosensing and Drug Delivery*

■ 17 May

**Miguel A. González Ballester**
Chief Research Officer, Alma IT Systems, S.L.
*Surgical planning and simulation research projects at Alma IT Systems*

■ 6 June

**Xavier Fernandez-Busquets**
Nanomalaria group, IBEC (joint group with CRESIB)
*Nanomedicine against malaria*

■ 14 June

**Ramon Pallás**
UPC
*Cardiovascular function assessment from 4+ measurement points*

■ 14 June

**Ann-Sofie Cans**
Chalmers University of Technology, Gothenburg, Sweden
*Cells, artificial cells and biosensors*

■ 19 June

**Sanjay Kumar**
UC Berkeley - UCSF Graduate Group in Bioengineering/Faculty Scientist, Lawrence Berkeley National Laboratory
*Dissecting, reconstructing, and rewiring cell-microenvironment biophysical crosstalk*

■ 20 June

**Sofía Rodríguez**
Nanoscribe GmbH
*High-Speed 3D Printing for Micro- and Nanofabrication*

■ 21 June

**Louise Jones**
Barts Cancer Institute, Queen Mary University of London
*Not such an innocent bystander: the role of the microenvironment in breast cancer initiation and progression*

■ 3 September

**Ada Cavalcanti-Adam**
University of Heidelberg / Max Planck Institute for Intelligent Systems, Stuttgart
*Cells at interfaces: regulating cellular functions with nanoscale spacing of extracellular ligands*

■ 20 September

**Eduard Torrents**
Bacterial infections: antimicrobial therapies group, IBEC
*Bacterial DNA synthesis: new strategies for the treatment of infectious diseases*

■ 26 September

**PhD Discussions Complementary Skill Session: Ignasi Labastida**
CRAI-Unitat de Recerca, Universitat de Barcelona
*Opening research results: open access, open data, open what?*

■ 11 October

**Francisco Andrade**
Universitat Rovira i Virgili
*Responding to new paradigms in chemical analysis: embedding chemical nanosensors for developing distributed analytical tools*

■ 18 October

**Ignacio Pagonabarraga Mora**
Universitat de Barcelona
*Emergent patterns in active matter; from molecular motors to microorganisms*

■ 6 November

**Assia Shisheva**
Wayne State University, Detroit, USA
*Protein machinery regulating synthesis and turnover of low-abundance signaling lipids is essential for health and life*

■ 8 November

**Catherine Picart**
Grenoble Institute of Technology and CNRS
*Layer-by-layer films as engineered biomaterial coatings : applications to muscle and bone tissue engineering*

■ 8 November

**Owen McCarty**
Oregon Health & Science University
*Platelet cytoskeletal remodeling*

■ 22 November

**Raúl Pérez**
Nanotechnology Platform, IBEC
*What's on your surface? ToF-SIMS can tell you*

■ 25 November

**Khalid Salaita**
Emory University, Atlanta
*Using Light to Visualize and Manipulate Molecular Forces in Cells*

■ 13 December

**Marino Arroyo**
Universitat Politècnica de Catalunya BarcelonaTech (UPC)
*Modeling dynamical reorganizations of lipid bilayers*

# Outreach activities in 2013

## Throughout the year

### Visits by Barcelona schools

Throughout the year, several groups of students from high schools in Barcelona and Catalonia visited IBEC: Centre Escolar Roig-Tesalia on 13th February (21 participants), Escuela Suiza Barcelona on 20th March (15 participants), Ins Montgròs on 11th June (17 participants), and Institut d'Educació Secundària El Til·ler on 26th November (23 participants). Researchers from the Robotics, Bacterial Infections: Antimicrobial Therapies, Signal and Information Processing for Sensing Systems and Control of Stem Cell Potency groups contributed to the visits with talks or activities.

### ESCOLAB

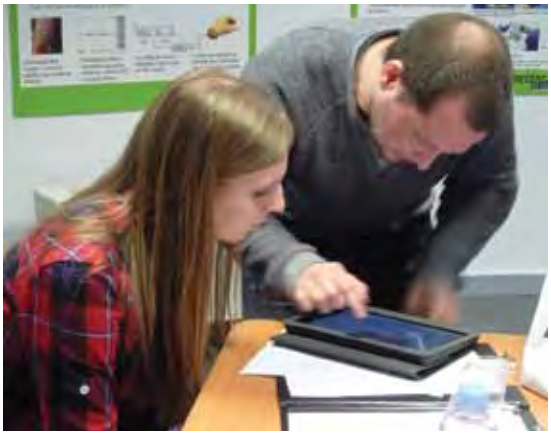
Every year, IBEC takes part in the ESCOLAB initiative of the City Council of Barcelona, which introduces groups high school students into the city's research laboratories to encourage scientific vocation.

In 2013 IBEC welcomed three groups of students to the institute as part of ESCOLAB: a group of 27 from Col·legi Lestonnac on February 7th; 20 from Institut d'Ensenyament Secundari Santa Coloma de Farners on 6th March; and 26 from Escola Santíssima Trinitat on 17th April. Researchers from the Control of Stem Cell Potency, Nanobioengineering, and Biomaterials for Regenerative Therapies groups provided the talks and activities.

### 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. Six such one-to-one encounters took place throughout 2013, with IBEC's young researchers from the Signal and Information Processing for Sensing Systems, Nanobioengineering, Integrative Cell and Tissue Dynamics, and Robotics groups resolving questions and

Below left: students form the Escuela Suiza Barcelona enjoy their visit to IBEC; below right, Lluís Fernández from the Signal and Information Processing for Sensing Systems helping out a high school student as part of the Entrevistas de Bachillerato scheme.



Left: 'rapid prototyping' with chocolate during the visit of the students from Escola Santíssima Trinitat; above, researchers from IBEC's Biomedical Signal Processing and Interpretation group helping visitors monitor their own biomedical signals at the Fira Recerca den Directe.

doubts and sharing new ideas to help with the school projects.

## Recerca a Secundària

The initiative Recerca a Secundària is addressed to 16-year-olds who are about to begin their research projects at school. This scheme offers these students the opportunity to be assessed by a tutor from the Parc Científic de Barcelona (PCB). During the year, the tutor gives advice on recommended reading, and students are also offered the chance to gain hands-on experience in their laboratory. In 2013 Andy Olivares, a PhD student in IBEC's Biomechanics and Mechanobiology group, tutored some students.

# February

■ 11 February

## Book launch at IEC

In February, then director Josep A. Planell took part in the public launch of a book to which he contributed, "Ciència i universitat a Catalunya: Projecció de futur". Published by the University of Barcelona, the book contains thirteen chapters by distinguished scientific experts on key issues relating to the university system, research and transfer of technology and knowledge in Catalonia today.

At the launch which took place at the Institut d'Estudis Catalans, editor David Bueno and Claudi Mans, Emeritus Professor of the UB's Department of Chemical Engineering, introduced the book, after which Josep and some of the other authors answered questions from the audience.

# March

■ 21 March

## Visit of students from the University of Cambridge

As part of the UPC's Programa Intercambio Lingüístico, a group of 12 University of Cambridge engineering students who were visiting their equivalents at the UPC's School of Industrial Engineering of Barcelona (ETSEIB) visited IBEC to learn about the institute's research areas.

# April

■ 23-25 April

## Fira Recerca en Directe

The 'Live Research' fair at Barcelona's La Pedrera 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.

In 2013 scientists from IBEC's Biomedical Signal Processing and Interpretation group took part with an activity that helps participants record and process their own biomedical signals. Visitors found out for themselves how the electrical activity of the heart, respiratory system, eye, muscles and brain are tracked using electrocardiographs, oculographs and electroencephalographs.

## June

■ 3 June

### Funding from BBVA for outreach project

At a ceremony in Sabadell, IBEC received its funding award for an outreach project from the Fundació Antigues Caixes Catalanes (formerly Unnim Caixa) of the BBVA. Pilar Jiménez, representing IBEC's Communications and Outreach Unit, and Head of Finance Ana González collected the prize, which went on to fund the unit's successful proposal for a series of scientific talks on nanobiotechnology, robotics and tissue engineering held at libraries and civic centres in Barcelona (see below). IBEC's project was one of the 42 chosen from nearly 250 proposals submitted.

■ 15 June

### Festa de la Ciència 2013

IBEC took part for the second time in the council-organised Festa de la Ciència in Barcelona's Parc de la Ciutadella, at which Nanobioengineering PhD student Ana Maria Oliva gave a presentation, 'Nanotecnologia: més petit que petit'.

## July

■ 1-12 July

### $E^2C^3$ Joves i Ciència programme

Two high-school students were hosted in an IBEC lab for a couple of weeks in July as part of Catalunya Caixa's $E^2C^3$ Youth and Science Programme, which exposes talented and motivated young students to 'real' scientific work to encourage more of them to embark on a scientific career. Júlia Uriach and Yentel Mateo joined Biomaterials for Regenerative Therapies group senior researcher Melba Navarro for some hands-on experience.

## October-December

### "Apropa't a la Ciència"

With its €10,000 award from the BBVA (see above), the Communications and Outreach Unit organised almost 20 talks on topics of interest to the general public in libraries and civic centres all over Barcelona throughput October, November and December.

The after-work talks, "Ens envaeixen els robots!", "Regeneració de teixits: como nou" and "Nanotecnologia: més petit que petit" were given by several researchers in rotation, namely Xavier Giralt and Manuel Vinagre (Robotics group), Melba Navarro, Miguel Angel Mateos and Oscar Castaño (Biomaterials for Regenerative Therapies), and Rosa Zaffino and Juan Pablo Agusil (Nanobioengineering).

All the events were well attended by mixed and extremely appreciative audiences of the participative lectures, which covered the history of the fields of research and their influence on popular culture, as well as outlining IBEC's current research.

### Dermoglass crowdfunding project

IBEC's very first venture into crowdfunding, which came about as an initiative of the Biomaterials for Regenerative Therapies group (page 90), went live in October on the crowdfunding website www.goteo.org. For the project, IBEC's Communications and Outreach Unit teamed up with Catalan actor and musician Andreu Rifé, who played doctor Josep in the TV3/Antena3 series 'Pulseras rojas', to make a video explaining the project, which aimed to develop and bring to market a special wound dressing that accelerates regeneration in hard-to-heal skin ulcers. The venture was also widely published on IBEC's social media pages such as Facebook and Twitter.

As a result, by 15th November 2013 Dermoglass had achieved the €8,000 minimum funding required - €8,007, to be exact - with 142 donors and still 10 days to go till the end of the first round.

# November

■ 4 November

## ‘Investiga amb RecerCaixa!’

Emili Boronat from IBEC’s Robotics group took part in the presentation of the initiative ‘Investiga amb RecerCaixa!’ at Cosmocaixa in Barcelona alongside nine other researchers from other institutions. Organized by the Catalan Association of Public Universities (ACUP) and Obra Social “la Caixa”, ‘Investiga amb RecerCaixa!’ promotes school pupils’ interest in science and helps them carry out projects associated with real research projects funded under the RecerCaixa programme, such as IBEC’s Robotics group’s InHands project, which Emili was representing.

In the auditorium full of fifth and sixth grade students, Emili explained why he decided to become a researcher, told the assembled kids a little bit about the daily life of a scientist, and outlined the concept and goals of the InHands project, whose researchers will now offer guidance and support to will help the children complete their related projects during this school year. The event appeared on TV3’s Info K programme the following day.

■ 7-9 November

## NanOpinion workshops

IrsiCaixa’s Unit of Public Engagement on Health Research, in a collaboration with IBEC, hosted two workshops to help teachers to introduce the concept of nanotechnology to their pupils. The initiative was part of the European project “NanOpinion”, which aims to monitor public opinion on nanotechnology, paying special attention to public education. The workshops formed part of the V Jornadas sobre la enseñanza de la Física y la Química, a conference for science teachers organised by the Col·legi de Llicenciats en Lletres i en Ciències de Catalunya and the Generalitat de Catalunya. They were introduced during a keynote talk by IBEC director Josep Samitier – who is also a member of the external advisory board of NanOpinion – entitled “Saps què li diu un àtom a un altre?: hola, nano” at IEC on Thursday 7th November, after which, on the Friday and Saturday at Cosmocaixa science museum in Barcelona, IBEC PhD student Teresa Galán gave a short introduction on nanotechnology and then ran one of the experiments in the workshops, which are entitled “Com apropar la recerca en nanotecnologia a l’aula”.

■ 15-24 November

## 18a Setmana de la Ciència

The “Apropa’t a la Ciència” talks (see previous page)were brought back into IBEC for this year’s Setmana de la Ciència, the Catalonia-wide science festival coordinated by the Fundació Catalana per a la Recerca i la Innovació.

Xavier Giralt, Oscar Castaño, and Rosa Zaffino and Juan Pablo Agusil presented the talks on three separate evenings during the festival, which were followed by visits to the relevant labs of the institute.

Left: Melba Navarro and the E²C³ Youth and Science placement students in July; below, Oscar Castaño giving an “Apropa’t a la Ciència” talk at the Centre Cívic Can Castelló in October.

# Media coverage in 2013

## January

■ 21 January

### 8TV

**'Investigant la investigació'**

Joan Aranda of the Robotics group and Head of Corporate Projects Arantxa Sanz featured on 8tv's 'Equip de Reporters' programme about public and private funding for science.

■ 31 January

### Diario Médico

**"Un paso hacia la reparación del sistema nervioso central"**

The press release about the Biomaterials for Regenerative Therapies group's work on the regeneration of the central nervous system was covered in *Diario Medico* and several other Spanish- and English-language news and science sites.

## February

■ 5 February

### Diario Vasco

**"Un robot para volver a andar"**

*Diario Vasco*, the daily newspaper published from San Sebastian, featured a report and video about the HYPER project, of which IBEC's Robotics group is a partner.

■ 6 February

### La Vanguardia and others

**"La UE ajudarà amb 150.000 dos investigadors espanyols"**

*La Vanguardia, Ara, Que!* and others reported the news that Pau Gorostiza, head of the Nanoprobes and Nanoswitches group, was one of the researchers selected to benefit from the European Research Council (ERC)'s top-up funding scheme 'Proof of Concept'.

■ 27-28 February

### El Mundo and others

**"Ficosa, IBEC y la UPC crean un aplicación para detectar la somnolencia al volante"**

The press release about the driver drowsiness alerter Somnoalert® developed by IBEC and Ficosa got lots of coverage in the news, including in *El Mundo, ABC*, *La Vanguardia,* TeleCinco and *El Economista*.

## March

■ 7 March

### La Razón and others

**"Un mecanismo biológico podría optimizar el tratamiento del párkinson"**

The press release about Ángel Raya's *Nature Neuroscience* paper gained coverage in *La Razón*, rTVE and many other science and news websites.

■ 12 March

### Radio Rubí

**"Entrevista a Alícia Casals, enginyera industrial especialitzada en robòtica"**

IBEC's Robotics group leader Alícia Casals was interviewed on local radio station Radio Rubí. The interview formed part of the *Rubí al dia* programme's celebration of International Women's Day, featuring women with interesting jobs.


La física 'guía' a las células


Left: Xavier Trepat in *El Périodico*; above, Sergio Oller on BTV.

## April

■ 2 April

### Ara

**"La mà més precisa d'un cirurgià"**

An April edition of Catalan daily magazine *Ara* featured an article about the minimally invasive robotic station for surgery, Bitrack, which is being developed by IBEC's spin-off company, Rob Surgical Systems.

■ 8 April

### La Vanguardia

**"Un cuerpo recambiable"**

*La Vanguardia* included a feature in the weekend magazine *Es* about the display in London of the first 'bionic man'. In the article, IBEC's former director Josep A. Planell explained that we are looking more and more towards regenerative medicine and tissue engineering to help the body repair and replace itself. The story also outlined the HYPER project involving IBEC's Robotics group, which aims to develop neurorobotic devices for the compensation and rehabilitation of motor disorders.

■ 15 April

### ABC and others

**"Primeros frutos del acuerdo entre la Generalitat y La Caixa de investigación"**

IBEC participated in an event and press conference to present the first results of the projects promoted by the five research centres included in the Obra Social "la Caixa"'s pilot scheme for funding research evaluation and technology transfer. *ABC*, *La Vanguardia* and EuropaPress covered the event.

■ 16 April

### Diario Médico

**"Herramientas para diseñar laboratorios que caben en un chip"**

In a *Diario Médico* Special on Diagnostic Therapies, IBEC acting director Josep Samitier's expert opinion was quoted in an article about lab-on-a-chip technologies.

■ 22 April

### Barcelona Televisió

**"El laboratori al 'Connexió': El nas electrònic del IBEC"**

PhD student Sergio Oller from the Signal and Information Processing for Sensing Systems was interviewed for BTV's "Connexió Barcelona" programme, talking about the group's research into the development of electronic noses based on the mammalian olfactory system.

■ 23 April

### El Periódico

**"Laboratorio a pie de calle"**

The "Recerca en directe" science fair in La Pedrera, where IBEC's Biomedical Signal Processing and Interpretation group took part with an activity that helped participants record and process their own biomedical signals, was reported on in *El Periódico*.



Medicaments que s'activen quan els toca la llum

Above: Emili Boronat (second from left) on TV3; right, the Nanoprobes and Nanoswitches group in *La Vanguardia*.

## May

■ 2 May

### Scientific American

**"9 Materials That Will Change the Future of Manufacturing'"**

The U.S. science magazine *Scientific American* featured IBEC alumnus Javier Fernandez who, along with the director of the Wyss Institute for Biologically Inspired Engineering where he is now a postdoc, developed a thin, clear, flexible material known as 'shrilk', made from discarded shrimp shells and proteins derived from silk, which is as strong as aluminum but weighs half as much. Javier began his work on materials based on chitin, one of the most abundant materials in nature, while doing his PhD in the Nanobioengineering group at IBEC, where he was awarded the prize for best thesis by the University of Barcelona in 2008.

■ 27 May

### El Mundo and others

**"Crean embriones humanos con la técnica empleada para clonar a la oveja 'Dolly'"**

Ángel Raya, group leader of IBEC's Control of Stem Cell Potency group, gave his expert opinion in several national and local newspapers on a breakthrough in Oregon, where scientists finally managed to derive human embryonic stem cells from adult tissue.

## June

■ 17 June

### Diario Médico and others

**"El movimiento de las células explicaría diversas patologías"**

*Diario Médico*, *ABC* and *El Dia* were among the press who covered the discovery by Xavier Trepat and his collaborators that appeared in *Nature Materials*.

■ 18 June

### Telecinco, Le Scienze and others

**"Descobreixen com controlar fàrmacs amb llum perquè actuïn en zones concretes"**

The news that researchers at IBEC and IRB achieved photo-switchable molecules to control protein-protein interactions in a remote and non-invasive manner was covered in national and international press including Telecinco and *Le Scienze*, the Italian version of *Scientific American*. The article, cover and "Very Important Paper" of *Angewandte Chemie* was a highlighted result of the European project "OpticalBullet", funded by the European Research Council (ERC) and in which the two institutes participate.

# July

■ 1 July

## El Periódico and others

**"La física 'guía' a las células"**

Integrative Cell and Tissue Dynamics group leader Xavier Trepat and his paper in *Nature Cell Biology* were the subject of an article in *El Périodico*. The news about the paper 'Chase-and-run between adjacent cell populations promotes directional collective migration' was also covered in several science and general news sites and magazines, including *La Razón*, in June.

■ 4 July

## El Mundo and others

**"Creado un hígado a partir de células madre"**

IBEC's Control of Stem Cell Potency group leader Ángel Raya appeared in *La Vanguardia* and *El Mundo* giving his expert opinion on some research published in *Nature* about a Japanese group that has managed to create a functional human liver using induced pluripotent stem cells.

■ 10 July

## El Periódico

**Victoria Englert: "Las notas no te definen como persona"**

IBEC got another mention in *El Periódico* when Victoria Englert, winner of the prestigious Intel ISEF prize of the Fundación Catalunya-La Pedrera, talked about her forthcoming internship in the Nanoprobes and Nanoswitches group.

■ 15 July

## Barcelona Televisió

**"El laboratori al 'Connexió': Institut de Bioenginyeria de Catalunya"**

Control of Stem Cell Potency group leader Ángel Raya appeared on an edition of current events programme Barcelona Connexió on Barcelona Televisió (BTV), in a special report on cloning.

■ 25 July

## UBTV

**"Nova aplicació mòbil que detecta la somnolència al volant"**

Santiago Marco was interviewed in a video forthe TV channel of the University of Barcelona (UBTV) about Somnoalert®, the mobile technology his group developed with them and industry partner FICOSA to detect drowsiness while driving.

■ 31 July

## Alma

**"El futur augura que tindrem la salut a l'abast de la mà"**

An interview with IBEC director Josep Samitier featured in the summer edition of *Alma*, the magazine of the Obra Social "La Caixa".


"EL FUTUR AUGURA QUE TINDREM LA SALUT A L'ABAST DE LA MÀ"

Left: Josep Samitier in *Alma;* below, Santiago Marco in the UBTV video.


Una gasa amb nanopartícules accelera la curació de les llagues


Left and above: coverage of the Biomaterials for Regenerative Therapies group's Dermoglass project: a full-page article in *El Périodico*, and Elisabeth Engel on 8TV's "8 al dia amb Josep Cuní" show.

## August

■ 1 August

### La Vanguardia

**"Medicaments que s'activen quan els toca la llum"**

Nanoprobes and Nanoswitches group leader Pau Gorostiza was the subject of a feature in *La Vanguardia*'s Sunday supplement magazine "*Diners*".

## October

■ 7 October

### La Vanguardia

**"El futuro de la educación no está en las aulas actuales"**

Founding director of IBEC Josep A. Planell appeared in *La Vanguardia*'s *Tendencias* section in an interview by journalist Maite Gutiérrez.

■ 15 October

### El Tribuno

**"El hombre biónico ya no es una utopía"**

IBEC appeared in an article about bionics and rebuilding the human body published in Argentine daily newspaper *El Tribuno* (Salta), when Josep Samitier was quoted as an expert opinion on the subject.

## November

■ 6 November

### TV3

**"Més de 450 nens de tot Catalunya faran recerca amb el suport d'investigadors del programa RecerCaixa"**

Emili Boronat from IBEC's Robotics group appeared on TV3's Info K programme after taking part in the presentation of the initiative 'Investiga amb RecerCaixa!' at Cosmocaixa in Barcelona alongside nine other researchers.

■ 7 November

### EuropaPress

**"Investigadors del Vall d'Hebron, Premi d'Investigació en Hemofília Europa Aspire 2013"**

EuropaPress reported on the collaboration between Vall d'Hebron Hospital and IBEC that led to the winning of Pfizer's prestigious ASPIRE Europe 2013 Hemophilia Research Award.

■ 12 November

### Ara

**"La ciència forja una aliança Catalunya-Israel"**

*Ara* reported that IBEC director Josep Samitier was one of 20 scientists who accompanied President Artur Mas on his official visit to Israel.

■ 12 November

## TV3

**“Lliurament de les ajudes de la Marató al Parc de Recerca Biomèdica”**

Junior group leader Pere Roca-Cusachs, who received funding from 2012’s La Marató de TV3 for his project “Stromal stiffness in Tumor Progression”, appeared on TV3 in their report about the awards ceremony.

■ 14 November

## 8TV

**“Una investigadora cerca finançament per desenvolupar un apòsit que regenera la pell”**

Elisabeth Engel, junior group leader in the Biomaterials for Regenerative Therapies group, appeared on 8tv’s “8 al dia amb Josep Cuní” show talking about the Dermoglass project.

■ 18 November

## Ara

**“Nanorobots de disseny per atacar la malària”**

IBEC Director and Head of Nanobioengineering, Josep Samitier, and the head of the joint IBEC/CRESIB unit on Nanomalaria, Xavier Fernández-Busquets, both featured in an article in the Catalan daily newspaper *Ara*.

■ 25 November

## Barcelona Televisió

**“Al laboratori al ‘Connexió’: Suma UPC, idees a la recerca de finançament”**

BTV’s Connexió programme reported on three of the projects which are currently raising funds by crowdfunding under the UPC’s SUMA initiative. One is the Biomaterials for Regenerative Therapies group’s ‘Dermoglass’, which had already achieved more than its minimum required funding, and another of the three also had a link to IBEC: the ‘Mosquiteras contra la malaria’ project coordinated by Manel Frigola, professor at the UPC, who is also a member of IBEC’s Robotics group.

# December

■ 10 December

## La Xarxa

**Dr. Samitier:’la nanotecnologia canviarà les nostres vides en 15 o 20 anys’**

Josep Samitier, Xavier Fernandez-Busquets, Santiago Marco and Sergio Oller all featured in a half-hour episode of science programme ‘El problema de Gettier’ devoted to nanotechnology.

■ 11 December

## La Vanguardia and others

**“Las células humanas construyen puentes colgantes para cicatrizar las heridas”**

The press release about the Integrative Cell and Tissue Dynamics group’s work published in *Nature Materials* appeared online in *La Vanguardia*, *ABC* and *El Diario*.


Creado un hígado a partir de células madre

Left: Ángel Raya in *La Vanguardia*; below, Xavier Fernández-Busquets in ‘*El problema de Gettier*’.

# PhD theses defended in 2013

# PhD theses in 2013

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.

■ 11 February

**Patricia Urbán**
Nanobioengineering
*Development of nanovectors for the targeted drug delivery of antimalarials (UB)*

■ 22 February

**Joana Mesquita**
Biomedical signal processing and interpretation
*Snoring and arousals in full-night polysomnographic studies from Sleep Apnea-Hypopnea Syndrome patients (UPC)*

■ 5 April

**Xavier Serra**
Integrative cell and tissue dynamics group
*Physical forces and mechanical waves during tissue growth (UPC)*

■ 23 July

**Victor Pomareda**
Signal and Information Processing for Sensing Systems
*Signal processing approaches to the detection and localization of gas chemical sources using partially selective sensors (UB)*

■ 30 July

**Sergio Martínez**
Nanobioengineering
*Desarrollo de una nueva tecnología para el ensamblaje selectivo de una monocapa ordenada de ADN:MCH por pulsos eléctricos; aplicación a sensores de ADN (UB)*

■ 26 September

**Arlyng González**
Biomaterials for regenerative therapies
*Implicaciones del Calcio Extracelular y su Receptor en Membrana (CaSR) en la Angiogénesis y la Osteogénesis. Relevancia en Ingeniería Tisular (UPC)*

■ 17 October

**Luis Amigo**
Robotics
*Estudio de Fuerzas de Interacción para Minimización de Esfuerzos en Rehabilitación Robotizada (UPC)*

■ 22 October

**Leonardo Sarlabous**
Biomedical signal processing and interpretation
*Evaluación no invasiva de la actividad de los músculos respiratorios mediante el análisis de señales Mecanomiográficas en pacientes con EPOC (UPC)*

■ 5 November

**Bogachan Tahirbegi**
Nanobioengineering
*Electrochemical multi-sensors for biomedical applications (UB)*

■ 6 November

**Mar Cendra**
Bacterial Infections: antimicrobial therapies
*Estudi de l'expressió i funció de les Ribonucleotidil Reductases d'Escherichia coli (UB)*

■ 29 November

**Patricia Carulla**
Molecular and cellular neurobiotechnology
*La proteína priónica celular: Análisis de su función neuroprotectora y reguladora del ciclo celular (UB)*

*Cover image: A field-emission scanning electron microscope image showing the good spreading and interactions of cells (appearing as green) with a scaffold made from the new fibers. Image courtesy of the Biomaterials for Regenerative Therapies group (page 90).*

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Texts by the Communications and Outreach Department and the staff and scientists of IBEC.

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