BIOENGINEERING
FOR HEALTHY AGEING

IBEC
Institute for Bioengineering of Catalonia

EXCELENCIA
SEVERO
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CONTENTS

About IBEC 4

Bioengineering for Halthy Ageing 6

Molecular Bionics 8

Protein phase transitions in health and disease 11

Molecular and cellular neurobiotechnology 14

Biomaterials for regenerative therapies 18

Nanoprobes and nanoswitches 21

Biomedical signal processing and interpretation 24

Molecular Imaging for Precision Medicine 28

Targeted therapeutics and nanodevices 30

Biosensors for bioengineering 33

Nanobioengineering 36

Smart nano-bio-devices 40

Bacterial infections: antimicrobial therapies 42

ABOUT IBEC

The Institute for Bioengineering of Catalonia (IBEC) is an interdisciplinary research centre, based in Barcelona, that conducts excellent interdisciplinary research at the frontiers of engineering and life sciences in order to generate new knowledge by putting together fields like nanomedicine, biophysics, biotechnology, tissue engineering and the applications of health information technology.

The institute currently has 22 research groups and 350+ researchers and staff from 25 different countries.

The IBEC model represents an evolution from 20th-century biomedical institutes and is part of a new wave of research initiatives set up in the last decade, with shared interests and points of view concerning how to advance the frontiers of knowledge in experimental science to benefit clinical and biomedical research. The common denominator shared by these new initiatives is their focus on the enormous challenge of how to make life science quantitative on any scale, taking full advantage of the unprecedented power of the convergence between nano, bio and ICT.

At IBEC, frontier research is combined with specific transfer targets to produce new applied technologies to be used in life and health sciences. We have the versatility to generate excellent research and, at the same time, work with clinicians and industry to develop new diagnostic or treatment systems. The model envisaged by IBEC is inspired by a creative, innovative new ecosystem based on interaction between research experts in different enabling technologies (nano-bio-info-cogno) to generate new knowledge and engineering solutions in health technology.

Early diagnosis, new therapies based on regenerative medicine, better quality of life compatible with an ageing population, and technological advances to increase efficiency and make healthcare sustainable: these are some excellent examples of areas where IBEC can contribute with its cutting-edge research to generate new technological advances of key importance to innovation.

Collaboration across research groups with complementary skills is the key factor behind IBEC's uniqueness. This is achieved through the convergence of talented researchers with very diverse backgrounds, access to state-of-the-art laboratory facilities and effective leadership able to efficiently coordinate and maximise the benefits of such a complex environment.

IBEC excellence was recognized by the Spanish Ministry of Economy and Competitiveness by its award as Severo Ochoa Research Centre in the 2014 call, which labels IBEC as one of Spain top research centres at the highest international level in terms of research, training, human resources, outreach and technology transfer. The award was renewed in the Severo Ochoa 2018 call.

The knowledge that exists in IBEC is structured in 4 broad avenues of knowledge: nanomedicine, mechanobiology, cell engineering and ICT for health:

Nanomedicine:
nanobiosensing; microfluidics; nanofabrication; beyond-AFM/ST microscopy tools to characterize biological samples at the nanoscale; nanorobotics; nanoscopy; drug delivery improvement; nano-scale characterization of bacterial-host interactions; organ/lab-on-chip.

Mechanobiology:
new technologies to measure physical forces at the cell-cell and cell-matrix interface; optogenetics to control cell mechanics; molecular mechanism that cells employ to sense and respond to rigidity. rigidity.

Cell Engineering:
cell reprogramming; control differentiation of stem cells; cell niches; biomaterials for regenerative medicine; cell-material interaction; biomimetics; cellular and molecular biology; antibacterial strategies

ICT for Health:
application of advanced information and communication technologies to healthcare, such as modelling; signaling processing; automatics/ control software for robotics; theory of mind and brain; cognition.

THESE ARE PLACED AT THE SERVICE OF SCIENCE AND SOCIETY TO PROGRESS IN THREE MAJOR RESEARCH PROGRAMMES:

BIOENGINEERING FOR FUTURE AND PRECISION MEDICINE, with the aim of developing technology that goes beyond the existing paradigm of medical care in hospital to incorporate new areas such as personalize medicine, tailoring diagnostic and therapies to the individual, optopharmacology, diagnosis and therapies based on mechanobiology and nanomedicine.

BIOENGINEERING FOR ACTIVE AGEING, with the aim of developing care and technology and improve the quality of life of an increasing older population. Assisted living technologies such as mobile health solutions, including home-based devices and services for remote monitoring, consultation and diagnosis, can help support independent living at home, keeping patients out of hospital and residential care for longer.

BIOENGINEERING FOR REGENERATIVE THERAPIES, with the aim of developing regenerative technologies to allow the creation of implants able to bring about the regeneration of damaged tissues or organs and to develop cell therapies.

BIOENGINEERING FOR HEALTHY AGEING

Population ageing is a long-term development that has been apparent for several decades in Europe. This process is being driven by historically low fertility rates, increasing life expectancy and, in some cases, migratory patterns. Population projections suggest that the ageing of the EU's population will quicken in the coming decades, with a rapid expansion in the number and share of older people.

The number of EU residents aged 65+ is expected to increase from 90.5 million at the start of 2019 to 129.8 million by 2050. The rapid growth of the oldest age groups will have a major impact on health care costs. The reasons are twofold: 1) The incidence of diseases that affect the elderly in particular will be soaring in the immediate future and 2) diseases and events that would have often been fatal become survivable and chronic.

This new paradigm requires a strong development of new solutions provided by bioengineering approaches. Engineering must play a substantial role mitigating and managing the effects of this surge in demand for healthcare and in providing care to be delivered in new ways. It also can be determinant to enable citizens to remain independent and able to live in their own homes as long as possible.

Bioengineering enables society to define, understand and solve highly complex problems in medicine, bringing together fields such as nanomedicine, biophysics, mechanobiology, biomaterials, biotechnology, tissue engineering, biosensors and the applications of ICT for health. These are put at the service of the understanding and quantification of all the mechanisms involved in human physiology and health.

IBEC works to find solutions in the following areas which present greater morbidity at older ages: cardiovascular diseases, diabetes and secondary diabetic diseases such as diabetic nephropathy, cardiac failure, traumatic brain injury, and neurodegenerative and respiratory diseases as well as nosocomial infections related to long stays in health care facilities.

Bioengineering is used at IBEC in a multidisciplinary way to fight diseases related to ageing by means of biosensors, organ-on-a-chip and organoids for disease modelling and drug screening, targeted drug delivery, high-throughput mutagenesis, light-regulated molecular neuroligands, regenerative therapies for neuroregeneration, bone, skin and heart substitution, biomarker identification, advanced signal processing to improve non-invasive monitoring, diagnosis and disease prevention and pathology treatment and ICT-based neurorehabilitation.

Since 2018, our researchers have published more than 90 publications focusing on healthy ageing, including contributions in top impact journals such as J Neurology, Neurosurgery, and Psychiatry, Acta Neuropathologica, Biofabrication or Science advances. In the last years, our research on healthy ageing has attracted competitive funding, including ERC grants, and national grants from the Ministry of Science as well as private funding from Fundació "La Caixa".

Bioengineering for Healthy Ageing is one of the Advanced Societal Health Challenges of the Severo Ochoa Strategic Plan of IBEC 2019-2023, designed to capitalize on IBEC's potential to apply a novel, non-conventional paradigm of bioengineering to contribute to the most acute challenges of medicine today.

The prevalence of diseases associated to ageing poses an unprecedented challenge to EU health systems. Biomedical engineering underpins many of the actions required to improve the quality of life of older people, including medical, social and infrastructure needs, so that the degree of independence and activity for ageing citizens can be greatly improved. Through the research and innovation activities described in the following pages and in collaboration with its international network of partner institutions, IBEC aims to contribute to a better quality of life of older people.

Molecular Bionics

Giuseppe Battaglia

In our lab, we are interested in how molecules, macromolecules, viruses, vesicles, and whole cells traffic across our body barriers. We combine novel microscopic tools with theoretical and computational physics to study biological transport from the single molecules, cell membrane, to the whole organism. We thus translate the acquired knowledge to bioengineer novel nanomedicines, combining soft matter physics with synthetic chemistry. Here, we design bionic units that mimic specific biological functions and introduce operations that do not exist in nature. We apply a constructionist approach where we mimic biological complexity in the form of design principles to produce functional units from simple building blocks and their interactions. We call such an effort, Molecular Bionics, and it involves inputs from physical science and engineering from one side and biomedical science.

"The blood-brain barrier (BBB) maintains the brain high metabolism and understanding how molecules shuttle through helps us to shed light on diseases and ageing, as well as to design new drugs."

Recent activities related to healthy ageing

We have recently been working on elucidating an unique mechanism that allow molecules to efficiently cross the blood brain barrier (BBB). We showed that depending on the cargo avidity (i.e. how many simultaneous bonds it forms), the BBB cells shuttle it through or keep it inside. We showed that large macromolecules cargos, including nanomedicines or misfolded proteins such as amyloid beta aggregates traffic across the BBB via tubular vesicles. These form and move fast across the cells via the coordinated work of membrane receptors (such as LRP1) and stabilised by cytosolic proteins such as syndapin-2 and actin. Such a transport is critical for the brain metabolism and indeed we observed that in Alzheimer and ageing, the shuttling machinery is less efficient leading to local accumulation of amyloid beta proteins. With this in mind, we are now shedding light on the relation between the BBB and the other brain cells stress, as well as the same mechanism is involved in other proteins associated with ageing and neurodegeneration including Tau proteins and alpha-synuclein. Most importantly, we are exploiting the same mechanism to design new carriers to deliver any type of therapeutic and diagnostic agent in the brain. At the same time, we are also designing new therapies to mend the faulty transport process and studying how this helps to cure diseases such as Alzheimer and other dementias.

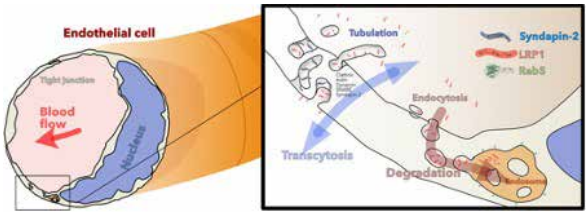


Diagram showing the syndapin-2–mediated transcellular route and the intracellular degradation of LRP1 in a brain endothelial cell, the main unit of the blood brain barrier.

Funded projects related to healthy ageing

CHEMOTACTIC SUPER-SELECTIVE TARGETING OF GLIOMAS	ERC
DEVELOPING A NOVEL STRATEGY TO DELIVER THERAPY-LOADED NANOPARTICLES SPECIFICALLY INTO THE BRAIN BY SELECTIVELY LABELLING THE BRAIN MICROVASCULATURE	CAIXA JUNIOR LEADER FELLOWSHIP (D. GONZALEZ PI)
DEFINING MACROMOLECULAR TRANSPORT AT THE BLOOD-BRAIN-BARRIER USING TARGETED NANOPROBES	BBSRC/ASTRAZENECA
MAPPING OUT GLIOMA HETEROGENEITY ALONG THE BLOOD BRAIN BARRIER USING SUPER-SELECTIVE BRAIN PENETRATING POLYMERSOMES	CRUK
BRAIN PENETRATING PRECISION NANOMEDICINES	MINECO PLAN NACIONAL

Main recent publications related to healthy ageing

Duro-Castano, A., Moreira Leite, D., Forth, J., Deng, Y., Matias, D., Noble Jesus, C., & Battaglia, G. (2020). Designing peptide nanoparticles for efficient brain delivery. Advanced Drug Delivery Reviews, 160, 52–77. https://doi.org/10.1016/j.addr.2020.10.001

Tian, X., Leite, D. M., Scarpa, E., Nyberg, S., Fullstone, G., Forth, J., Matias, D., Apriceno, A., Poma, A., Duro-Castano, A., Vuyyuru, M., Harker-Kirschneck, L., Šarić, A., Zhang, Z., Xiang, P., Fang, B., Tian, Y., Luo, L., Rizzello, L., & Battaglia, G. (2020). On the shuttling across the blood-brain barrier via tubule formation: Mechanism and cargo avidity bias. Science Advances, 6(48), eabc4397. https://doi.org/10.1126/sciadv.abc4397

M Leite, D., Matias, D., & Battaglia, G. (2020). The Role of BAR Proteins and the Glycocalyx in Brain Endothelium Transcytosis. Cells, 9(12), 2685. https://doi.org/10.3390/cells9122685

X. Tian, S. Angioletti-Uberti, G Battaglia* On the design of precision nanomedicines. Science Advances 2020, 6, 4 , eaat0919 10.1126/sciadv.aat0919

E.S.Kim,D.Kim,S.Nyberg,A.Poma,D.Cecchin,S.Jain,K.A.Kim,Y.J.Shin,E.H.Kim, M. Kim , S. H. Baek ,J. K. Kim , T. Doeppner , A. Ali , J. Redgrave , G. Battaglia* , O. N. Bae*, A. Majid*. LRP-1 functionalized polymersomes enhance the efficacy of carnosine in experimental stroke Scientific Reports 2020, 10(1), 699. https://doi.org/10.1038/s41598-020-57685-5

M.Liu, A. Apriceno, M. Sipin, E. Scarpa, L. Rodriguez Arco, A.Poma, G.Marchello, G. Battaglia*, S. Angioletti-Uberti*. Combinatorial entropy behaviour leads to range selective binding in ligand-receptor interactions. Nature Communications 11, 4836 (2020). https://doi.org/10.1038/s41467-020-18603-5

Protein phase transitions in health and disease

Benedetta Bolognesi

We aim to understand how protein sequences can become toxic upon mutation. We are particularly interested in amino acid sequences that can adopt different conformations and undergo a process of self-assembly which results in distinct physical states. In order to understand how mutations affect these delicate equilibria and when and why a sequence becomes toxic for the cell in the context of different types of disease, our lab integrates experimental and computational approaches in different model systems.

Currently, we focus mainly on classical amyloids, such as the amyloid-beta peptide found in Alzheimer's disease brains, but we are also exploring prion-like domains. Prion-like domains are frequently mutated in several rare neurodegenerative conditions, such as Amyotrophic Lateral Sclerosis. Just like most disordered protein regions, prion-like domains are particularly difficult to study in vitro. In this perspective, in vivo approaches such as the ones we develop, can provide a unique opportunity to investigate these sequences in a systematic way.

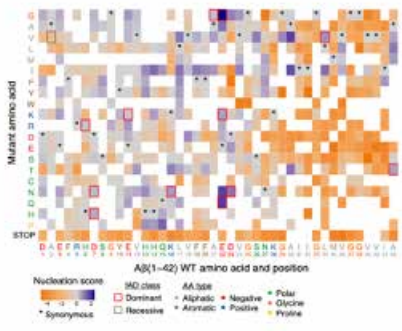
"We have developed a high throughput method to quantify the effects of thousands of mutations in the amyloid beta peptide, which forms insoluble plaques in the brains of Alzheimer's disease patients."

Recent activities related to healthy ageing

Development of a massively parallel assay for amyloid nucleation and application to amyloid beta

We have developed a new high throughput method to quantify the effects of thousands of mutations in parallel on the nucleation of amyloid fibrils. We have applied the method to the amyloid beta peptide (AB), which forms insoluble plaques in the brains of Alzheimer's disease patients. Here, we could quantify how more than 15,000 mutations influence the formation of new aggregates. Remarkably, the scores obtained through this approach accurately classify all of the known familial Alzheimer's disease mutations which cause horrific rare forms of dementia. Our work also provides many mechanistic insights into the process of amyloid nucleation which we are currently extending to other amyloid diseases. This work was recently published: https://elifesciences.org/articles/63364

In collaboration with the CRG, we have also used high-throughput mutagenesis to study Amyotrophic Lateral Sclerosis (ALS). Amyotrophic lateral sclerosis is a devastating and incurable nervous system disease that affects nerve cells in the brain and spinal cord, causing loss of muscle control and normally death within a few years of diagnosis. We focused on TDP-43, a protein that aggregates in the motor neurons of nearly all ALS patients. We made over 50,000 mutants of TDP-43 and tracked their toxicity to yeast cells. The results showed that mutant forms that aggregated into solid aggregates were, actually, less toxic than other versions of the protein which instead formed more dynamic condensates in the cell (https://www.nature.com/articles/s41467-019-12101-z). We have also succeeded in using genetic interactions to infer the structure that this putatively disordered protein domain adopts inside the cell. The group is currently studying if the aggregation of TDP-43 is also protective in mammalian cells and neurons. If this proves to be the case, the way in which ALS is therapeutically addressed will have to be entirely changed.



The amyloid nucleation propensity of amino acid substitutions in the amyloid beta peptide mapped by combining deep mutagenesis to our nucleation assay. Familial AD mutations are highlighted by red squares.

Funded projects related to healthy ageing

MASSIVELY PARALLEL MUTAGENESIS TO UNDERSTAND, PREDICT AND PREVENT AMYLOID NUCLEATION IN NEURODEGENERATIVE DISEASES.	FUNDACIÓ LA CAIXA
PRIOMUT ESCANEADO EXHAUSTIVO DE MUTACIONES EN UN DOMINIO PRIÓNICO PARA ENTENDER LA TOXICIDAD INDUCIDA POR PROTEÍNAS	MICIU, RETOS INVESTIGACIÓN: PROYECTOS I+D

Main recent publications related to healthy ageing

Seuma, M., Faure, A. J., Badia, M., Lehner, B., Bolognesi, B. (2021). The genetic landscape for amyloid beta fibril nucleation accurately discriminates familial Alzheimer's disease mutations. eLife, 10, e63364.

Badia, M., Bolognesi, B. (2021). Assembling the right type of switch: Protein condensation to signal cell death. Current opinion in cell biology, 69, 55–61.

Bolognesi, B.; Faure, A.J.; Seuma, M.; Schmiedel, J.M.; Tartaglia, G.G.; Lehner, B. (2019). The mutational landscape of a prion-like domain Nature Communications 10, 4162

Molecular and cellular neurobiotechnology

José Antonio del Río

Inflammation is a physiological process protective against acute infections or tissue damage but becomes harmful when it enters a chronic state. Recruitment of circulating leukocytes and inflammation is a general mechanism and hallmark of many pathological disorders of the central nervous system (CNS) including multiple sclerosis (MS) and spinal cord injuries (SCI). Neuroinflammation in the CNS, however, is also necessary for proper healing, and current anti-inflammatory interventions depleting immune cells or directly targeting their trafficking into the CNS usually have serious unwanted side effects. These highlights the need for better immunomodulatory strategies in CNS diseases, additionally the unwanted effects of neuroinflammation are worsened with aging.

In our laboratory we investigate the cellular and molecular mechanisms underlying the different phases of the inflammatory response and their effects on neurons and glial cells, after axonal injuries or autoimmune demyelinating diseases, such as multiple sclerosis. Our aim is to identify putative treatments or targets that allow us to tailor the inflammatory response in CNS sensorimotor pathologies such as SCI or MS.

"We study the biology of neurodegenerative diseases to understand their pathogenesis and determine new biomarkers and putative therapeutical approaches."

Recent activities related to healthy ageing

We are analyzing epigenetic tags related to cellular prion protein (PrPC) expression changes, as future prodromal biomarkers of Alzheimer's disease (AD) in peripheral blood of asymptomatic population. Using brain human samples from diagnosed AD patients at different Braak stages (from I to VI) our results show an increase of H3K9 histone acetylation associated with PRNP promoter in the first steps of the disease when compared to non-AD control samples and, a decrease at later stages, correlating with PrPC expression profile. On the other hand, the finding of a methylated cytosine near the AP-1 site, in samples from patients with advanced AD, points this mechanism of regulation of PRNP transcription as a candidate to be evaluated in the progression of the disease.

Funded projects related to healthy ageing

STOPTAUPATHOL · MODULATION OF TAU SEEDING AND PATHOLOGY IN TAUOPATHIES BY BBBNANOCARRIERS, EPITOPE SELECTIVE VACCINATION AND ECTOPRP TAU RECEPTOR BODIES (2019-2022)	OBRA SOCIAL "LA CAIXA"
PRIONET-SPAIN. RED DE EXCELENCIA NACIONAL DE PRIONES	MICIU (REDES TEMÁTICAS DE INVESTIGACIÓN)
CNED2016/2 . MONITORING THE ONSET AND EVOLUTION OF NEURONAL DYSFUNCTIONS IN PROPAGATIVE NEURAL DISORDERS USING MICROFLUIDIC DEVICES AND TRANSLATIONAL APPROACHES	SPANISH NETWORK OF NEURODEGENERATIVE DISEASES (CIBERNED), INSTITUTE OF HEALTH CARLOS III.
CNED2018/2 . ANÁLISIS CELULAR Y MOLECULAR DE LA SIEMBRA Y PROGRESIÓN DE TAU EN MODELOS ANIMALES Y CELULARES DE DISTINTAS TAUOPATIAS HUMANAS.	SPANISH NETWORK OF NEURODEGENERATIVE DISEASES (CIBERNED), INSTITUTE OF HEALTH CARLOS III.

Main recent publications related to healthy ageing

Ferrer, I., Andrés-Benito, P., Ausín, K., Pamplona, R., Del Rio, J. A., Fernández-Irigoyen, J., & Santamaría, E. (2021). Dysregulated protein phosphorylation: A determining condition in the continuum of brain aging and Alzheimer's disease. Brain pathology (Zurich, Switzerland), e12996. Advance online publication. https://doi.org/10.1111/bpa.12996

Mesquida-Veny, F., Del Río, J. A., & Hervera, A. (2021). Macrophagic and microglial complexity after neuronal injury. Progress in neurobiology, 200, 101970. https://doi.org/10.1016/j.pneurobio.2020.101970

Lidón, L., Llaó-Hierro, L., Nuvolone, M., Aguzzi, A., Ávila, J., Ferrer, I., Del Río, J. A., & Gavín, R. (2021). Tau Exon 10 Inclusion by PrPC through Downregulating GSK3β Activity. International journal of molecular sciences, 22(10), 5370. https://doi.org/10.3390/ijms22105370

Hervera, A., De Virgiliis, F., Palmisano, I., Zhou, L., Tantardini, E., Kong, G., Hutson, T., Danzi, M. C., Perry, R. B., Santos, C., Kapustin, A. N., Fleck, R. A., Del Río, J. A., Carroll, T., Lemmon, V., Bixby, J. L., Shah, A. M., Fainzilber, M., & Di Giovanni, S. (2018). Reactive oxygen species regulate axonal regeneration through the release of exosomal NADPH oxidase 2 complexes into injured axons. Nature cell biology, 20(3), 307–319. https://doi.org/10.1038/s41556-018-0039-x

Diaz-Lucena, D., Kruse, N., Thüne, K., Schmitz, M., Villar-Piqué, A., da Cunha, J., Hermann, P., López-Pérez, Ó., Andrés-Benito, P., Ladogana, A., Calero, M., Vidal, E., Riggert, J., Pineau, H., Sim, V., Zetterberg, H., Blennow, K., Del Río, J. A., Marín-Moreno, A., Espinosa, J. C., … Llorens, F. (2021). TREM2 expression in the brain and biological fluids in prion diseases. Acta neuropathologica, 141(6), 841–859. https://doi.org/10.1007/s00401-021-02296-1

Ferrer, I., Andrés-Benito, P., Sala-Jarque, J., Gil, V., & Del Rio, J. A. (2020). Capacity for Seeding and Spreading of Argyrophilic Grain Disease in a Wild-Type Murine Model; Comparisons With Primary Age-Related Tauopathy. Frontiers in molecular neuroscience, 13, 101. https://doi.org/10.3389/fnmol.2020.00101

Sala-Jarque, J., Mesquida-Veny, F., Badiola-Mateos, M., Samitier, J., Hervera, A., & Del Río, J. A. (2020). Neuromuscular Activity Induces Paracrine Signaling and Triggers Axonal Regrowth after Injury in Microfluidic Lab-On-Chip Devices. Cells, 9(2), 302. https://doi.org/10.3390/cells9020302

Del Rio, J. A., & Ferrer, I. (2020). Potential of Microfluidics and Lab-on-Chip Platforms to Improve Understanding of "prion-like" Protein Assembly and Behavior. Frontiers in bioengineering and biotechnology, 8, 570692. https://doi.org/10.3389/fbioe.2020.570692

Gil, V., & Del Río, J. A. (2019). Functions of Plexins/Neuropilins and Their Ligands during Hippocampal Development and Neurodegeneration. Cells, 8(3), 206. https://doi.org/10.3390/cells8030206

Diaz-Lucena, D., Escaramis, G., Villar-Piqué, A., Hermann, P., Schmitz, M., Varges, D., Santana, I., Del Rio, J. A., Martí, E., Ferrer, I., Baldeiras, I., Zerr, I., & Llorens, F. (2020). A new tetra-plex fluorimetric assay for the quantification of cerebrospinal fluid β-amyloid42, total-tau, phospho-tau and α-synuclein in the differential diagnosis of neurodegenerative dementia. Journal of neurology, 267(9), 2567–2581. https://doi.org/10.1007/s00415-020-09870-9

Gavín, R., Lidón, L., Ferrer, I., & Del Río, J. A. (2020). The Quest for Cellular Prion Protein Functions in the Aged and Neurodegenerating Brain. Cells, 9(3), 591. https://doi.org/10.3390/cells9030591

Lidón, L., Vergara, C., Ferrer, I., Hernández, F., Ávila, J., Del Rio, J. A., & Gavín, R. (2020). Tau Protein as a New Regulator of Cellular Prion Protein Transcription. Molecular neurobiology, 57(10), 4170–4186. https://doi.org/10.1007/s12035-020-02025-x

Lidón, L., Urrea, L., Llorens, F., Gil, V., Alvarez, I., Diez-Fairen, M., Aguilar, M., Pastor, P., Zerr, I., Alcolea, D., Lleó, A., Vidal, E., Gavín, R., Ferrer, I., & Del Rio, J. A. (2020). Disease-Specific Changes in Reelin Protein and mRNA in Neurodegenerative Diseases. Cells, 9(5), 1252. https://doi.org/10.3390/cells9051252

Diaz-Lucena, D., Escaramis, G., Villar-Piqué, A., Hermann, P., Schmitz, M., Varges, D., Santana, I., Del Rio, J. A., Martí, E., Ferrer, I., Baldeiras, I., Zerr, I., & Llorens, F. (2020). A new tetra-plex fluorimetric assay for the quantification of cerebrospinal fluid β-amyloid42, total-tau, phospho-tau and α-synuclein in the differential diagnosis of neurodegenerative dementia. Journal of neurology, 267(9), 2567–2581. https://doi.org/10.1007/s00415-020-09870-9

La Montanara, P., Hervera, A., Baltussen, L. L., Hutson, T. H., Palmisano, I., De Virgiliis, F., Kong, G., Chadwick, J., Gao, Y., Bartus, K., Majid, Q. A., Gorgoraptis, N., Wong, K., Downs, J., Pizzorusso, T., Ultanir, S. K., Leonard, H., Yu, H., Millar, D. S., Istvan, N., … Di Giovanni, S. (2020). Cyclin-dependent-like kinase 5 is required for pain signaling in human sensory neurons and mouse models. Science translational medicine, 12(551), eaax4846. https://doi.org/10.1126/scitranslmed.aax4846

Ferrer, I., Andrés-Benito, P., Zelaya, M. V., Aguirre, M., Carmona, M., Ausín, K., Lachén-Montes, M., Fernández-Irigoyen, J., Santamaría, E., & Del Rio, J. A. (2020). Familial globular glial tauopathy linked to MAPT mutations: molecular neuropathology and seeding capacity of a prototypical mixed neuronal and glial tauopathy. Acta neuropathologica, 139(4), 735–771. https://doi.org/10.1007/s00401-019-02122-9

Ferrer, I., Zelaya, M. V., Aguiló García, M., Carmona, M., López-González, I., Andrés-Benito, P., Lidón, L., Gavín, R., Garcia-Esparcia, P., & Del Rio, J. A. (2020). Relevance of host tau in tau seeding and spreading in tauopathies. Brain pathology (Zurich, Switzerland), 30(2), 298–318. https://doi.org/10.1111/bpa.12778

Ferrer, I., Aguiló García, M., Carmona, M., Andrés-Benito, P., Torrejón-Escribano, B., Garcia-Esparcia, P., & Del Rio, J. A. (2019). Involvement of Oligodendrocytes in Tau Seeding and Spreading in Tauopathies. Frontiers in aging neuroscience, 11, 112. https://doi.org/10.3389/fnagi.2019.00112

Palmisano, I., Danzi, M. C., Hutson, T. H., Zhou, L., McLachlan, E., Serger, E., Shkura, K., Srivastava, P. K., Hervera, A., Neill, N. O., Liu, T., Dhrif, H., Wang, Z., Kubat, M., Wuchty, S., Merkenschlager, M., Levi, L., Elliott, E., Bixby, J. L., Lemmon, V. P., … Di Giovanni, S. (2019). Epigenomic signatures underpin the axonal regenerative ability of dorsal root ganglia sensory neurons. Nature neuroscience, 22(11), 1913–1924. https://doi.org/10.1038/s41593-019-0490-4

Hervera, A., Zhou, L., Palmisano, I., McLachlan, E., Kong, G., Hutson, T. H., Danzi, M. C., Lemmon, V. P., Bixby, J. L., Matamoros-Angles, A., Forsberg, K., De Virgiliis, F., Matheos, D. P., Kwapis, J., Wood, M. A., Puttagunta, R., Del Río, J. A., & Di Giovanni, S. (2019). PP4-dependent HDAC3 dephosphorylation discriminates between axonal regeneration and regenerative failure. The EMBO journal, 38(13), e101032. https://doi.org/10.15252/embj.2018101032

Hutson, T. H., Kathe, C., Palmisano, I., Bartholdi, K., Hervera, A., De Virgiliis, F., McLachlan, E., Zhou, L., Kong, G., Barraud, Q., Danzi, M. C., Medrano-Fernandez, A., Lopez-Atalaya, J. P., Boutillier, A. L., Sinha, S. H., Singh, A. K., Chaturbedy, P., Moon, L., Kundu, T. K., Bixby, J. L., … Di Giovanni, S. (2019). Cbp-dependent histone acetylation mediates axon regeneration induced by environmental enrichment in rodent spinal cord injury models. Science translational medicine, 11(487), eaaw2064. https://doi.org/10.1126/scitranslmed.aaw2064

Hervera, A., Santos, C. X., De Virgiliis, F., Shah, A. M., & Di Giovanni, S. (2019). Paracrine Mechanisms of Redox Signalling for Postmitotic Cell and Tissue Regeneration. Trends in cell biology, 29(6), 514–530. https://doi.org/10.1016/j.tcb.2019.01.006

Biomaterials for regenerative therapies

Elisabeth Engel

Research in the Biomaterials for Regenerative Therapies group is devoted to the development and knowledge transfer for biomedical applications. They design, fabricate and characterize bioactive and biodegradable materials and investigate their interactions with biological entities, both in terms of fundamental research aspects and as specific applications for tissue engineering and disease modelling purposes in mind. The aim is to repair and restore tissue and organ functions, as well as closely replicate 3D disease microenvironments such as cancer, for a better and personalized diagnose and treatment. By means of combining 3D scaffolds, cells, their generated extracellular matrix and their own signalling cues, researchers pretend to engineer innovative biomaterials and cell-derived scaffolds that mimic complex human structures and their biochemical properties, with promising industrial applications.

"Our work on regenerative therapies focuses on the regeneration of cardiac tissue, cartilage and also in wound healing, all major problems in the ageing population."

Recent activities related to healthy ageing

Chronic wounds are one of the most prominent clinical manifestations of diabetes, however, they lack satisfactory treatment options. We have developed polymeric composites that deliver ions having wound healing properties. The evaluation of its performance using a pressure ulcer model in diabetic mice proved that these polymeric composites offer an optimum approach for chronic wound healing without adding cells or external biological factors.

Another major problem for the world ageing population are degenerative cartilage pathologies. We have been working on the development of a three-dimensional bioengineered platform for articular cartilage regeneration. This 3D-bioengineered platform allows for long-term hMSC culture resulting in chondrogenic differentiation and has mechanical properties resembling native articular cartilage. These promising results suggest that this approach could be potentially used in articular cartilage repair and regeneration.

We are also working on the generation of bioactive scaffolds that can be novel implants for stimulating neovascularization of tissue-engineered constructs in regenerative medicine field. In addition, we have developed a new methodology for in-house fabrication of microtissues with angiogenic potential for downstream use in various tissue regenerative strategies.

Another research line in our laboratory is focussing on the generation of cardiac tissue models for preclinical testing. We have recently presented a microfluidic platform that aims to provide a range of signaling cues to immature cardiac cells to drive them towards an adult phenotype. The device combines topographical electrospun nanofibers with electrical stimulation in a microfabricated system. This platform is a powerful tool for the tissue engineering community due to its low cost, high imaging compatibility, versatility, and high-throughput configuration capabilities.

Funded projects related to healthy ageing

NANGIODERM · MATERIALES LIBERADORES DE IONES PARA PROMOVER LA ANGIOGÉNESIS EN REGENERACIÓN DÉRMICA (2019-2022)	MINECO, ACCIONES DE PROGRAMACIÓN CONJUNTA INTERNACIONAL
BIOCARDIO · BIOINGENIERÍA DE CONSTRUCTOS BASADOS EN BIOMATERIALES PARA LA REGENERACIÓN CARDIACA (2019-2021)	MICIU, RETOS INVESTIGACIÓN: PROYECTOS I+D

Main recent publications related to healthy ageing

López-Canosa, A., Perez-Amodio, S., Yanac-Huertas, E., Ordoño, J., Rodriguez-Trujillo, R., Samitier, J., Castaño, O., & Engel, E. (2021). A microphysiological system combining electrospun fibers and electrical stimulation for the maturation of highly anisotropic cardiac tissue. Biofabrication, 13(3), 10.1088/1758-5090/abff12. https://doi.org/10.1088/1758-5090/abff12

Li, J., Castaño, O., Tomasello, A., de Dios Lascuevas, M., Canals, P., Engel, E., & Ribo, M. (2021). Catheter tip distensibility substantially influences the aspiration force of thrombectomy devices. Journal of neurointerventional surgery, neurintsurg-2021-017487. Advance online publication. https://doi.org/10.1136/neurintsurg-2021-017487

Perez-Amodio, S., Rubio, N., Vila, O. F., Navarro-Requena, C., Castaño, O., Sanchez-Ferrero, A., Marti-Munoz, J., Alsina-Giber, M., Blanco, J., & Engel, E. (2021). Polymeric Composite Dressings Containing Calcium-Releasing Nanoparticles Accelerate Wound Healing in Diabetic Mice. Advances in wound care, 10(6), 301–316. https://doi.org/10.1089/wound.2020.1206

Rubí-Sans, G., Cano-Torres, I., Pérez-Amodio, S., Blanco-Fernandez, B., Mateos-Timoneda, M. A., & Engel, E. (2021). Development and Angiogenic Potential of Cell-Derived Microtissues Using Microcarrier-Template. Biomedicines, 9(3), 232. https://doi.org/10.3390/biomedicines9030232

Soriente, A., Amodio, S. P., Fasolino, I., Raucci, M. G., Demitri, C., Engel, E., & Ambrosio, L. (2021). Chitosan/PEGDA based scaffolds as bioinspired materials to control in vitro angiogenesis. Materials science & engineering. C, Materials for biological applications, 118, 111420. https://doi.org/10.1016/j.msec.2020.111420

Blanco-Fernandez, B., Castaño, O., Mateos-Timoneda, M. Á., Engel, E., & Pérez-Amodio, S. (2021). Nanotechnology Approaches in Chronic Wound Healing. Advances in wound care, 10(5), 234–256. https://doi.org/10.1089/wound.2019.1094

Rubí-Sans, G., Recha-Sancho, L., Pérez-Amodio, S., Mateos-Timoneda, M. Á., Semino, C. E., & Engel, E. (2019). Development of a Three-Dimensional Bioengineered Platform for Articular Cartilage Regeneration. Biomolecules, 10(1), 52. https://doi.org/10.3390/biom10010052

Bertuoli, P. T., Ordoño, J., Armelin, E., Pérez-Amodio, S., Baldissera, A. F., Ferreira, C. A., Puiggalí, J., Engel, E., Del Valle, L. J., & Alemán, C. (2019). Electrospun Conducting and Biocompatible Uniaxial and Core-Shell Fibers Having Poly(lactic acid), Poly(ethylene glycol), and Polyaniline for Cardiac Tissue Engineering. ACS omega, 4(2), 3660–3672. https://doi.org/10.1021/acsomega.8b03411

Nanoprobes and nanoswitches

Pau Gorostiza

Research in the laboratory focuses on developing nanoscale tools to study biological systems. These include a set of tools based on engineered molecular actuators that can be switched with light (photopharmacology). They include peptide inhibitors of protein-protein interactions, small molecule enzymatic inhibitors, and photoswitchable ligands of a diversity of other proteins. Among several applications to basic research and advanced therapies for healthy ageing, these compounds have enabled photoactivated chemotherapy, photocontrol of cellular signalling mediated by ion channels and G protein-coupled receptors, photocontrol of cardiac activity and locomotion, sensory restoration, and photocontrol of brain waves. Based on these tools, we have also developed two-photon pharmacology to manipulate and study the activity of neurons and glia in intact brain tissue with pharmacological selectivity and sub-cellular three-dimensional resolution.

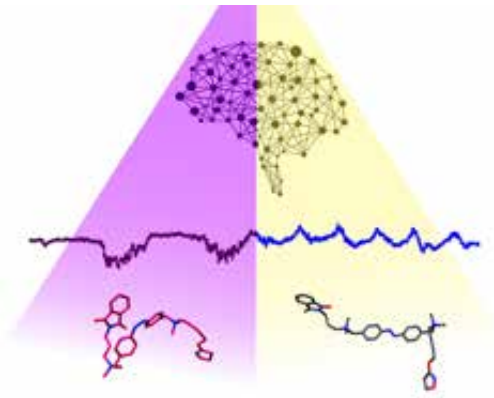
"Our photoswitchable drugs enable both basic and applied research, including safe and accurate therapeutic interventions in the brain and other organs with pharmacological and spatiotemporal selectivity."

Recent activities related to healthy ageing

In the last years, the nanoprobes and nanoswitches group has been working in the development of photoswitchable drugs and neurotransmitters that will help with the treatment and understanding of brain diseases.

As part of the European consortium, (Modulightor), two compounds targeting glycine receptors in a light dependent manner have been developed. Glycine receptors (GlyRs) are inhibitory receptors broadly distributed in the central nervous system of vertebrates and play a key role in regulating (inhibiting) the transmission of the signals through neurons. They are involved in disorders such as hyperekplexia (excessive startle response), inflammatory pain sensitization, autism, temporal lobe epilepsy, breathing disorders, alcoholism, and motor neuron disease. These new molecules pave the way to the development of photoswitchable drugs that can specifically modulate receptors in every disease, reducing side effects and increasing the effectiveness of the treatment.

Another recent study led by researchers from the nanoprobes and nanoswitches group in collaboration with IDIBAPS achieves, for the first time, the control of brain state transitions using a molecule responsive to light, named PAI. The results pave the way to act on the brain patterns activity, and also lead to the development of photomodulated drugs for the treatment of brain lesions or diseases such as depression, bipolar disorders or Parkinson's or Alzheimer's diseases.



The muscarinic agonist PAI (structures below below) can be reversibly switched with light (left: inactive isomer under violet light; right: active isomer under blue or while light) and allows controlling the frequency of emerging brain waves in vitro and in vivo (representative time course of electrophysiological oscillations shown above each isomer). From Barbero-Castillo, A., Riefolo, F., et al. (2021). Control of Brain State Transitions with a Photoswitchable Muscarinic Agonist. Advanced Science 8:e2005027.

Funded projects related to healthy ageing

DEEPER · DEEP BRAIN PHOTONIC TOOLS FOR CELL-TYPE SPECIFIC TARGETING OF NEURAL DISEASES (2021-2025)	EUROPEAN COMMISSION, ICT
HUMAN BRAIN PROJECT SPECIFIC GRANT AGREEMENT 3 (2020-2023)	EUROPEAN COMMISSION, FET FLAGSHIPS
DEEP RED · NEUROMODULACIÓN DE LAS VÍAS INHIBITORIAS MEDIANTE FOTOFARMACOLOGÍA ACTIVADA POR LUZ ROJA E INFRARROJA (2020-2023)	MINECO, RETOS INVESTIGACIÓN: PROYECTOS I+D
DECA CECH · CLUSTER EMERGENTE DEL CEREBRO HUMANO (2019-2021)	RIS3CAT – TECNOLOGIES EMERGENTS

Main recent publications related to healthy ageing

Riefolo, F., Sortino, R., Matera, C., Claro, E., Preda, B., Vitiello, S., Traserra, S., Jiménez, M., & Gorostiza, P. (2021). Rational Design of Photochromic Analogues of Tricyclic Drugs. Journal of medicinal chemistry, 64(13), 9259–9270. https://doi.org/10.1021/acs.jmedchem.1c00504

Barbero-Castillo, A., Riefolo, F., Matera, C., Caldas-Martínez, S., Mateos-Aparicio, P., Weinert, J. F., Garrido-Charles, A., Claro, E., Sanchez-Vives, M. V., & Gorostiza, P. (2021). Control of Brain State Transitions with a Photoswitchable Muscarinic Agonist. Advanced science (Weinheim, Baden-Wurttemberg, Germany), 8(14), e2005027. https://doi.org/10.1002/advs.202005027

Prischich, D., Gomila, A., Milla-Navarro, S., Sangüesa, G., Diez-Alarcia, R., Preda, B., Matera, C., Batlle, M., Ramírez, L., Giralt, E., Hernando, J., Guasch, E., Meana, J. J., de la Villa, P., & Gorostiza, P. (2021). Adrenergic Modulation With Photochromic Ligands. Angewandte Chemie (International ed. in English), 60(7), 3625–3631. https://doi.org/10.1002/anie.202010553

Gomila, A., Rustler, K., Maleeva, G., Nin-Hill, A., Wutz, D., Bautista-Barrufet, A., Rovira, X., Bosch, M., Mukhametova, E., Petukhova, E., Ponomareva, D., Mukhamedyarov, M., Peiretti, F., Alfonso-Prieto, M., Rovira, C., König, B., Bregestovski, P., & Gorostiza, P. (2020). Photocontrol of Endogenous Glycine Receptors In Vivo. Cell chemical biology, 27(11), 1425–1433.e7. https://doi.org/10.1016/j.chembiol.2020.08.005

Biomedical signal processing and interpretation

Raimon Jané

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.

"The design and development of tools, apps and devices for healthcare has produced important advances to design new systems for diagnosing and monitoring to improve health and wellbeing."

Recent activities related to healthy ageing

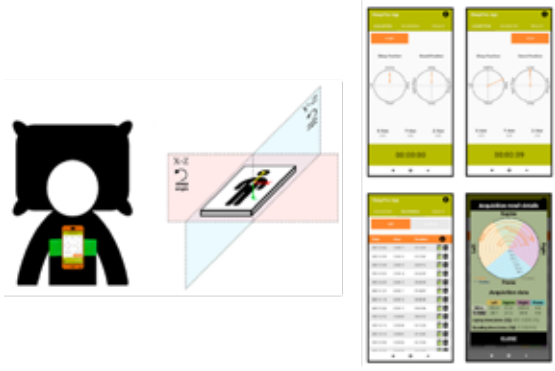
We are contributing to the smart health ecosystem, designing tools, apps and devices for personalized medicine and healthcare, with a common methodology, based on estimation, tracking and interpretation of non-invasive physiological biomarkers. We propose a combined use of multimodal sensors, health patches, wireless devices and smartphones, with novel computational and advanced data processing, that permits a significant advance in health diagnostic and monitoring for personalised medicine and healthcare.

We also working on identifying and validating novel physiological biomarkers estimated from multimodal biosignals that will be acquired using the smart health tools, apps and devices designed and developed in the SappHiRES project.

Together with international partners at IMEC in the Netherlands and a Hospital in Belgium, we have developed an innovative procedure to evaluate pulmonary diseases. The novel methodology, non–invasive and quantifiable, was applied to COPD patients and is based on the combination of bioimpedance and myographic signals to measure the contribution of inspiratory muscle activity into pulmonary ventilation.

We have also developed a portable, cheap and non-invasive system to detect obstructive sleep apnea (OSA) at home in order to improve the diagnosis of this diseases that remain undiagnosed and untreated on most patients due to the complexity and intrusiveness of the previous diagnosis technique. We designed a novel mHealth tool for screening and monitoring of sleep disorders, based on a smartphone using the built-in sensors. This research has been conducted with the Hospital Clínic, Barcelona.

Moreover, we are working in the characterization of muscle activity and movement patterns to contribute to assessing patients' condition and guiding neurorehabilitation interventions. We develop, with the Institut Guttmann, a new technique by measuring thoracic function during a reaching task performed by healthy human subjects sitting in a chair.



A smartphone system developed for screening of sleep disorders in healthy people, including an app for high resolution sleep position monitoring and acoustic analysis of respiratory activity.

Funded projects related to healthy ageing

SAPPHIRES · ECOSISTEMA DE SALUD INTELIGENTE PARA LA MEDICINA PERSONALIZADA Y LA ASISTENCIA SANITARIA EN ENFERMEDADES RESPIRATORIAS Y TRASTORNOS DEL SUEÑO (2019 – 2021)	MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
DEEPDREAM · A DATA-DRIVEN COMPUTATIONAL METHOD FOR PERSONALIZED HEALTHCARE IN CHRONIC RESPIRATORY DISEASES THROUGH BIG-DATA ANALYTICS AND DYNAMICAL MODELLING (2020-2022)	EUROPEAN COMISSION · MARIE CURIE

Main recent publications related to healthy ageing

Blanco-Almazan, D., Groenendaal, W., Lozano-Garcia, M., Estrada-Petrocelli, L., Lijnen, L., Smeets, C., Ruttens, D., Catthoor, F., & Jane, R. (2021). Combining Bioimpedance and Myographic Signals for the Assessment of COPD During Loaded Breathing. IEEE transactions on bio-medical engineering, 68(1), 298–307. https://doi.org/10.1109/TBME.2020.2998009

Castillo-Escario, Y., Kumru, H., Valls-Solé, J., García-Alen, L., Vidal, J., Jané, R. (2021). Assessment of trunk flexion in arm reaching tasks with electromyography and smartphone accelerometry in healthy human subjects. Scientific Reports, 11 (1), 5363.

Estrada-Petrocelli, L., Torres, A., Sarlabous, L., Rafols-de-Urquia, M., Ye-Lin, Y., Prats-Boluda, G., Jané, R., Garcia-Casado, J. (2021). Evaluation of respiratory muscle activity by means of concentric ring electrodes. IEEE Transactions on Biomedical Engineering, 68(3), 1005–1014.

Lozano-García, M., Estrada-Petrocelli, L., Torres, A., Rafferty, G.F., Moxham, J., Jolley, C.J., Jané, R. (2021). Noninvasive assessment of neuromechanical coupling and mechanical efficiency of parasternal intercostal muscle during inspiratory threshold loading. Sensors, 21(5), 1781.

D. Romero and R. Jané, "Global and Transient Effects of Intermittent Hypoxia on Heart Rate Variability Markers: Evaluation Using an Obstructive Sleep Apnea Model," in IEEE Access, vol. 9, pp. 19043-19052, 2021, doi: 10.1109/ACCESS.2021.3053310.

Ferrer-Lluis, I.; Castillo-Escario, Y.; Montserrat, J.M.; Jané, R. Ferrer-Lluis I., et al. SleepPos app: an automated smartphone application for angle based high resolution sleep position monitoring and treatment. Sensors, 21(13): 4531, 2021.

Ferrer-Lluis I., Castillo-Escario Y., Montserrat J. M. and Jané R. (2021). Enhanced monitoring of sleep position in sleep apnea patients: smartphone triaxial accelerometry compared with video-validated position from polysomnography. Sensors, 21(11): 3689

Ferrer-Lluís, I., Castillo-Escario, Y., Montserrat, J. M., Jané, R., (2020). Analysis of smartphone triaxial accelerometry for monitoring sleep disordered breathing and sleep position at home. IEEE Access, 8, 71231–71244.

Fletcher, H.V., Cho, P.S.P., Loong, S.L., Estrada-Petrocelli, L., Patel, A.S., Birring, S.S., Lee, K.K. (2020). Effect of continuous positive airway pressure on maximal exercise capacity in patients with obstructive sleep apnea: A systematic review and meta-analysis. Journal of Clinical Sleep Medicine 16(11), 1847–1855.

Calvo, M., González, R., Seijas, N., Vela, E., Hernández, C., Batiste, G., Miralles, F., Roca, J., Cano, I., Jané, R. (2020). Health outcomes from home hospitalization: Multisource predictive modelling. Journal of Medical Internet Research, 22(10), e21367.

Castillo-Escario, Y., Rodríguez-Cañón, M., García-Alías, G., Jané, R., (2020). Identifying muscle synergies from reaching and grasping movements in rats. IEEE Access, 8, 62517–62530.

Hall, J.I., Lozano, M., Estrada-Petrocelli, L., Birring, S., Turner, R. (2020). The present and future of cough counting tools. Journal of Thoracic Disease, 12(9), 5207–5223.

Romero, D., Lázaro, J., Jané, R., Laguna, P., Bailón, R., (2020). A quaternion-based approach to estimate respiratory rate from the vectorcardiogram Computers in Cardiology (CinC) 2020 Computing in Cardiology , IEEE (Rimini, Italy) 47, 1-4

Valls-Margarit, M., Iglesias-García, O., Di Guglielmo, C., Sarlabous, L., Tadevosyan, K., Paoli, R., Comelles, J., Blanco-Almazán, D., Jiménez-Delgado, S., Castillo-Fernández, O., Samitier, J., Jané, R., Martínez, Elena, Raya, Á. (2019). Engineered macroscale cardiac constructs elicit human myocardial tissue-like functionality. Stem Cell Reports, 13(1), 207–220.

Rafols-de-Urquia, M., Estrada, L., Estevez-Piorno, J., Sarlabous, L., Jane, R., Torres, A. (2019). Evaluation of a wearable device to determine cardiorespiratory parameters from surface diaphragm electromyography. IEEE Journal of Biomedical and Health Informatics, 23(5), 1964–1971.

Calvo, M., Le Rolle, V., Romero, D., Béhar, N., Gomis, P., Mabo, P., Hernández, A. I., (2019). Recursive model identification for the analysis of the autonomic response to exercise testing in Brugada syndrome. Artificial Intelligence in Medicine, 97, 98–104.

Blanco-Almazán, D., Groenendaal, W., Catthoor, F., Jané, R. (2019). Chest movement and respiratory volume both contribute to thoracic bioimpedance during loaded breathing. Scientific Reports, 9(1), 20232.

Castillo-Escario, Y., Ferrer-Lluis, I., Montserrat, J. M., Jané, R. (2019). Entropy analysis of acoustic signals recorded with a smartphone for detecting apneas and hypopneas: A comparison with a commercial system for home sleep apnea diagnosis. IEEE Access, 7, 128224–128241.

Lozano-García, M., Estrada-Petrocelli, L., Moxham, J., Rafferty, G. F., Torres, A., Jolley, C. J., Jané, R. (2019). Noninvasive assessment of inspiratory muscle neuromechanical coupling during inspiratory threshold loading. IEEE Access, 7, 183634–183646.

Blanco-Almazan, D., Groenendaal, W., Catthoor, F., Jane, R., (2019). Wearable bioimpedance measurement for respiratory monitoring during inspiratory loading. IEEE Access, 7, 89487–89496.

Rodríguez, J., Schulz, S., Giraldo, B. F., Voss, A. (2019). Risk stratification in idiopathic dilated cardiomyopathy patients using cardiovascular coupling analysis. Frontiers in Physiology, 10, 841.

Sarlabous, L., Estrada, L., Cerezo-Hernández, A., Leest, Sietske V. D., Torres, A., Jané, R., Duiverman, M., Garde, Ainara, (2019). Electromyography-based respiratory onset detection in COPD patients on non-invasive mechanical ventilation. Entropy, 21(3), 258.

Lozano-García, M., Estrada, L., Jané, R., (2019). Performance evaluation of fixed sample entropy in myographic signals for inspiratory muscle activity estimation. Entropy, 21(2), 183.

Lozano-García, Manuel, Sarlabous, Leonardo, Moxham, John, Rafferty, Gerrard F., Torres, Abel, Jané, Raimon, Jolley, Caroline J., (2018). Surface mechanomyography and electromyography provide non-invasive indices of inspiratory muscle force and activation in healthy subjects. Scientific Reports 8, (1), 16921.

Estrada, L., Torres, A., Sarlabous, L., Jané, R., (2018). Onset and offset estimation of the neural inspiratory time in surface diaphragm electromyography: A pilot study in healthy subjects IEEE Journal of Biomedical and Health Informatics 22, (1), 67-76

Molecular Imaging for Precision Medicine

Irene Marco

Our research line is to detect, identify and validate biomarkers of disease. We focus on developing molecular imaging tools to study cell metabolism in human disease and predict treatment efficacy. Particularly, we use Bioengineering solutions using Chemistry and Physics tools to study Biological problems. Specifically, we develop Magnetic Resonance (MR) imaging to study the metabolic pathways in bioengineered systems and in vivo.

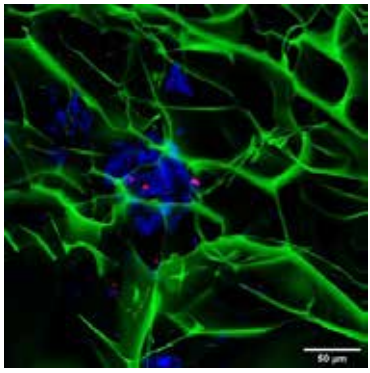
MR is chemically specific and can directly relate response of a single (or many) chemical compound to biological events in biofluids, cell models in vitro, excised tissue and perfused organs ex vivo, animal models in vivo and patients. The rich variety of MR experiments developed over the past decades allows precise quantification of metabolites, diffusion, perfusion, and tissue oxygenation. These parameters constitute a fingerprint of the sample, which encodes physiological and pathological factors that can be used to monitor and study disease in real time.

"We work at the forefront of molecular imaging with a technique that increases MR signal over 10.000 times. We can see molecular processes in real time and non-invasively in a wide range of biological models."

Recent activities related to healthy ageing

We are working on the development of a platform to monitor the progression of non-alcoholic fatty liver disease (NAFLD) - a highly prevalent disease in the aging population - in vitro. We are developing organ-on-a-chip (OOC) systems with validated in vivo-like metabolism. The objective is to better understand disease evolution within subjects and transition between disease stages while providing a platform for personalised screening on OOC.

The key goal is to probe the pathways of gluconeogenesis, glycolysis and lipid synthesis non-invasively by injecting DNP-MR substrates into a bioengineered liver OOC. The long-term aim is to apply the same approach to cells from human liver biopsy or excised tissue as a step towards personalised medicine.



Hepatic spheroid inside a Cellulose scaffold. Scaffold fibres in green, hepatocyte nuclei in blue, apoptotic cells in red

Funded projects related to healthy ageing

ANALISIS METABOLICO EN TIEMPO REAL DE MODELOS DE CULTIVO DE CELULAS 3D DE LA ENFERMEDAD DEL HIGADO GRASO NO ALCOHOLICO: ORGANOS EN UN CHIP Y RESONANCIA MAGNETICA NUCLEAR	ACCIONES DINAMIZACIÓN EUROPA INVESTIGACIÓN/ EIN2020-112209
"BLOC: BENCHTOP NMR FOR LAB-ON-CHIP."	EUROPEAN COMMISSION FET OPEN. GA-863037
"OOC-MR: REAL-TIME, IN SITU MONITORING OF DISEASE METABOLISM IN ORGAN-ON-CHIP SYSTEMS WITH MAGNETIC RESONANCE".	FUNDACIÓN LA CAIXA. LCF/ BQ/PI18/11630020
"NARMYD: NMR-BASED ASSAYS TO REVEAL MYOTONIC DYSTROPHY 1 BIOMARKERS".	MINISTERIO DE CIENCIA E INOVACIÓN

Targeted therapeutics and nanodevices

Silvia Muro

Our research sits at the interface between molecular-cellular biology and nanotechnology-drug delivery. We study the biological mechanisms by which cells transport cargoes to precise destinations within our bodies, and apply this knowledge to design nanodevices for improved delivery of therapeutic agents to specific disease sites.

Focusing on endothelial cell adhesion molecules as accessible targets and on genetic conditions that serve as models for metabolic, neurodegenerative and cardiovascular syndromes, our ultimate goal is to enable effective treatment for these life-threatening disorders, as well as other maladies characterized by similar pathological traits. Our main programmatic efforts during the last year focused on drug delivery across the blood-brain barrier, a major bottleneck for current development of treatment strategies against neurodegenerative diseases that affect both rare diseased and common maladies associated with aging. Some of these efforts are described below.

"We are studying which parameters & biological routes are more relevant for BBB transport in order to guide the design of nanodevices for brain delivery of drugs or diagnostics for neurological ailments, e.g. Alzheimers, Parkinsons."

Recent activities related to healthy ageing

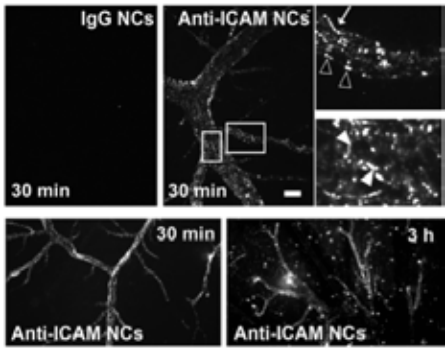
Accessing the brain is key to study brain pathologies relative to aging and other neurodegenerative maladies, and for designing efficient therapeutics. However, this is hindered by the blood-brain barrier (BBB), a natural filter that stop brain access for most drugs. To overcome this obstacle, novel drug nanocarriers are being designed to target the routes that body substances use to cross this interface, without much translational success. Scarce knowledge about how these diseases impact natural BBB routes, lack of systematic analyses on the design parameters ruling nanocarrier transport across the BBB, and limited tools suitable for translation, are at fault. We are investigating all these aspects.

1-Using natural ligands and polymeric nanocarriers targeted to key blood-to-brain transport routes, we are investigating how rare and common neurodegenerative pathologies affect these pathways and brain access. We have identified alterations in the nano-scale distribution and mobility of receptors and/or their interaction with endocytic machinery, leading to altered interactions and transport of therapeutic nanocarriers depending on the particular route they target.

2-We are studying how design parameters of polymeric nanocarriers targeted to key routes across the endothelium influence brain delivery of therapeutics. We have found that intertwined biological processes made it difficult to predict the impact of these parameters, yet have identified key players such as the optimal nanocarrier targeting valency depending on the route that regulate their transport.

3-We are developing new antibodies as targeting tools to direct drugs and their carriers to specific organs and subcellular compartments, including neurons in the brain. These new tools will be suitable for research stage in diverse cellular models, testing in multiple animal species during pre-clinical development, and finally readily translatable to the clinics for human application.

intermediate valency delivered higher amounts of a therapeutic protein for enzyme replacement therapy of acid sphingomyelinase deficiency, holding considerable translational potential.



Brain transport of ICAM-1 targeting nanocarriers in mice. Fluorescence microscopy of cortical blood vessels in brain specimens from mice 30 minutes or 3 hour after intravenous injection with fluorescently-labeled nanocarriers targeted to ICAM-1 (anti-ICAM NCs) compared to control untargeted formulations (IgG NCs). Scale bar = 10 µm. Reproduced from Manthe et al., J. Controlled Rel. (2021) 324, 181-193.

Funded projects related to healthy ageing

CROSSTARGET · DESARROLLO DE NUEVAS HERRAMIENTAS TRASLACIONALES MULTI-ESPECIE PARA EL DIRECCIONAMIENTO DE TERAPIAS CON PRECISIÓN DE ÓRGANO Y SUBCELULAR	MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
BBB2GATE · CONTROL DIFERENCIAL DEL TRANSPORTE DE VEHICULOS TERAPEUTICOS DENTRO VERSUS A TRAVES DE LA BARRERA HEMATOENCEFALICA	MINECO
NANO-GBA · ASSESSING HOW GLUCOCEREBROSIDASE DEFECTS ALTER RECEPTOR MEMBRANE NANOARCHITECTURE TO DESIGN IMPROVED NANOMEDICINES.	BIST

Main recent publications related to healthy ageing

Muro S. (2021). Drug Delivery Systems: A Few Examples of Applications, Drug Cargoes, and Administration Routes. Current pharmaceutical design, 27(17), 1975–1976. https://doi.org/10.2174/1381612827172105241617 45

Qamar, B., Solomon, M., Marin, A., Fuerst, T. R., Andrianov, A. K., Muro, S., (2021). Intracellular delivery of active proteins by polyphosphazene polymers. Pharmaceutics, 13(2), 249.

Roki, N., Solomon, M., Casta, L., Bowers, J., Getts, R. C., Muro, S., (2021). A method to improve quantitative radiotracing-based analysis of the in vivo biodistribution of drug carriers. Bioengineering and Translational Medicine Early View, e210208

Manthe, R.L., Loeck, M., Bhowmick, T., Solomon, M., Muro, S. (2020). Intertwined mechanisms define transport of anti-ICAM nanocarriers across the endothelium and brain delivery of a therapeutic enzyme. Journal of Controlled Release, 324, 181-193

Roki N, Tsinas Z, Salomon M, Bowers J, Getts R, Muro S. (2019) Unprecedently high targeting specific to lung ICAM-1 using 3DNA nanocarriers. J Control Release. 305:41-49.

Manthe R, Rappaport J, Solomon M, Gugutkov D, Hildreth M, Velovolu V, Long Y, Marugan J, Zheng W, Muro S. (2019) ?-Tocopherol Effect on Endocytosis and its Combination with Enzyme Replacement Therapy for Lysosomal Disorders: a New Type of Drug Interaction? J Pharm Exp Ther. 379(3):823-833.

Muro S. (2018) Alterations in cellular processes involving vesicular trafficking and implications in drug delivery. Biomimetics. 3(3), 19; https://doi.org/10.3390/biomimetics3030019

Biosensors for bioengineering

Javier Ramón

Our research is focused on multi tissues organs-on-a-chip (OOC) and more specifically in the metabolic crosstalk within tissues and their relationship with metabolic diseases. Our projects are focused on four key tissues regulating glucose homeostasis, namely, the pancreas, liver, skeletal muscle, and adipose tissue.

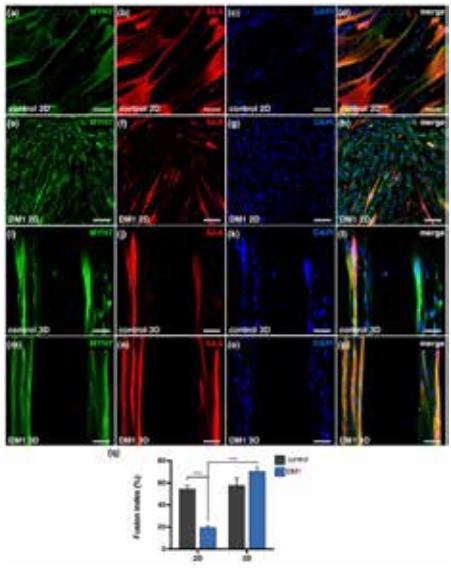
"Integrating biosensors in an organ-on-a-chip, we are studying with in situ electrochemical biosensors the release of insulin under the effect of external stimuli, changes in glucose levels and myokines secreted by skeletal muscle (multi-OOC approach)."

Recent activities related to healthy ageing

One of the goals of the group is the fabrication of a biomimetic multi organ-on-a-chip integrated device composed of skeletal muscle and pancreatic islets for studying metabolism glucose diseases and for drug screening applications. Engineered muscle tissues and pancreatic islets are integrated with the technology to detect the glucose consumption, contraction induced glucose metabolism, insulin secretion and protein biomarker secretion of cells. We aim to design a novel therapeutic tool to test drugs with a multi organ-on-a-chip device. Such finding would improve drug test approaches and would provide for new therapies to prevent the loss of beta cell mass associated with T2D and defects in the glucose uptake in skeletal muscle.

To fully exploit the potential of the organs-on-a-chip, there is a need to interface them to integrated sensing modules, capable to monitor in real-time their biochemical response to external stimuli, like stress or drugs. Our goal is to answer this need, by developing a novel technology based on integrating localized surface plasmon resonance (LSPR) sensing module to organs-on-a-chip devices to monitor disease and evaluate drug response in organs-on-a-chip models.

Biosensors for Bioenginering is also developing skeletal muscle models to study different muscular dystrophies, such as myotonic dystrophy type 1 (see figure 1). The group is also funded by Duchenne Parent Project Spain asociation (https://www.duchenne-spain.org/) to develop a 3D model to study Duchenne muscle degenerative disease.



*Cell differentiation is improved in 3D cultures. (a-p) Representative confocal images of 2D (a-h) and 3D (i-p) cultures stained for myosin heavy chain 7 (MYH7, green), sarcomeric ⍰-actinin (SAA, red), and nuclei (DAPI, blue) after 7 days in differentiation conditions (scale bars: 50 μm). (q) Graph showing comparison of fusion index expressed as the percentage of differentiated myotubes with respect to the total cell number. ****p<0.0001.*

Funded projects related to healthy ageing

DAMOC · 'DIABETES APPROACH BY MULTI-ORGAN-ON-A-CHIP' (2017-2021)	ERC
TATAMI THERAPEUTIC TARGETING OF MBNL MICRORNAS AS INNOVATIVE TREATMENTS FOR MYOTONIC DYSTROPHY (HR17-00268)	LA CAIXA FOUNDATION (CAIXA HEALTH PROGRAMME 2017)

Main recent publications related to healthy ageing

Fernández-Garibay, X., Ortega, M.A., Cerro-Herreros, E., Comelles, J., Martínez, E., Artero, R., Fernández-Costa, J.M. & Ramón-Azcón, J. (2021) Bioengineered in vitro 3D model of myotonic dystrophy type 1 human skeletal muscle, Biofabrication, 13(3), 035035. http://iopscience.iop.org/article/10.1088/1758-5090/abf6ae

De Chiara, F., Ferret-Miñana, A., & Ramón-Azcón, J. (2021). The Synergy between Organ-on-a-Chip and Artificial Intelligence for the Study of NAFLD: From Basic Science to Clinical Research. Biomedicines, 9(3), 248.

Velasco-Mallorquí, F., Rodríguez-Comas, J., & Ramón-Azcón, J. (2021). Cellulose-based scaffolds enhance pseudoislets formation and functionality. Biofabrication, 13(3), https://doi.org/10.1088/1758-5090/ac00c3

Ortega, M. A., Rodríguez-Comas, J., Yavas, O., Velasco-Mallorquí, F., Balaguer-Trias, J., Parra, V., Novials, A., Servitja, J. M., Quidant, R., & Ramón-Azcón, J. (2021). In Situ LSPR Sensing of Secreted Insulin in Organ-on-Chip. Biosensors, 11(5), 138. https://doi.org/10.3390/bios11050138

Nanobioengineering

Josep Samitier

The Nanobioengineering group is a multidisciplinary team composed by researchers coming from very diverse backgrounds working together in applying nanotechnology for the development of new biomedical systems and devices, mainly for diagnostic purposes, and integrated microfluidic Organ-on-Chip devices for the study of organ physiology, disease etiology, or drug screening for main clinical problems, including cancer and rare diseases.

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

The goal is to fabricate microsystems containing living cells that recapitulate tissue and organ level functions in vitro and new portable diagnosis devices that can be used as Point-of-Care systems.

"3D in vitro models to resemble the physiological conditions of the brain. We try to assess the compatibility of neural progenitor cell culture in GelMA and AlgMA composites with hyaluronic acid."

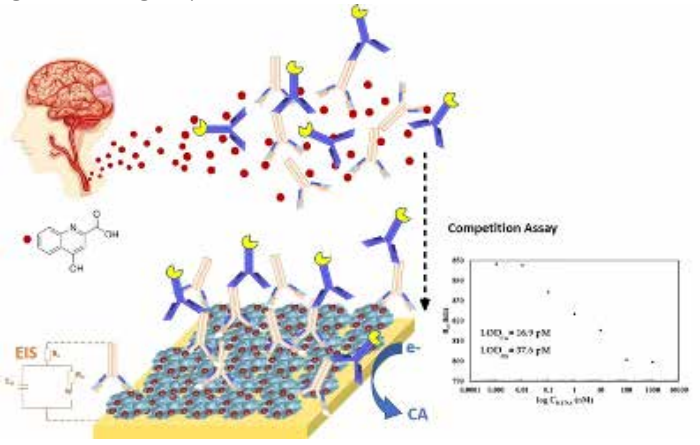
Recent activities related to healthy ageing

The group has been recently working on the development of a micro-implantable sensor for ischemia or hypoxia monitoring in tissue and blood based on acidosis detection. The most common causes of hypoxia are acute arterial thrombus formation due to cardiovascular diseases, atherosclerotic disease, arterial or by other specific prothrombotic situations such as a trauma that causes compartmental syndrome or incorrect micro-reconnection of vascular vessels in post-surgery of tissue anastomosis. All the described medical situations are common in hospitals at high prevalence. Early diagnosis will be of great importance to avoid further problems for the patient and reduce health system costs.

We have also worked in collaboration with the Bacterial infections: antimicrobial therapies group, on the development of a microfluidic platform with an integrated interdigitated sensor (BiofilmChip). This device allows an irreversible and homogeneous attachment of bacterial cells of clinical origin, even directly from clinical specimens. It has proved to be suitable to study polymicrobial communities, as well as to measure the effect of antimicrobials on biofilms without introducing disturbances due to manipulation, thus better mimicking real-life clinical situations.

The group has developed as well, a robust, reliable, and non-invasive detection platform based on an electrochemical immunosensor for the analysis of KYNA concentrations in blood, to move towards an automated platform for the non-invasive early diagnosis of AD that contains different bioreceptors for the detection of blood biomarkers in an array format.

In the field of regeneration therapies, we have participated in the cardiac tissue regeneration project leaded by the Biomaterials for regenerative therapies group an we have leaded a project on chondreogenesis, studying the best conditions for the initial stages of cartilage repair.



The alteration of the KYNA levels in blood has been related with inflammatory processes in the brain, produced as a protective function when neurons are damaged. We have developed a novel electrochemical immunosensor for KYNA detection, based on successive functionalization multi-electrode array

Funded projects related to healthy ageing

ISCHEMSURG · MINIATURIZED ELECTROCHEMICAL SENSOR FOR MONITORING OF FREE FLAP ISCHEMIA IN POST-SURGERY (2019-2021)	AGAUR
ASCTN-TRAINING, GRANT NUMBER 813851 (2019-2022)	EUROPEAN COMMISSION MARIE SKŁODOWSKA-CURIE PROGRAM
RTI2018-097038-B-C21 MICROPHYSIOLOGICAL SYSTEM TO MIMIC THE BLOOD-CENTRAL NERVOUS SYSTEM BARRIERS (2019-2021)	MINISTERIO CIENCIA E INNOVACIÓN

Main recent publications related to healthy ageing

Marrugo-Ramírez, J., Rodríguez-Núñez, M., Marco, M. P., Mir, M., & Samitier, J. (2021). Kynurenic Acid Electrochemical Immunosensor: Blood-Based Diagnosis of Alzheimer's Disease. Biosensors, 11(1), 20. https://doi.org/10.3390/bios11010020

Blanco-Cabra, N., López-Martínez, M. J., Arévalo-Jaimes, B. V., Martin-Gómez, M. T., Samitier, J., & Torrents, E. (2021). A new BiofilmChip device for testing biofilm formation and antibiotic susceptibility. NPJ biofilms and microbiomes, 7(1), 62. https://doi.org/10.1038/s41522-021-00236-1

López-Canosa, A., Perez-Amodio, S., Yanac-Huertas, E., Ordoño, J., Rodriguez-Trujillo, R., Samitier, J., Castaño, O., & Engel, E. (2021). A microphysiological system combining electrospun fibers and electrical stimulation for the maturation of highly anisotropic cardiac tissue. Biofabrication, 13(3), 10.1088/1758-5090/abff12. https://doi.org/10.1088/1758-5090/abff12

Dulay, S., Rivas, L., Miserere, S., Pla, L., Berdún, S., Parra, J., Eixarch, E., Gratacós, E., Illa, M., Mir, M., & Samitier, J. (2021). in vivo Monitoring with micro-implantable hypoxia sensor based on tissue acidosis. Talanta, 226, 122045. https://doi.org/10.1016/j.talanta.2020.122045

Pla, L., Berdún, S., Mir, M., Rivas, L., Miserere, S., Dulay, S., Samitier, J., Eixarch, E., Illa, M., & Gratacós, E. (2021). Non-invasive monitoring of pH and oxygen using miniaturized electrochemical sensors in an animal model of acute hypoxia. Journal of translational medicine, 19(1), 53. https://doi.org/10.1186/s12967-021-02715-7

Casanellas, I., Lagunas, A., Vida, Y., Pérez-Inestrosa, E., Andrades, J. A., Becerra, J., & Samitier, J. (2020). The Janus Role of Adhesion in Chondrogenesis. International journal of molecular sciences, 21(15), 5269. https://doi.org/10.3390/ijms21155269

Rodríguez-Pereira, C., Lagunas, A., Casanellas, I., Vida, Y., Pérez-Inestrosa, E., Andrades, J. A., Becerra, J., Samitier, J., Blanco, F. J., & Magalhães, J. (2020). RGD-Dendrimer-Poly(L-lactic) Acid Nanopatterned Substrates for the Early Chondrogenesis of Human Mesenchymal Stromal Cells Derived from Osteoarthritic and Healthy Donors. Materials (Basel, Switzerland), 13(10), 2247. https://doi.org/10.3390/ma13102247

Rivas, L., Dulay, S., Miserere, S., Pla, L., Marin, S. B., Parra, J., Eixarch, E., Gratacós, E., Illa, M., Mir, M., & Samitier, J. (2020). Micro-needle implantable electrochemical oxygen sensor: ex-vivo and in-vivo studies. Biosensors & bioelectronics, 153, 112028. https://doi.org/10.1016/j.bios.2020.112028

Valls-Margarit, M., Iglesias-García, O., Di Guglielmo, C., Sarlabous, L., Tadevosyan, K., Paoli, R., Comelles, J., Blanco-Almazán, D., Jiménez-Delgado, S., Castillo-Fernández, O., Samitier, J., Jané, R., Martínez, E., & Raya, Á. (2019). Engineered Macroscale Cardiac Constructs Elicit Human Myocardial Tissue-like Functionality. Stem cell reports, 13(1), 207–220. https://doi.org/10.1016/j.stemcr.2019.05.024

Smart nano-bio-devices

Samuel Sánchez

The smart nano-bio-devices group develops different systems ranging from active nanoparticles (nanobots), 3D Bioprinted Actuators and flexible biosensors. We are interested in fundamental studies of active matter, the use of nanobots for future nanomedicine and environmental applications and the bioengineering of new devices based on hybrid systems. In the research line of soft bio-hybrid robotics, the group explores the integration of biological tissue and artificial materials at larger length scales. In particular, we take advantage of the 3D bioprinting technique to develop bio-robotic systems composed of skeletal muscle cells embedded in biocompatible hydrogels, which can be 3D bioprinted alongside other artificial materials. These materials can act as scaffolds, support, or flexible parts, as well as be responsive upon certain stimuli. By controlling the contractions of skeletal muscle cells via electric fields, we can measure the forces exerted by these bio-actuators against artificial 3D-printed posts.

"We have engineered 3D platforms that can elegantly recapitulate the properties of aged skeletal muscle tissues and used it for testing of commercial anti-aging active principles."

Recent activities related to healthy ageing

We have developed a 3D-printed platform of bioengineered human skeletal muscle which can efficiently model the three-dimensional structure of native tissue, while providing information about force generation and contraction profiles.

By the addition of TNF-⍰ to the skeletal muscle cells we have mimicked some phenotypical aspects of aged muscle, and we have shown its effects both in morphology (by immunostaining) and functionality (by contraction profiles), characterized by a reduction in fiber diameter and loss of nuclei, as well as loss of maximum and baseline forces.

This 3D-bioengineered human muscle platform could be used to assess morphological and functional changes in the aging process of muscular tissue with potential applications

Schematic of the fabrication method of three-dimensional human skeletal muscle constructs, based on casting on 3D-printed molds and subsequent transfer into 3D-printed PDMS posts, which is then stimulated with a home-made setup of carbon-based electrodes.

Main recent publications related to healthy ageing

Mestre, R., García, N., Patiño, T., Guix, M., Fuentes, J., Valerio-Santiago, M., Almiñana, N., & Sánchez, S. (2021). 3D-bioengineered model of human skeletal muscle tissue with phenotypic features of aging for drug testing purposes. Biofabrication, 13(4), 10.1088/1758-5090/ac165b. https://doi.org/10.1088/1758-5090/ac165b

Bacterial infections: antimicrobial therapies

Eduard Torrents

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. Special interest is in older people who are more vulnerable to infectious diseases because their immune system becomes weaker with age.

There is an urgent need for reliable and rapid detection of infecting bacteria and its pattern of resistance to antibiotics.

Our lab aims to investigate new antimicrobial therapies and strategies to combat bacterial (chronic) infections with these objectives: to establish the molecular basis for the gene regulation in virulence and biofilm formation; to identify and screen new antibacterial; to develop new drug delivery systems; to develop new methodologies to treat chronic bacterial infections; to study a new type of antibacterial vaccines; to develop new strategies for bacterial co-culture system and to use lab-on-a-chip technology for bacteria identification.

"We have investigated and developed novel therapies to treat chronic and nosocomial infections as well as new drug delivery systems and antimicrobials to treat bacterial multiresistant strains. "

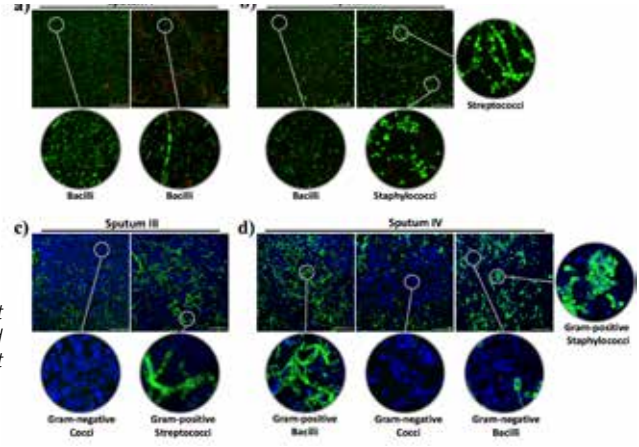
Recent activities related to healthy ageing

Over 60% of all human infections treated by physicians are characterized by the formation of a biofilm, which is involved in a wide variety of pathological conditions. In the case of human biofilm infections, these are typically associated with major chronic diseases, which is important in older adults. The control and treatment of biofilms remain an urgent unmet medical need, and it is occurring at the same time when there is a dearth of new and effective antibiotics available on the market or in late-stage development. These infections are not readily amenable to be treated with the current antimicrobial therapies or by using single "magic bullet" approaches.

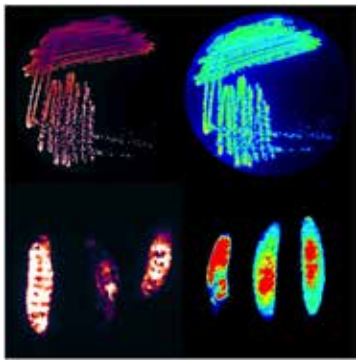
Our group is focused on identifying new antimicrobials and therapies specifically indicated to treat this chronic lung infection or with the capacity to remove pre-existing biofilms. We concentrate on this problem by applying basic research and more applied investigations to bring new technologies identified in our laboratory close to the market.

Firstly, we investigate the molecular basis for bacteria to establish a chronic infection or a polymicrobial biofilm and how crucial oxygen availability and bacterial strain type are. At the same time, we are setting in vitro conditions to develop polymicrobial biofilms to resemble the real situations found in chronically infected patients and valuable for investigating new antibiofilm molecules. Furthermore, we are exploring new antibiofilm and antibacterial molecules to inhibit bacterial and biofilm proliferation and study their potential bacterial or biofilm targets.

In our laboratory, we are bringing the nanotechnology close to the patients by developing new drug delivery systems based on nanoparticles with real capabilities to be used in patients with the availability to degrade pre-existing biofilms and kill bacteria. Finally, we are optimizing different invertebrate animal models of infection and developing a new type of bacterial vaccine to be used primarily to treat infected patients.



Biofilms formed from four different sputum samples (I–IV) with enlarged images showing the different bacterial shapes found.



Variable gene expression levels of Galleria mellonella infected with Pseudomonas aeruginosa were successfully measured in the larvae at different time points.

Funded projects related to healthy ageing

COMBATRNR · COMPRENDER LA SÍNTESIS DEL ADN EN PATÓGENOS BACTERIANOS: NUEVAS ESTRATEGIAS PARA EL TRATAMIENTO DE ENFERMEDADES INFECCIOSAS (2019 – 2021)	MICIU RETOS INVESTIGACIÓN: PROYECTOS I+D
BIOVAC2; ARTIFICIAL BACTERIA: A NOVEL GENERATION OF BIOINSPIRED VACCINES (2020 – 2021)	BIST IGNITE PROGRAM
NOVES STRATEGIES ANTIMICROBIANES PEL TRACTAMENT DE LES ENFERMETATS INFECCIOSES EN MALALTS DE FIBROSIS QUÍSTICA (2017 – 2021)	FUNDACIÓ LA CAIXA

Main recent publications related to healthy ageing

Vilela, D., Blanco-Cabra, N., Eguskiza, A., Hortelao, AC., Torrents, E., Sanchez, S. (2021). Drug-Free Enzyme-Based Bactericidal Nanomotors against Pathogenic Bacteria. ACS Appl. Mater. Interfaces. 13, 13, 14964–14973.

Abdelrahman, F., Easwaran, M., Daramola, O. I., Ragab, S., Lynch, S., Oduselu, T. J., Khan, F. M., Ayobami, A., Adnan, F., Torrents, E., Sanmukh, S., & El-Shibiny, A. (2021). Phage-Encoded Endolysins. Antibiotics, 10(2), 124. https://doi.org/10.3390/antibiotics10020124

Vilela, D., Blanco-Cabra, N., Eguskiza, A., Hortelao, A. C., Torrents, E., & Sanchez, S. (2021). Drug-Free Enzyme-Based Bactericidal Nanomotors against Pathogenic Bacteria. ACS applied materials & interfaces, 13(13), 14964–14973. https://doi.org/10.1021/acsami.1c00986

Blanco-Cabra, N., López-Martínez, M. J., Arévalo-Jaimes, B. V., Martin-Gómez, M. T., Samitier, J., & Torrents, E. (2021). A new BiofilmChip device for testing biofilm formation and antibiotic susceptibility. NPJ biofilms and microbiomes, 7(1), 62. https://doi.org/10.1038/s41522-021-00236-1

Cendra, M., & Torrents, E. (2021). Pseudomonas aeruginosa biofilms and their partners in crime. Biotechnology advances, 49, 107734. https://doi.org/10.1016/j.biotechadv.2021.107734

Moya-Andérico, L., Vukomanovic, M., Cendra, M., Segura-Feliu, M., Gil, V., Del Río, J. A., & Torrents, E. (2021). Utility of Galleria mellonella larvae for evaluating nanoparticle toxicology. Chemosphere, 266, 129235. https://doi.org/10.1016/j.chemosphere.2020.129235

Del Mar Cendra, M., & Torrents, E. (2020). Differential adaptability between reference strains and clinical isolates of Pseudomonas aeruginosa into the lung epithelium intracellular lifestyle. Virulence, 11(1), 862–876. https://doi.org/10.1080/21505594.2020.1787034

Moya-Andérico, L., Admella, J., Fernandes, R., & Torrents, E. (2020). Monitoring Gene Expression during a Galleria mellonella Bacterial Infection. Microorganisms, 8(11), 1798.

https://doi.org/10.3390/microorganisms8111798

Blanco-Cabra, N., Paetzold, B., Ferrar, T., Mazzolini, R., Torrents, E., Serrano, L., & LLuch-Senar, M. (2020). Characterization of different alginate lyases for dissolving Pseudomonas aeruginosa biofilms. Scientific reports, 10(1), 9390. https://doi.org/10.1038/s41598-020-66293-2

Pedraz, L., Blanco-Cabra, N., & Torrents, E. (2020). Gradual adaptation of facultative anaerobic pathogens to microaerobic and anaerobic conditions. FASEB journal: official publication of the Federation of American Societies for Experimental Biology, 34(2), 2912–2928. https://doi.org/10.1096/fj.201902861R

Cendra, M., Blanco-Cabra, N., Pedraz, L., & Torrents, E. (2019). Optimal environmental and culture conditions allow the in vitro coexistence of Pseudomonas aeruginosa and Staphylococcus aureus in stable biofilms. Scientific reports, 9(1), 16284. https://doi.org/10.1038/s41598-019-52726-0

Blanco-Cabra, N., Vega-Granados, K., Moya-Andérico, L., Vukomanovic, M., Parra, A., Álvarez de Cienfuegos, L., & Torrents, E. (2019). Novel Oleanolic and Maslinic Acid Derivatives as a Promising Treatment against Bacterial Biofilm in Nosocomial Infections: An in Vitro and in Vivo Study. ACS infectious diseases, 5(9), 1581–1589. https://doi.org/10.1021/acsinfecdis.9b00125

Ohui, K., Afanasenko, E., Bacher, F., Lim Xue Ting, R., Zafar, A., Blanco-Cabra, N., Torrents, E., Dömötör, O., May, NV., Darvasiova, D., Enyedy, EA., Popović-Bijelić, A., Reynisson, J., Rapta, P., Babak, MV., Pastorin, G., Arion, VB. (2019). New Water-Soluble Copper(II) Complexes with Morpholine-Thiosemicarbazone Hybrids as Potential Anticancer and Antibacterial Drugs. J. Med. Chemistry. 62(2): 512-530. https://doi.org/10.1021/acs.jmedchem.8b01031

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