

Activity **REPORT** 2021

CICbiomaGUNE

MEMBER OF
BASQUE RESEARCH
& TECHNOLOGY ALLIANCE

 EXCELEXIA
MARÍA
DE MAEZTU
07/2018 - 06/2022

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DIRECTORS' MESSAGE



Aitziber L. Cortajarena, Scientific Vice Director (left)
Luis M. Liz-Marzán (middle)
José M Mato, Director General (right)

This report summarizes the main strengths and achievements concerning research activity and scientific leadership of CIC biomaGUNE during 2021. We are proud to show excellent output, in terms of research, technological development, resources, and capacities, which reflects the great enthusiasm and skills of our researchers, platform managers, as well as support and management teams. The achievements attained thus far show both qualitative and quantitative improvement in our performance along the years, positioning CIC biomaGUNE as a consolidated research center, specialized in biomaterials, with high international recognition.

The volume of R&D activity has grown significantly in comparison with previous years, as can be seen by the number of grants and industrial contracts (**38 new projects, of which 5 international: 9.1 M€ granted in total**). The scientific production of our researchers features remarkable quality and impact, with **146 articles** published in high profile journals, and **over 10,000 citations**. From these articles, 47% were led by CIC biomaGUNE researchers, 59% include international collaboration, 54% national collaboration, and 23% internal collaboration.

From a **knowledge & technology transfer** perspective, CIC biomaGUNE also made significant progress, as reflected in the **increased level of funding from private sources, reaching 19% in 2021**. Several actions were implemented under CIC biomaGUNE's strategic program, to promote collaboration with the private and clinical sectors, to enhance technology transfer and to attract industrial funding. This resulted in **31 agreements, service contracts and research contracts** with industrial or external partners. Additionally, we pushed forward the **validation of 4 technologies**, 2 of which are currently seeding the creation of spin-off companies.

During 2021, **3 new patent families** were initiated, **1 trade secret** deposited and **2 patents** were **granted**. Also, **3 licenses** were **signed** for the exploitation of CIC biomaGUNE's intellectual property rights.

CIC biomaGUNE has gradually built up a network of partnerships with leading research centers and universities around the world, aiming at high-quality research and outstanding academic programs, supported by our successful participation in European and other International Programs. **30 EU and International collaborative projects** were active throughout 2021, **11 led/coordinated by CIC biomaGUNE researchers**.

In the competitive framework of Horizon 2020, 5 projects started during 2021: **1 ERC Advanced Grant** (Maurizio Prato) was launched, which adds to the 7 previously granted ERC grants, **3 FET projects** (**1 coordinated** by Aitziber L. Cortajarena), and **1 MSCA-RISE coordinated** by Sergio Moya.

International recognition of academic excellence is also reflected by **prestigious awards**, including the Lilly Biomedical Research Award, RSC Materials Chemistry Division Horizon Prize, honorary doctorates, and the recognition of one group leader as Highly Cited Researcher.

It is also noteworthy that our researchers globally served in **40 Editorial Boards** of prominent international Journals. In 2021, our researchers have organized or co-organized **8 International conferences and workshops**.

CIC biomaGUNE has an average workforce of **160 people**, with a balanced gender distribution, **57% of our staff being women**, as well as an international profile with more than **29% of our staff coming from foreign countries**. During 2021, gender balance was maintained in practically all professional categories, except in the group leader positions, and **increased the number of women Research Fellows**, from 2 in 2016 to 6 in 2021, as well **in management positions**, including the General Manager (since September 2019) and the Scientific Director (from 2022). In terms of training, we had an average of **35 postdoctoral researchers** and **42 predoctoral researchers**, with **9 PhD theses completed**.

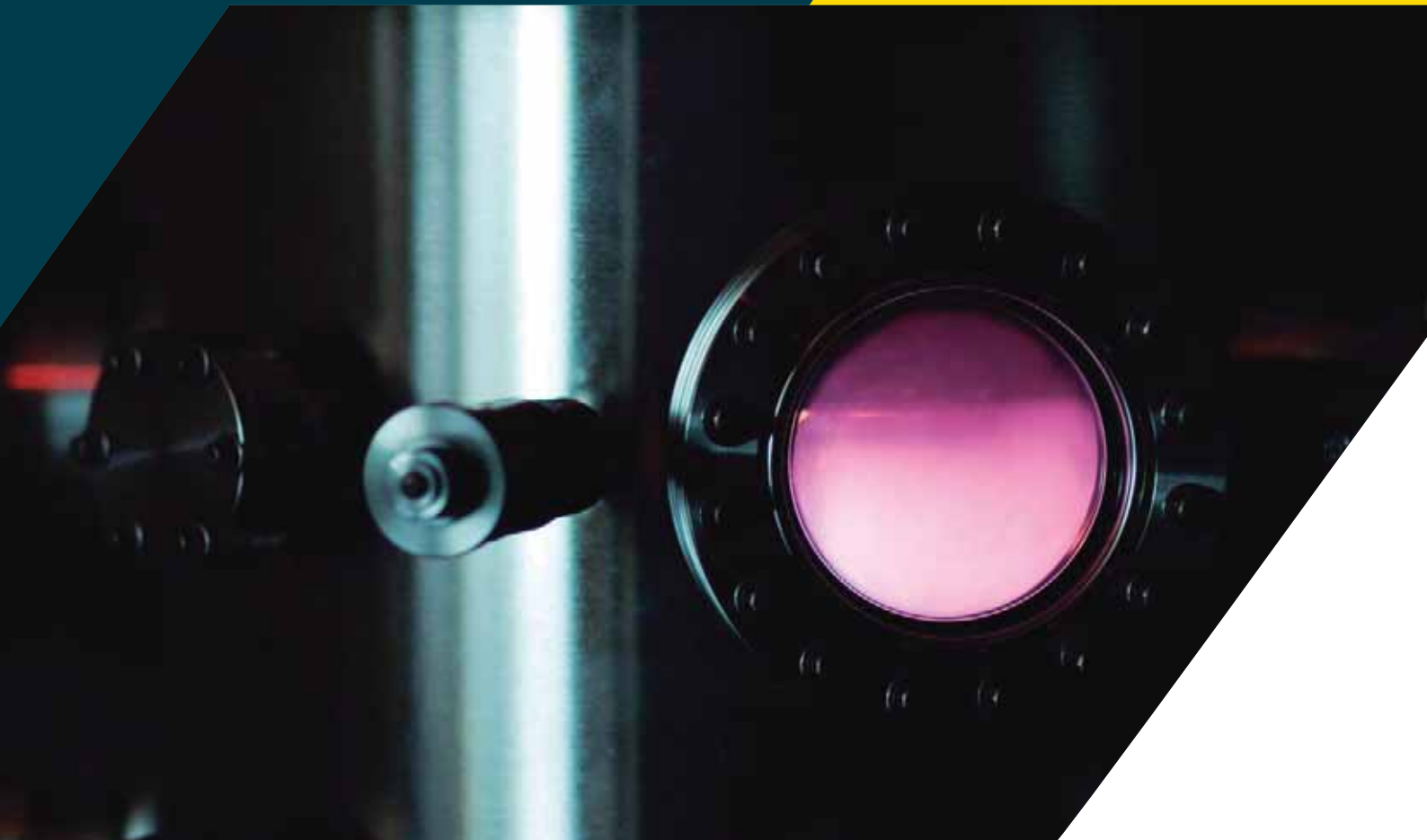
As part of our commitment to achieve excellence in the management of human resources and equality, we developed a **harassment prevention protocol**, and obtained the **HR Excellence in Research seal** from the European Commission. Our RD&I management system renewed the accreditation according to the **UNE 166002** standard and we also renewed **AAALAC accreditation** for high quality animal care and use for research.

As part of our commitment to dissemination and outreach, in particular for promotion of STEAM careers in young girls and visibility of women in science, we organized and participated in more than **44 outreach activities**. CIC biomaGUNE's visibility has been increased through fruitful efforts on social media and public communication, while our work was featured in over **400 media impacts**.

Luis M. Liz- Marzán, Scientific Director

Aitziber L. Cortajarena, Scientific Vice-Director

José M. Mato, Director General



PRESENTATION

The Center for Cooperative Research in Biomaterials- CIC biomaGUNE, member of the **Basque Research and Technology Alliance (BRTA)**, is a non-profit research organization created to promote scientific research and technological innovation at the highest levels in the Basque Country following the BioBasque policy, to help create a new business sector based on biosciences.

Located in the Science and Technology Park of Gipuzkoa (Donostia-San Sebastián), the activity of CIC biomaGUNE is conducted by an average of **11 international and dynamic research groups**, which develop high-level research at the interface between chemistry, physics and biology, with particular emphasis on the properties of nanostructures and biomaterials, and their applications in biomedicine.

The scientific strategy of the Center for the 2017-2021 period has been structured around **three main research priorities**: Biofunctional Nanomaterials, Molecular and Functional Imaging, and Regenerative Medicine.

The main research lines deal with the design, preparation and characterization of biofunctional nanostructures and their *in vitro* and *in vivo* biological evaluation to be used in the study of biological processes and the development of biomedical tools such as diagnostic, theranostic, or multimodal imaging platforms.

To carry out this ambitious program of research, the Center counts with a unique research infrastructure, equipped with advanced nanoscience, chemistry, biochemistry, cell biology, and molecular imaging facilities, including fully equipped research laboratories, **Technological Platforms** and the **Molecular Imaging**

CIC biomaGUNE building





Facility, selected as a Singular Scientific and Technical Infrastructure (ICTS) by the Spanish Government and one of the **most complete preclinical imaging research infrastructures in Europe**.

CIC biomaGUNE started its activity in December 2006. In the course of almost fifteen years, with an average critical mass of around 160 people, the Center has obtained national and international recognition as a scientific leader and knowledge builder in the field of biomaterials. Among other achievements, our activity has resulted in the generation of knowledge (publications, patents, PhD theses) the internationalization of research through collaboration with

international bodies and institutions, as well as opening our facilities to the scientific community and the industrial sector.

In 2018 CIC biomaGUNE earned the accreditation as a “María de Maeztu Unit of Excellence”, the highest recognition of scientific excellence in Spain awarded by the Spanish State Research Agency (AEI). The center counts with additional certifications and recognitions such as the Seal of Excellence in Human Resources “HR Excellence in Research”, UNE 166002:2014 for RD&I Management and the AAALAC accreditation for the care and use of animals in science.

AT A GLANCE



2021 Organization

01. Research Groups

1. Glycotechnology
2. Biomolecular Nanotechnology
3. Soft Matter Nanotechnology
4. Bionanoplasmonics
5. Bioengineered Particles
6. Carbon Bionanotechnology
7. Heterogeneous Biocatalysis
8. Regenerative Medicine
9. Computational Biophysics
10. Radiochemistry & Nuclear Imaging
11. Magnetic Resonance Imaging
12. Molecular & Functional Biomarkers

02. Molecular & Functional Imaging Facility

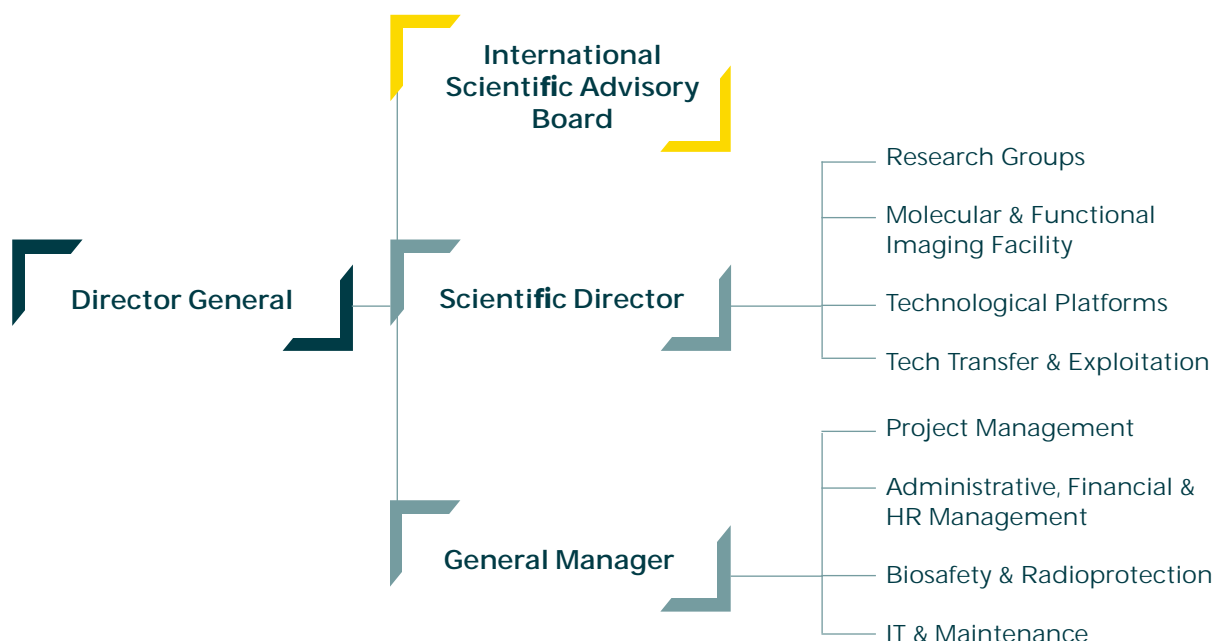
1. Radiochemistry
2. Nuclear Imaging (PET/SPECT/CT)
3. Magnetic Resonance Imaging (MRI)
4. Image Analytics
5. Animal House

03. Technological Platforms

1. Nuclear Magnetic Resonance
2. Electron Microscopy
3. Mass Spectrometry
4. Surface Analysis & Fabrication
5. Colloidal Nanofabrication
6. Optical Spectroscopy

04. Support

1. Direction
2. General Management
3. Administration, Financial & HR Management
4. Project Management
5. Tech Transfer & Exploitation
6. Biosafety & Radioprotection
7. Information Technology
8. Maintenance



Staff

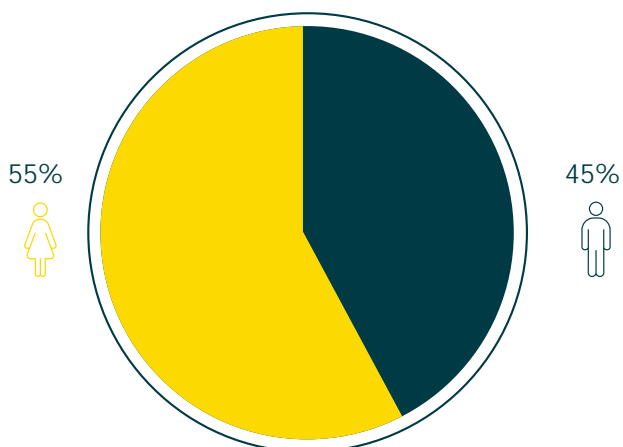
156.13

AVERAGE STAFF FTE
(55% women, 45% men)

27

NATIONALITIES REPRESENTED
(29% of staff born outside Spain)

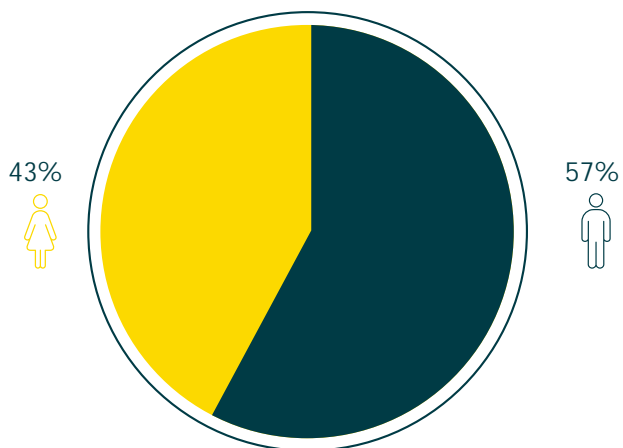
GENDER DISTRIBUTION



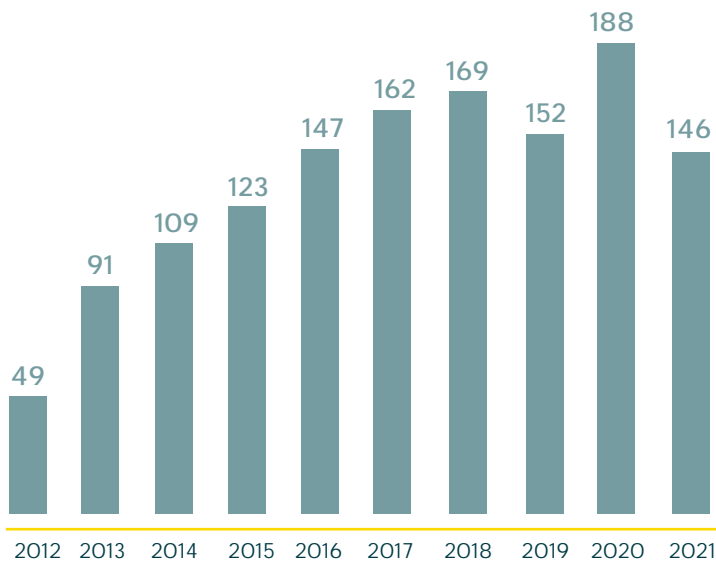
Scientific Output

Scientific Publications	146
Citations	10,826
Average Impact Factor	9.28
1 st Quartile	78%
1 st Decile	44%
HIRSCH Index	101
Open acces (gold or green)	82%

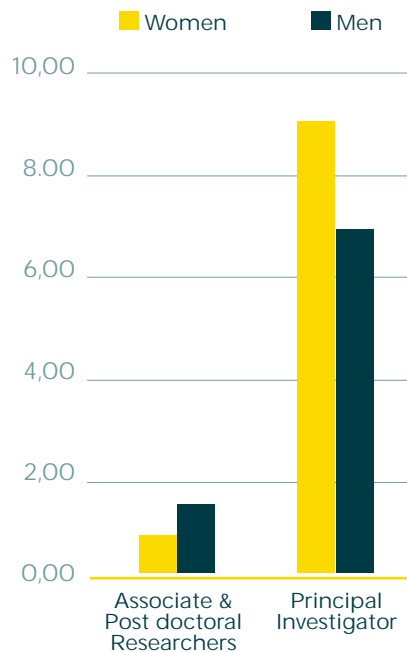
PUBLICATIONS BY GENDER PUBLICATIONS 1ST AUTHORSHIP



PUBLICATIONS EVOLUTION



AVERAGE ARTICLES CORRESPONDING AUTHORSHIP PER CATEGORY



2021 Budget

14,609,461 €

TOTAL BUDGET

European Commission 19%

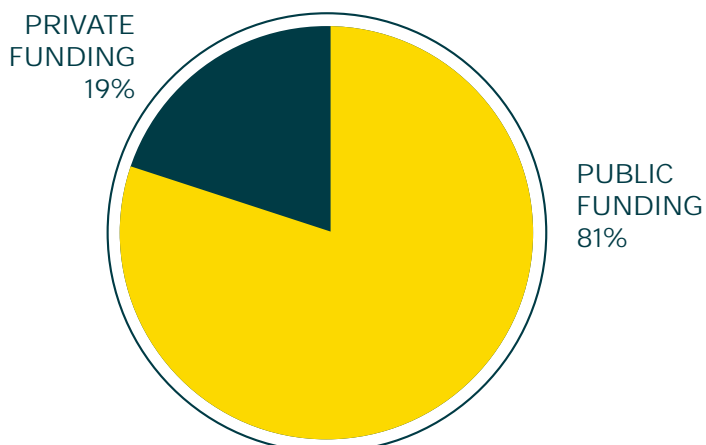
Spanish Government 13%

Basque Government 19%

Base Funding 30%

Private 19%

PRIVATE-PUBLIC FUNDING



Technology Transfer

New Patent Families 3

Trade secrets 1

Granted patents 2

Licensed Patents & Other IP Rights 3

Ongoing Valorisation Projects 4

Agreements, Research Contracts 31

Training & Career Development

9

COMPLETED
PhD THESES
(55% women,
44% men)

63

ONGOING PhD
THESES
(62% women,
38% men)

97

INCOMING
RESEARCH
STAYS
(56% women,
44% men)

12

OUTGOING
RESEARCH
STAYS
(33% women,
66% men)

34

SEMINARS
(36% women
speakers,
64% men speakers)

114

INTERNAL
SCIENTIFIC &
TECHNOLOGY
TRAININGS
(59% women
participants,
41% men
participants)

3

ORGANIZED
WORKSHOPS &
CONFERENCES

5

CO-ORGANIZED
WORKSHOPS &
CONFERENCES

218

CIC BIOMAGUNE
EMPLOYEES
PARTICIPATED
TO
WORKSHOPS &
CONFERENCES
(67% women,
33% men)

108

CIC BIOMAGUNE
EMPLOYEES
DELIVERED
ORAL & POSTER
CONTRIBUTIONS
TO WORKSHOPS &
CONFERENCES
(54% women,
46% men)

Dissemination & Public Engagement



44

OUTREACH
ACTIVITIES
(19 of which aimed
to promote STEAM
careers in young girls
and improve visibility
of women in science)



407

MEDIA
APPEARANCES



55,142

WEB VISITS



2,726

TWITTER
FOLLOWERS



3,368

LINKEDIN
FOLLOWERS



235

FACEBOOK
FOLLOWERS



208

FACEBOOK LIKES

Awards & Recognitions

CIC biomaGUNE Accreditations

- ✓ **AAALAC Accreditation to CIC biomaGUNE's animal facilities** CIC biomaGUNE received the **AAALAC accreditation** in 2015 for the first time, and the accreditation was renewed in 2018 and 2021.
- ✓ **Maria de Maeztu Unit of Excellence** accredited by the Spanish State Research Agency (Ministry of Science, Innovation and Universities).
- ✓ The Molecular & Functional Imaging Facility renewed its recognition as **Singular Scientific and Technical Infrastructure** (ICTS in Spanish).
- ✓ **Certification** of CIC biomaGUNE RD&I management system according to **UNE 166002:2014** standard.
- ✓ **Seal of Excellence in Human Resources "HR Excellence in Research"** from the European Commission since 2021.

Awards

- ✓ **Antonio Aires Trapote**, awarded with the **ACS Applied Materials & Interfaces #MyACSAMI Prize**. 14/04/2021
- ✓ **Luis M. Liz-Marzán** awarded with the **Lilly Foundation Award for Preclinical Biomedical Research**. 14/06/2021
- ✓ **Aitziber L. Cortajarena**, awarded with **Materials Chemistry Division Horizon Prize** from the Royal Society of Chemistry to the collaborative team in which Aitziber L. Cortajarena participates for their work on stabilisation of fluorescent proteins in polymer coatings and their use in bio-based lighting technology. 08/06/2021
- ✓ **Susana Carregal Romero** awarded with the **2020 Michael Balls Award** for the best article published in the 2020 volume of ATLA for the collaborative work with Gaiker and CIC bioGUNE entitled, '*Evaluation of the influence of astrocytes on in vitro blood-brain barrier models*'; **ATLA 48, 184-200**. 22/09/2021
- ✓ **Jesús Ruiz-Cabello**, awarded with the **2021 Dr. Antoni Esteve Foundation Research Award** In 2019, for the collaborative work with CNIC, CNIO and University Hospital of Salamanca, entitled "*p38 gamma is essential for cell cycle progression and liver tumorigenesis*", *Nature* 2019, 568, 557-560. 10/10/2021
- ✓ **Luis M. Liz Marzán**, **Highly Cited researcher** (Clarivate Analytics) in the Cross-field category. 16/11/2021

Academy Membership and Honorary Degrees

- ✓ **Wolfgang W. Parak** elected **Fellow of the American Institute for Medical and Biological Engineering (AIMBE)**. 16/02/2021
- ✓ **Maurizio Prato** received the "**Honoris Causa**" honorary degree in "Medical Biotechnology and Nanobiotechnology" from the Università del Salento (Italy). 30/06/2021
- ✓ **Luis M. Liz-Marzán**, joins the **Spanish Royal Academy of Sciences (RAC - Real Academia de Ciencias Exactas, Físicas y Naturales de España)** as **Full Member**. 27/10/2021
- ✓ **Fernando López-Gallego**, joins the **Young Academy of Spain** as **Numerary Member**. 26/11/2021

Best Talk/Poster

- ✓ **Gabriela Guedes Faria** awarded with the **Best Graduate Student Poster Award** in the Protein Society Annual Meeting 2021. 14/07/2021
- ✓ **Cristina de la Encarnación Bermúdez**, awarded with the **Best Flash Talk** in the Spanish Conference in Nanophotonics 2021 (CEN2021). 22/09/2021
- ✓ **Pedro Ramos Cabrer & Maurizio Prato** awarded "**Best v-EMIM Poster-Pitches**" prize in the "Structural & Functional Neuroimaging category" of the 16th European Molecular Imaging Meeting (EMIM), for the collaborative work entitled "Functional rewiring across spinal injuries via biomimetic nanofiber scaffolds". 30/08/2021
- ✓ **Damián Pérez Martínez**, received the **Best poster Award** at the European Chemical Biology Symposium 2021. 11/11/2021
- ✓ **Damián Pérez Martínez**, received the **Best Poster Award** at the New Frontiers Symposium on Translational Glycoscience. 19/11/2021

ORGANIZATION



General Assembly

PUBLIC ADMINISTRATIONS

BIO Foundation



berrikuntza + ikerketa + osasuna eusko fundazioa
fundación vasca de innovación e investigación sanitarias

Provincial Council of Gipuzkoa



Gipuzkoako Foru Aldundia
Diputación Foral de Gipuzkoa

Technology Parks Network



Univ. of the Basque Country



Universidad del País Vasco Euskal Herriko Unibertsitatea

Provincial Council of Bizkaia



BTI



COMPANIES

Curium Pharma



Industrial Química del Nalón, S.A.



Mondragon Corporation



International Scientific Advisory Board



Prof. Peter Morris

Sir Peter Mansfield
Magnetic Resonance
Centre University of
Nottingham, UK



Prof. Monica Olvera de la Cruz

Department of Chemistry
Northwestern University,
USA



Prof. Itamar Willner

Institute of Chemistry
The Hebrew University of
Jerusalem, Israel



Prof. Peter Seeberger

Max Plank Institute of
Colloids and interfaces,
Germany



Prof. Aránzazu del Campo

INM - Leibniz Institute for
New Materials, Germany



Prof. Samuel I. Stupp

Institute for
BioNanotechnology in
Medicine Northwester
University, USA



Prof. Patrick Couvreur

Université Paris-Sud,
France

Research Groups

The main research lines deal with the design, preparation and characterization of biofunctional nanostructures and their *in vitro* and *in vivo* biological evaluation, to be used in the study of biological processes and the development of biomedical tools such as diagnostic, theranostic, or multimodal imaging platforms.

GLYCOTECHNOLOGY

Niels Reichardt
Principal Investigator
Sonia Serna -
Research Associate

The Glycotechnology Laboratory carries out projects in basic and applied glycoscience, the science and technology of carbohydrates with a large untapped potential to provide innovative solutions to important social challenges such as personalized medicine, pharmaceutical products, food and biomaterials.

The group applies carbohydrate synthesis, materials science and molecular biology to the design of tools, probes and devices to elucidate the role and exploit the potential of sugars for cancer immune therapy, as biomarkers and biomaterials for biomedical applications.

BIOMOLECULAR NANOTECHNOLOGY

Aitziber López Cortajarena
Principal Investigator
(Ikerbasque Professor)
Valery Pavlov - Associated
Principal Investigator
Ivan R. Sasselli - Research
Associate (Fellow Gipuzkoa)
Aitor Manteca - Research
Associate (Fellow Gipuzkoa)



The group focuses on protein engineering toward the generation of functional nanostructures and bioinspired materials for applications in nanobiotechnology and nanomedicine. The research focuses mainly on protein engineering in order to develop versatile platforms for the bottom-up fabrication of protein-based hybrid functional biomaterials. We are also interested in the tailored biofunctionalization of nanomaterials for biomedical applications, from disease treatment to diagnosis.

The group also carries out research aimed at the development of new analytical and bioanalytical techniques, using metal and semiconductor nanoparticles and has also focused on the fabrication of novel biosensors employing different read-out methods, such as UV-visible and fluorescence spectroscopy, quartz crystal microbalance, electrochemistry and photo-electrochemistry.

SOFT MATTER NANOTECHNOLOGY

Sergio Moya
Principal Investigator

The Soft Matter Nanotechnology Laboratory makes use of elements of soft matter, mainly polyelectrolytes, in nanofabrication and in the development of hybrid materials for biomedical applications.

The group has expertise in several physico-chemical characterization techniques, especially in fluorescence spectroscopy. The group interests include the synthesis of polyelectrolytes, self-assembly, physical characterization, the development of drug delivery systems, and hybrid materials for tissue engineering.

RADIOCHEMISTRY & NUCLEAR IMAGING

Jordi Llop
Principal Investigator

The activity of the Radiochemistry and Nuclear Imaging Laboratory focuses on the development of innovative radiochemistry and the application of positron emission tomography (PET) and single photon emission computed tomography (SPECT) tracers toward the investigation of biological, physiological and pathological processes in the fields of oncology, neurology, pneumology, infection and cardiovascular diseases.



BIONANOPLASMONICS

Luis M. Liz-Marzan

Principal Investigator (Ikerbasque Professor)

Isabel García - Research Associate (CIBER-BBN)

Dorleta Jiménez de Aberasturi - Research Associate (Ikerbasque Fellow)

Óscar F. Silvestre - Research Associate (Fellow Gipuzkoa)

Carlos D. Lima de Albuquerque

- Research Associate (Fellow Gipuzkoa)

Malou Henriksen-Lacey - Research Associate

The activity of the Bionanoplasmonics Laboratory focuses on the biomedical applications of plasmonic nanomaterials, including new chemical methods for the synthesis of colloidal metal nanoparticles with tailored size, shape and surface chemistry, their directed self-assembly and applications in biosensing, diagnostics and therapy, mainly based on plasmonic effects. One of the current central topics of the group is the development of platforms that can be used for ultrasensitive detection based on SERS. The group is interested in the incorporation of such nanostructured substrates within devices for implementation of real detection techniques.

BIOENGINEERED PARTICLES (UNTIL 08/2021)

Wolfgang J. Parak

Principal Investigator

Carlos Sánchez Cano - Research Associate (Fellow Gipuzkoa)

The Bioengineered Particles Laboratory focuses on understanding the interaction of colloidal nanomaterials with the biological matter, such as proteins and cells.

Our work is dedicated to the synthesis of highly defined nanoparticle libraries, their physicochemical characterization, and correlation of biological effects to their physicochemical properties. We also develop new methods toward novel methodologies for physicochemical characterization in situ and in complex environments.



CARBON BIONANOTECHNOLOGY

Maurizio Prato

Principal Investigator

(Ikerbasque Professor & AXA Chair)

The mission of the Carbon Bionanotechnology Laboratory is the design and synthesis of tailored carbon nanostructures for bionanotechnology applications and solar energy conversion through biomimetic approaches.

The group explores new synthetic protocols and new analytical methods, enabling innovative, controlled and reproducible ways toward the designer functionalization of carbon nanostructures, such as fullerenes, carbon nanotubes, graphene and carbon nanodots.



HETEROGENEOUS BIOCATALYSIS

Fernando López Gallego

Principal Investigator

(Ikerbasque Professor)

The Laboratory of Heterogeneous Biocatalysis is applying multi-enzyme systems to synthetic, environmental, medical and analytical chemistries by harnessing the exquisite selectivity of enzymes (biological catalysts) for the development of more sustainable and effective chemical processes. We are mimicking the spatial organization found inside the living organisms, but using *ex-vivo* systems supported on solid materials. To address such goal, we are interfacing chemistry and biology utilizing multidisciplinary tools that involve molecular biology, enzymology and materials chemistry.

REGENERATIVE MEDICINE

Ander Abarrategi
Junior Group Leader
(Ikerbasque and Ramón y Cajal Fellow)

The Regenerative Medicine Laboratory uses biomaterial based approaches to boost knowledge in stem-cell biology, both in physiological and in pathological contexts. For this aim, we generate bioactive and cell-laden 3D structures potentially useful for regenerative medicine and disease modelling studies.

The understanding of bone tissue is the core of our research. Briefly, we design, characterize and test different kinds of implantable devices to gain insight into specific tissue formation processes. From this information we define and modulate relevant mechanisms in the context of tissue regeneration and tissue pathology.

COMPUTATIONAL BIOPHYSICS

Ivan Coluzza
Principal Investigator
(Ikerbasque Professor)
Ivan Sasselli Ramos -
Research Associate (Fellow
Gipuzkoa)

The Computational Biophysics Laboratory is composed by an interdisciplinary team of scientists from different backgrounds but all with experience in computational modeling of biological systems and statistical mechanics.

The research focuses on the application of statistical mechanics to soft-matter and complex biological systems.

The goal is to build simple models of natural complex systems, such as proteins, and in doing so learn their fundamental function and copy it into artificial systems.

MAGNETIC RESONANCE IMAGING

Pedro Ramos Cabrer
Principal Investigator
(Ikerbasque Professor)

The Magnetic Resonance Imaging (MRI) Laboratory makes use of nanomaterials and magnetic resonance imaging techniques on animal models.

On one hand, we intend to characterize the onset and evolution of diseases of the central nervous system, from development of early markers to imaging methods that quantify the progression of the pathological processes and their consequences at anatomical and functional levels.

We additionally develop new therapeutic approaches to treat such diseases, with special emphasis on the penetration through the blood-brain-barrier and monitoring the effective release of drugs in the brain parenchyma.

MOLECULAR & FUNCTIONAL BIOMARKERS

Jesús Ruiz-Cabello
Principal Investigator
(Ikerbasque Professor)
Susana Carregal - Research
Associate (CIBER-BBN)

The Molecular & Functional Biomarkers Laboratory studies cardio-pulmonary and vascular diseases through functional and molecular imaging and system biology approaches.

The group is particularly interested in the potential of new imaging techniques, including nanotechnology-based applications, in early diagnosis of pulmonary and cardiovascular remodelling, the assessment of metabolic changes associated with cell growth, the structure and function of the right ventricle and cardiovascular coupling signals.

Directorate & Management Area

DIRECTORATE

José M. Mato - Director General
Luis M. Liz Marzán - Scientific Director
Aitziber L. Cortajarena - Scientific Vice-Director

Design, define and coordinate the Center's scientific strategies and activities.

GENERAL MANAGEMENT

Anna Llanes Pallàs - General Manager

The General Manager is responsible for supervising the management of the Administration Department, Project Management, as well as the IT, Maintenance and Biosafety units of the Center.

ADMINISTRATION

Sheyla García Medel - Administration & HR Manager
Elizabeth Noguera Olaechea - Finance & Control Manager

This department is responsible for the management of finances, accounting, administration, and the human resources of the Center.

RD&I MANAGEMENT UNIT

Cristina Díez García - Project Manager
Marcos Simón Soria - Technology Transfer Manager

A dedicated office to support and strengthen the capacities of the Center, in terms of attracting funding from various Research Programs, in particular, international ones, strengthening links between academic and industrial environments, and promoting the transfer of research results to society and industry, especially to the biotechnology sector.

BIOSAFETY & RADIOPROTECTION

Paola Ferreira Cabeza - Biosafety & Radioprotection Manager

Dedicated to establish safe working conditions of all CIC biomaGUNE's personnel by promoting good laboratory practices. The service is also in charge of the appropriate operation of the Center's Radioactive Facility.

COMPUTING & COMMUNICATIONS

Mikel Gonzalez Lacunza - IT Manager

The IT service is in charge of supporting the staff of the Center with setting up and maintaining computer-related equipment, software, data storage, e-mail servers, as well as the website and other social media.

MAINTENANCE

Álvaro Ruiz Fernández - Maintenance Manager

This department takes care of the preventive, predictive and corrective maintenance of all facilities at CIC biomaGUNE.

Research Facilities

All the research lines, framed within the strategic research program of CIC bio-maGUNE, are strongly supported by the Molecular & Functional Imaging Facility and the Technological Platforms, which constitute a major strength of the Center.



Molecular & Functional Imaging Facility

Designed, built and equipped to tackle longitudinal and multimodal pre-clinical projects and to develop applications in the areas of Preclinical Molecular and Functional Imaging and Nanomedicine. The research-oriented preclinical imaging facility offers state-of-the-art imaging resources in: (i) radiochemistry (dual particle-high current cyclotron capable to routinely produce ^{18}F , ^{11}C and ^{13}N ; versatile synthesis boxes housed in shielded hot cells; and state-of-the-art analytical equipment including radio-HPLC, radio-GC, radio-TLC, and gamma spectrometry); and (ii) small-animal imaging including PET and SPECT (both as hybrid systems with CT) and a trimodal PET-SPECT-CT, optical imaging and high field Magnetic Resonance Imaging (MRI, 7.0 and 11.7 T). The MRI unit and the Nuclear Imaging unit sandwich a dedicated animal housing area, which holds since 2015 accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) and is prepared to house up to 800 mice and 400 rats in individually ventilated cages, with an experimental area specifically devoted to perform longitudinal studies. The animal house is complemented with microsurgery areas for animal preparation. Four workstations and a data storage system in the Terabyte scale enable image reconstruction, processing, quantification and archiving.

Personnel with extensive scientific background and experience in handling and operating specific equipment, technologies, methodologies or experimental animals complete the scientific-technical staff.

The Facility is currently integrated in the "Distributed Biomedical Imaging Network" (ReDIB, www.redib.net), recognized by the Spanish Government as a Singular Scientific and Technical Infrastructure (ICTS).





RADIOCHEMISTRY PLATFORM

Vanessa Gómez-Vallejo
Platform Manager

The platform is equipped with an **IBA Cyclone 18/9 cyclotron** able to accelerate protons (18 MeV) and deuterons (9 MeV) and is equipped with 7 targets for the routine production of [¹⁸F] F-, [¹⁸F]-F2, [¹³N]-NH⁴⁺, [¹⁵O]-O₂, [¹¹C]-CO₂ and [¹¹C]-CH₄. It also has a solid target for the production of ⁸⁹Zr and ⁶⁴Cu.

The radiochemistry laboratory equipped with 5 shielded hot cells housing versatile automatic synthesis, suitable for the production (synthesis, purification and quality control) of PET and SPECT radiotracers. The facility has specially designed modules for:

- Synthesis of [¹¹C] CH₃I / [¹¹C] CH₃OTf from [¹¹C] CO₂ / [¹¹C] CH₄, and subsequent methylation reaction
- ¹⁸F-fluorination by nucleophilic and electrophilic substitution
- Radiotracer synthesis using microfluidics technology
- Chelation reactions using radiometals (⁶⁸Ga, ⁶⁷Ga, ⁶⁴Cu, ⁸⁹Zr, etc.)

The quality control lab, sited into the production lab, is equipped with state of art equipment to perform the complete quality control of the synthesized radiotracers, including radio-HPLC, radio-GC, radio-TLC, and gamma spectrometry.



PRE-CLINICAL IMAGE ANALYTICS

Unai Cossío
Platform Manager

The Image Analytics service takes care of processing all the outgoing multimodal images obtained within the Molecular Imaging Unit (PET, SPECT, CT, and MRI).

Working on different operating systems, we carry out co-registration, segmentation, and quantification of multimodal images. The combination of all multimodal imaging techniques confined in the Imaging Unit with a reliable image analysis process offers a complete and powerful Imaging facility to researchers. Four workstations and a data storage system in the Terabyte scale enable image reconstruction, processing, quantification and archiving.



MAGNETIC RESONANCE IMAGING (MRI)

Daniel Padró
Platform Manager

Equipped with instrumentation to conduct advanced imaging and spectroscopic experiments applied to biological samples including small rodents, samples or tissue extracts and cell cultures is available. CIC biomaGUNE provides the instrumentation and the expertise to carry out a wide range of **MRI** and **MRS** experiments, and is equipped with surgery rooms for animal preparation and implementation of surgical models. Ancillary equipment is also available: anesthesia systems, MRI-compatible physiological monitoring systems, infusion pumps, and temperature regulation systems. Equipment available: MRI 7T/30 cm (70/30 USR), MRI 11.7T/16 cm (117/16 USR).



NUCLEAR IMAGING

Unai Cossío
Platform Manager

The Radioimaging platform offers state-of-the-art imaging resources in preclinical Positron Emission Tomography (PET), Single Photon Emission Computerized Tomography (SPECT) and Computerized Tomography (CT). It is equipped with a hybrid PET-CT scanner (GE Healthcare eXplore Vista-CT), two standalone high-performance PET imagers (2x MOLECUBES β -CUBE), one high-sensitivity, high-resolution SPECT imager (MOLECUBES γ -CUBE) and one high-throughput CT (MOLECUBES X-CUBE) system. The platform is designed to perform *in vivo* studies from various imaging modalities in an interleaved fashion from the same animal. The combination of these potent and non-invasive imaging techniques facilitates performing multimodal approaches to biological, physiological and medical problems, obtaining images with significant functional and anatomical information. The platform is furthermore equipped with an autoradiography system for end point-high resolution nuclear imaging.



ANIMAL FACILITY

Ainhoa Cano
Platform Manager

The MRI Unit and the Nuclear Imaging Unit sandwich a dedicated animal housing area, which holds accreditation of the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) since 2015 and is prepared to house up to 800 mice and 400 rats in individually ventilated cages, with an experimental area specifically devoted to perform longitudinal studies. The animal house is complemented with microsurgery areas for animal preparation.

Technological Platforms

Managed by specialized Platform Managers, provide technical and scientific support to the research activities conducted at CIC biomaGUNE. They include the following state-of-the-art research infrastructures:



NUCLEAR MAGNETIC RESONANCE (NMR)

Daniel Padró
Platform Manager

Equipped with a **500 MHz NMR** spectrometer, it provides essential service for the characterization of molecules with biological activity, from complex glycans to molecules used in the design of nanostructures for biomedical applications.



ELECTRON MICROSCOPY

Marco Möller
Platform Manager

Equipped with **SEM-EDX, TEM – 120 keV and 200 keV**, it offers techniques to study nanoparticles and biological or soft polymer materials (cryo-TEM) at the micrometer and nanometer scale to determine the materials dimensions, shape and composition.



MASS SPECTROMETRY

Javier Calvo
Platform Manager

Equipped with **MALDI-TOF, ICP-MS**, it provides several high-quality mass spectrometry techniques for the analysis of small molecules, complex biomolecules and nanomaterials. The platform is equipped with modern instrumentation and offers different ionization methods.



Surface Analysis & Fabrication

SURFACE ANALYSIS AND FABRICATION

Desiré Di Silvio
Platform Manager

Equipped with XPS, 3 x AFM, **sputtering system**, it focuses on the analysis of materials at the surface level, including spectroscopic and microscopic techniques especially suited to surfaces. The platform offers also service for the deposition of thin layers with controlled manufacture at the nanoscale.



Colloidal Nanofabrication

COLLOIDAL NANOFABRICATION

Ana Sánchez Iglesias
Platform Manager

Within the priority area of biofunctional nanomaterials and nanomedicine, colloidal synthesis plays an essential role. This platform provides knowledge, training and service for the manufacture of nanoparticles with a wide variety of compositions and morphologies.



Optical Spectroscopy

OPTICAL SPECTROSCOPY & IMAGING

Irantzu Llarena & Judith Langer
Platform Managers

Equipped with 2 x Confocal and 2 x Confocal-Raman microscopes, UV-VIS-NIR and FT-IR spectrometers, Fluorimeter, Flow Cytometer, Cell Observer, CD, DLS, DCS, ITC, TGA, SPR, this platform offers a wide variety of techniques for the spectroscopic characterization of biomaterials and biosurfaces. Also included are optical microscopy techniques (confocal, Raman, etc.), to investigate the interaction of nanomaterials with cellular systems of diverse complexity.

HUMAN RESOURCES & EQUALITY



Human Resources

Several actions directed towards the attraction and retention of scientific talent have been implemented, in particular regarding the recruitment of PhD students and postdoctoral researchers. Such actions have additionally been supported by external funding from specific HR calls.

We have worked on the definition of a **Career Plan** at CIC biomaGUNE and started working on developing a **performance appraisal system**. Between 2020 and 2021 we elaborated a GAP analysis and a corresponding Action Plan, towards obtaining the **seal of “Excellence in HR in Research”**. The Human Resources Strategy for Researchers - HRS4R - is an initiative of the European Commission (EC) to encourage research institutions to implement the European Charter for Researchers and the Code of Conduct for the recruitment of research staff.



Equality

CIC biomaGUNE formalized in 2020 a journey and a commitment to equality that has been developing since the beginning of the activity and that it intends to maintain over time.

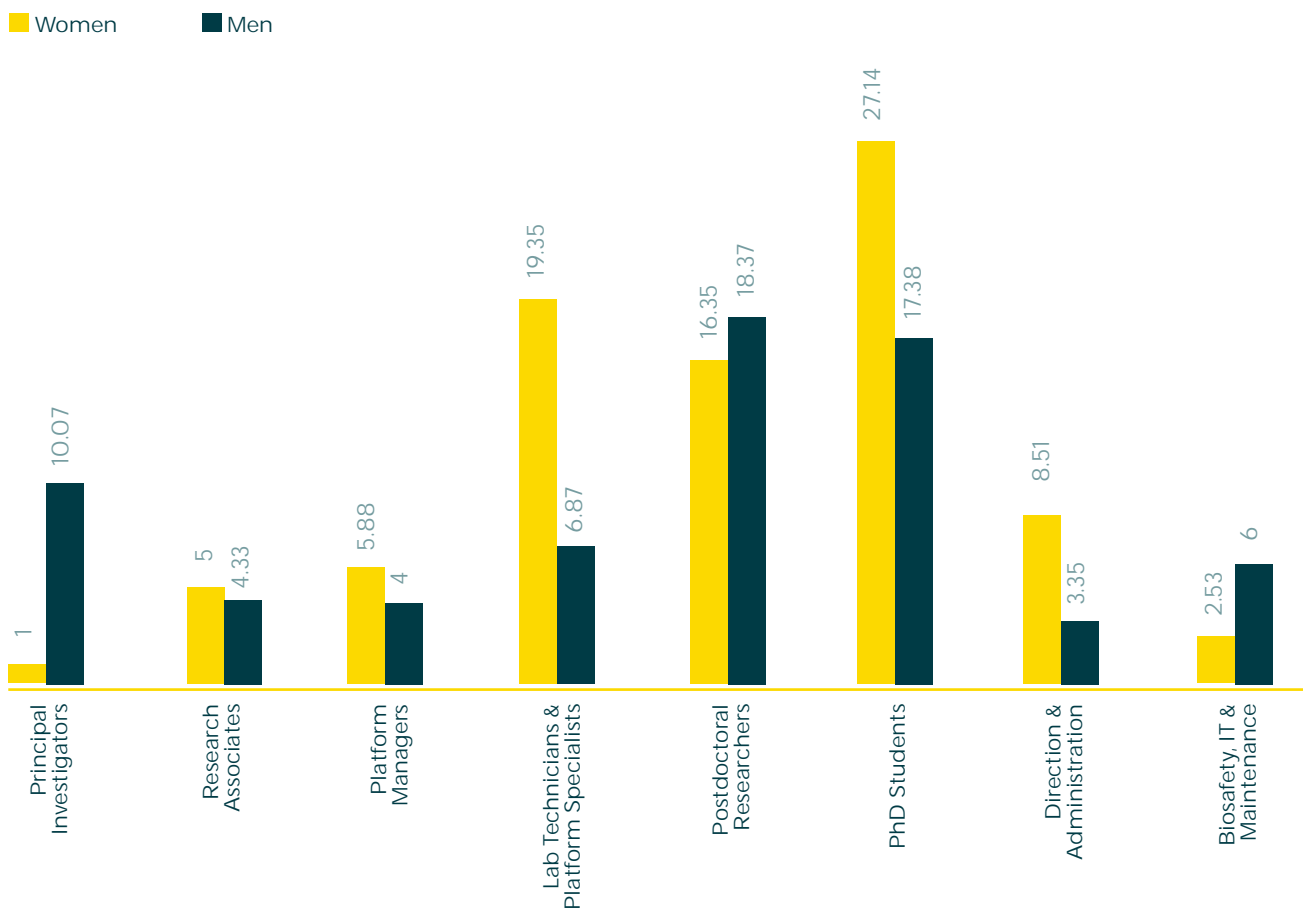
Our commitment stems not only from legal compliance but also from the opportunity represented by being able to generate a consensus that allows us to deepen and improve our culture, based on shared values and made explicit through our R&D&I Policy and other directives that we have been adopting over the years.

An equality committee was constituted in 2018, which has since engaged with the organization of multiple outreach activities and actions aimed at promoting scientific-technological vocation among girls and the figure of women in science. Together with the Direction of the Center, the committee has been working on the diagnosis and equality plan of CIC biomaGUNE, which aims at **ensuring equality, equal recruitment policies and reconciliation between work and private life**. The COVID-19 crisis has abruptly bursted into this process, radically transforming the organization of work, and combining work at the Center and remote work. We have implemented flexibility measures, to support conciliation and offering the possibility of remote work for those positions whose functions might allow it.

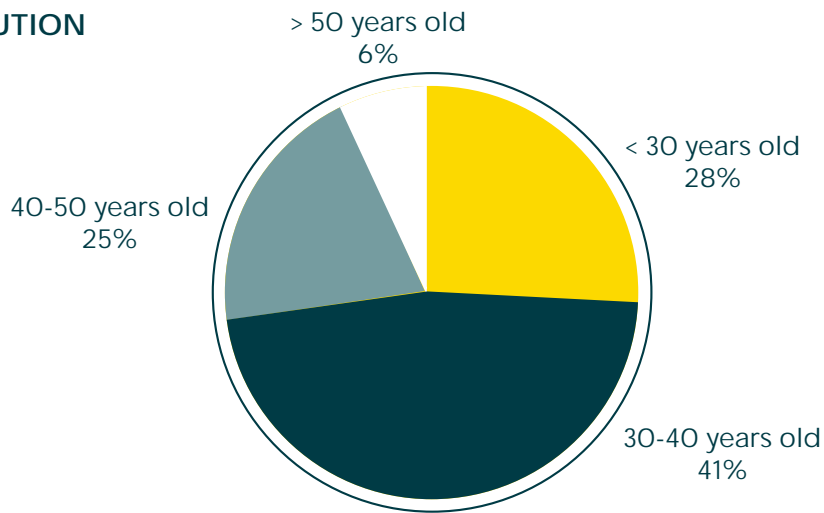
The table below provides the distribution of CIC biomaGUNE's personnel during 2021 in FTE.

POSITION		%		%	TOTAL	%
Principal Investigators	1	9%	10.07	91%	11.07	7%
Research Associates	5	54%	4.33	46%	9.33	6%
Platform Managers	5.88	60%	4	40%	9.88	6%
Lab Technician/Platform Specialists	19.35	74%	6.87	26%	26.22	17%
Postdoctoral Researchers	16.35	47%	18.37	53%	34.72	22%
PhD Students	27.14	61%	17.38	39%	44.52	29%
Direction & Admin	8.51	72%	3.35	28%	11.86	8%
Biosafety & Radioprotection	1	100%	0	0%	1	1%
IT & Maintenance	1.53	20%	6	80%	7.53	5%
TOTAL	85.76	55%	70.37	45%	156.13	100%

STAFF DISTRIBUTION BY POSITION



AGE DISTRIBUTION

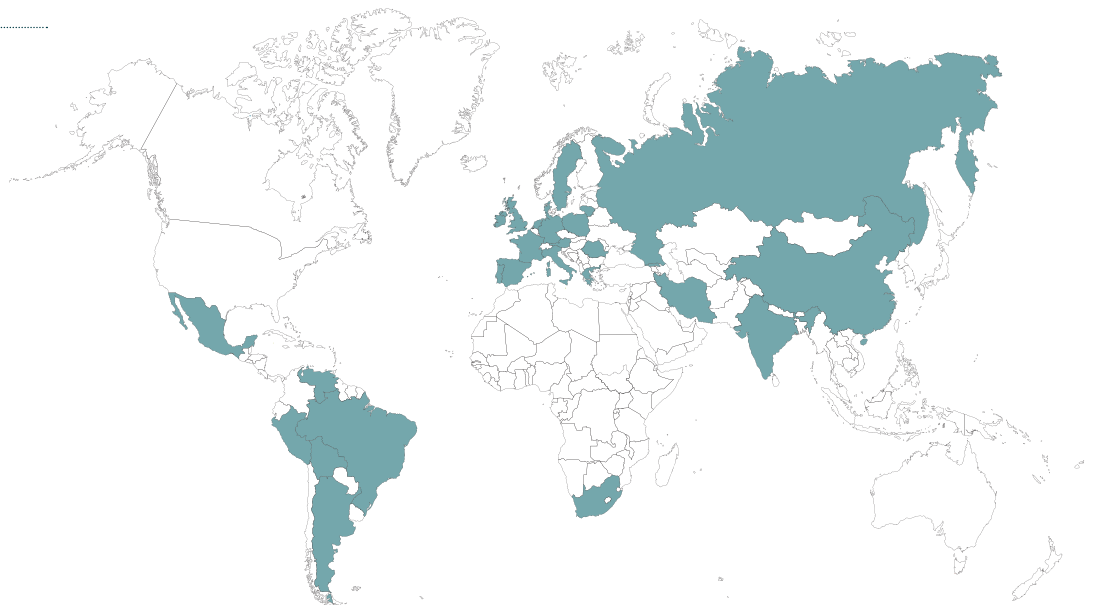
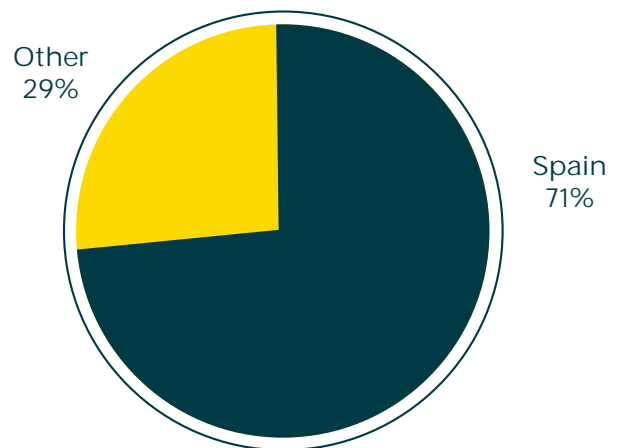


COUNTRIES

CIC biomaGUNE is a **multicultural organization**, people from 27 different countries work at CIC biomaGUNE and 29% of employees were born outside Spain.

COUNTRY	TOTAL	COUNTRY	TOTAL
Argentina	2	Lithuania	1
Austria	1	Mexico	2
Bolivia	1	Peru	1
Brasil	2	Poland	1
China	2	Portugal	2
Denmark	1	Romania	1
France	2	Russia	1
Germany	6	South Africa	1
Greece	1	Spain	144
India	6	Sweden	1
Iran	1	The Netherlands	1
Ireland	1	United Kingdom	1
Italy	25	Venezuela	1
Lebanon	1		

NATIONALITY



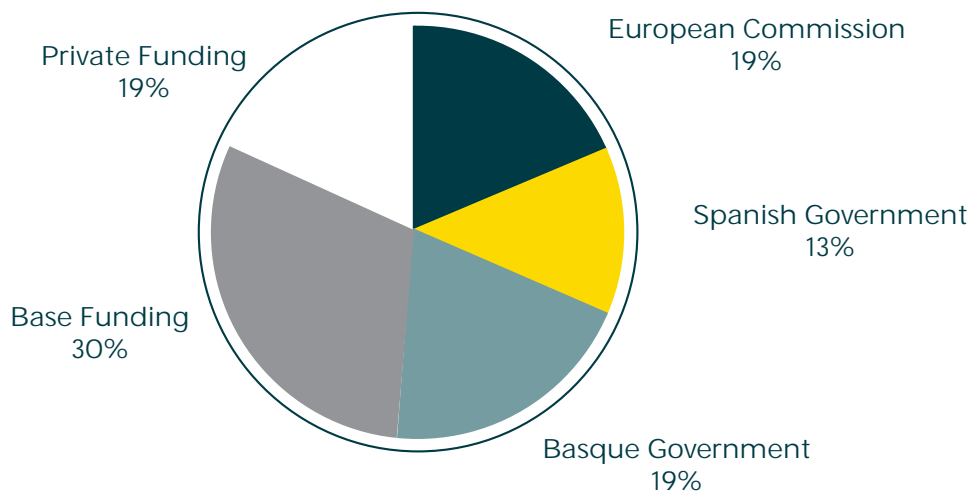
FUNDING



2021 Budget

The **total budget** for 2021 has amounted 14,609,461 €, 81% of which came from public sources and 19% from private sources.

2021 BUDGET FUNDING SOURCES



Launched projects

38 new projects (from competitive funding sources) have been launched in 2021 with a **total contribution of 9,172,565 €**

From the new launched projects, we highlight **1 ERC AdG**, **3 FET projects** (1 of them coordinated) and **1 MSCA-RISE** (coordinated) funded under Horizon 2020.

	TOTAL PROJECTS	TOTAL FUNDING (€)
European Commission	4	1,771,617
European Research Council (ERC)	1	1,820,231
Spanish Research State Agency (AEI)	16	2,802,603
Basque Government	6	2,057,273
BIOEF	1	29,766
Gipuzkoa Provincial Council (DFG)	8	364,998
La Caixa Foundation	2	326,077
	38	9,172,565

LIST OF FUNDED PROJECTS STARTING IN 2021



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Maurizio Prato	ERC-2019-ADG Advanced Grant	1,820,231.25	2021 - 2025	e-DOTS - Small molecule-derived carbon nanodots for challenging applications



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Luis M. Liz-Marzán / Aitziber L. Cortajarena	FET-Open Challenging Current Thinking (4) - FETOPEN-01- 2018-2019-2020	353,750.00	2021 - 2024	DNA FAIRYLIGHTS - DNA-flash light driven data technology with multiplexed optical encoding and read-out
Aitziber L. Cortajarena	FET-Open Challenging Current Thinking (4) - FETOPEN-01- 2018-2019-2020	541,790.25	2021 - 2025	e-Prot - Engineered conductive proteins for bioelectronics
Valery Pavlov / Aitziber L. Cortajarena	FET-Open Challenging Current Thinking (4) - FETOPEN-01- 2018-2019-2020	314,001.25	2021 - 2024	DeDNAed - Cluster decorated recognition elements on DNA origami for enhanced raman spectroscopic detection methods
Sergio Moya	H2020-MSCA- RISE-2020	562,074.00	2021 - 2026	SUPRO-GEN - Supramolecular Polyamine Gene Vectors for Cancer Therapy



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Jesús Ruiz-Cabello	Proyectos de prueba de concepto (PDC 2021)	138,000.00	2021-2023	PV4D - Clinically relevant tools to analyze complex 4D flow MRI data: application for the diagnosis of pulmonary vascular pathology associated with left heart disease
Jordi Llop	Proyectos de prueba de concepto (PDC 2021)	143,750.00	2021-2023	VentiPET - Gases radio-perfluorados como marcadores de ventilación para tomografía por emisión de positrones
Aitziber L. Cortajarena	Proyectos de prueba de concepto (PDC 2021)	149,500.00	2021-2023	NanoIVDAb - Platform for the rapid development of quantitative antibody monitoring IVD tests
Jordi Llop	«Proyectos I+D+i» 2020 - Modalidad «Retos Investigación»	290,400.00	2021-2024	TheADnostics - Development of new diagnostic tools and therapeutic strategies targeting Alzheimer's Disease: a multimodal imaging approach

Sergio Moya	«Proyectos I+D+i» 2020 - Modalidad «Retos Investigación»	205,700.00	2021-2025	GENNANOPOL - Non viral Gene Vectors based on supramolecular Polyamine Nanoparticles: Self Assembly, Physical Chemistry, Translocation studies and Transfection
Luis M. Liz-Marzán	«Proyectos I+D+i» 2020 - Modalidad «Retos Investigación»	350.900,00	2021-2023	ChirPlasThera - Design of Chiral Plasmonic Nanostructures for Theranostics
Niels Reichardt	«Proyectos I+D+i» 2020 - Modalidad «Retos Investigación»	254,100.00	2021-2024	Immunotheralec - Targeting human immune lectins with N-glycomimetics and glycoengineered exosomes as potential new avenues in cancer therapy
Pedro Ramos-Cabrer	«Proyectos I+D+i» 2020 - Modalidad «Retos Investigación»	119,790.00	2021-2024	Tear-This-Wall - To the other side of the Blood-brain barrier: development of effective biomaterials and protocols to deliver drugs to the Central Nervous System
Luis M. Liz-Marzán	Equipamiento Científico-Técnico (EQC 2021)	599,251.00	2021-2023	FESEM - Field Emission Scanning Electron Microscope
PI (FELLOW)				
Fernando López Gallego (Sergio Pacheco)	Ayudas para contratos predoctorales 2020	98,960.00	2021-2025	
Maurizio Prato (Michele Cesco)	Ayudas para contratos predoctorales 2020	98,960.00	2021-2025	
Luis M. Liz-Marzán (Paula Piñeiro)	Ayudas para contratos predoctorales 2020	98,960.00	2021-2021	
Maurizio Prato (Bahaa Daou)	Ayudas para contratos predoctorales 2019	98,250.00	2021-2024	
Luis M. Liz-Marzán (Clara García Astrain)	Juan de la Cierva - Incorporación 2019	93,000.00	2021-2024	
Luis M. Liz-Marzán (Paula Piñeiro)	Ayudas para la formación de profesorado universitario (FPU 2020)	58,311.660	2021-2025	
Luis M. Liz-Marzán (Javier Plou)	Ayudas a la movilidad para estancias breves y traslados temporales de beneficiarios (FPU 2021)	4,770.00	2021-2021	



PI (FELLOW)	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Aitziber L. Cortajarena / Ivan Coluzza (Ivan Sasselli)	Programa Fellows Gipuzkoa de atracción y retención de talento 2021	35,000.00	2021 - 2022	EINPySB-3 - Estudio de la Interfase entre Nanomateriales Peptídicos y Sistemas Biológicos
Luis M. Liz-Marzán (Oscar Ferreira Silvestre)	Programa Fellows Gipuzkoa de atracción y retención de talento 2021	35,000.00	2021 - 2022	NanoMito4Imaging-3 - Nanoterapias dirigidas a la mitocondria y herramientas de imagen de precisión avanzadas para la administración de medicamentos
Luis M. Liz-Marzán (Carlos Lima de Albuquerque)	Programa Fellows Gipuzkoa de atracción y retención de talento 2021	48,998.00	2021 - 2022	Deep-SERS - Nueva generación de (bio)sensores SERS de alto rendimiento usando un microscopio computacional en chip
Aitziber L. Cortajarena (Aitor Manteca)	Programa Fellows Gipuzkoa de atracción y retención de talento 2021	48,998.00	2021 - 2022	FLUIDEVOPRO - Sistemas de cribado y selección microfluidica para evolución dirigida de proteínas
Jordi Llop	TXEKINTEK / EKINTZAILE 2021	45,000.00	2021 - 2022	VentiPET - Análisis de la viabilidad económica de gases radiofluorados como trazadores de ventilación pulmonar
Jordi Llop	Programa de apoyo especializado para valorar el potencial de transferencia de proyectos de I+D+i biotecnológicos cercanos el mercado		2021 - 2022	Ventilation markers for Positron Emission Tomography
Jesús Ruiz-Cabello	Programa de Red guipuzcoana de Ciencia, Tecnología e Innovación 2021 - Inversión	60,991.00	2021 - 2022	PRECLINIC_BMG - Ampliación de la infraestructura de imagen preclínica avanzada en CIC biomaGUNE
Fernando López Gallego	Programa de Red guipuzcoana de Ciencia, Tecnología e Innovación 2021 - I+D	91,011.00	2021 - 2022	TERPROT - Desarrollo de un nuevo concepto de terapia basada en síntesis proteica extracelular in situ



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Niels Reichardt	IKERBILERAK 2021-2	3,090.00	2021	Glycobasque - 4th Glycobasque Meeting
Jesús Ruiz-Cabello / Jordi Llop / Pedro Ramos Cabrer	Azpitek 2021	345,872.11	2021-2022	PET - Proyecto de adquisición de un sistema de imagen de tomografía por emisión de positrones

Sergio Moya	Elkartek 2020	870,710.00	2021-2022	bmG20-2 - Desarrollo de vectores no virales para terapia génica con aplicaciones oncológicas y en inmunoterapia
Pedro Ramos Cabrer	Elkartek 2021	805,004.00	2021 - 2022	bmG21-1 - Desarrollo de herramientas y protocolos efectivos para transporte y liberación de fármacos por diferentes rutas de administración
Aitziber L. Cortajarena	Ayudas a proyectos de investigación y desarrollo en salud 2021	21,282.58	2021 - 2022	NKTPH-3 - Papel de las células NK humanas en el trasplante autólogo de precursores hematopoyéticos en el tratamiento del cáncer
Ander Abarrategi	Ayudas a proyectos de investigación y desarrollo en salud 2021	11,314.42	2021-2021	Fragilidad 2 - Validación de un patrón molecular para el diagnóstico y estratificación de la fragilidad



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Aitziber L. Cortajarena	Ayudas 2021 a proyectos de investigación en COVID-19	29,9766.00	2021 - 2023	COVID - Desarrollo y validación de técnicas de diagnóstico de precisión para la era post-pandémica



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Jordi Llop	Health Research Call 2021	164,500.00	2021 - 2024	BREAST-BRAIN-N-BBB - Protecting the brain from metastatic breast cancer
Jordi Llop	Health Research Call 2021	161,576.50	2021 - 2024	BLADDEBOTS - Enzyme propelled nanobots as efficient nanotech platform for bladder cancer therapy

KNOWLEDGE & TECHNOLOGY TRANSFER



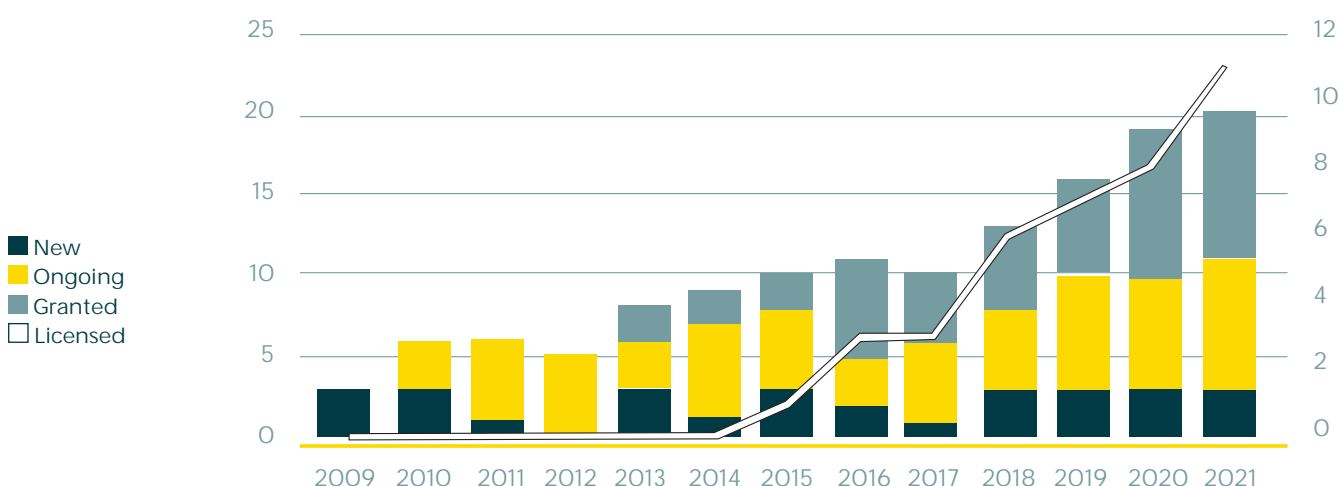
Effort devoted by our researchers with the support of the Technology Transfer Unit in 2021 resulted in **3 new patent families, 1 trade secret, 2 granted patents** and **3 licenses for exploitation** of CIC biomaGUNE intellectual property rights. Moreover, a total of **31 Research Contracts, Services and Collaboration Agreements** were signed with companies or other RD&I institutions.



Patents

The generation of patents is one of the instruments that indicate the transfer of knowledge from CIC biomaGUNE to Society and to business development. The graph below shows the evolution over the years:

IP PORTFOLIO



2021 Priority Patent Applications

- ✓ **Microfluidic devices and methods.**
V. Pavlov, B. Díez-Buitrago, N. Briz, G. Bijelic. [EP21382293.5](#) (07/04/2021)
- ✓ **Nanoparticles for the control of one-pot multi-enzymatic reactions.**
F. López-Gallego, J. García Ovejero, I. Armenia, S. Veintemillas, J. Martínez de la Fuente, M.P. Morales, V. Grazú, J. Manuel Guisán, B. Nidetzky, D. Roether, N. Cassinelli, G. B. Bernardini. [EP21382585.4](#) (01/07/2021)
- ✓ **Uric acid liposomes.**
P. Ramos, A. M. Planas, A. Chamorro. [EP21382979](#) (29/10/2021)

2021 Granted Patents

- ✓ **Synthesis and use of isotopically-labelled glycans.**
N.C. Reichardt, B. Echeverria, J. Etxebarria, J. Calvo, N. Ruiz. [CA2908446](#) (02/03/2021) - Canada. Previously granted in Japan, Australia, USA and Europe.
- ✓ **Pharmaceutical composition comprising fluorine-18 labelled gases.**
J. Llop, T. Reese, V. Gómez-Vallejo, A. Lecuona. [EP3474902B1](#) (09/07/2021) - Europe. Previously granted in USA.

Agreements, Services & Research Contracts

CIC biomaGUNE develops joint research activities in collaboration with different types of organizations and companies, including spin-offs, SMEs, large companies and research organizations. This research activity has a sharp focus on innovation, to which CIC biomaGUNE contributes with scientific knowledge. Joint projects under development include privately funded research activities as well as research contracts and consultancy services.

During 2021, the following agreements and services **with public and private partners were signed.**



Spin-Offs

Asparia Glycomics

www.aspariaglycomics.com

In 2016, CIC biomaGUNE researchers and private investors joined efforts to set up Asparia Glycomics, a spin-off company specialized in the production and marketing of reagents, reference standards, kits and software, intended for glycan analysis in clinical diagnosis and for quality control of biopharmaceuticals.

The business initiative markets the leading technology developed by CIC biomaGUNE's Glycotechnology Laboratory, directed by Niels C. Reichardt, to quantify and identify glycans more accurately and faster than existing solutions on the market. Asparia Glycomics offers unique, stable, isotope labeled glycans as internal standards, custom made quantification software and reagents for glycan analysis by mass spectrometry.

Asparia Glycomics' line of work is based on the development of its own technology that can be useful for the diagnosis and prognosis of cancer, diabetes or autoimmune diseases such as rheumatoid arthritis, among others.

The products and technology developed by the Glycotechnology Laboratory, reviewed and validated by the CIC biomaGUNE Development Unit are aimed at researchers, academia and pharmaceutical companies around the world.

Since 2020 and after a change of management, the company has been able to break even and has established a position as a reliable provider of cutting-edge glycan analysis and synthesis projects for leading biotech companies and academic researchers worldwide.

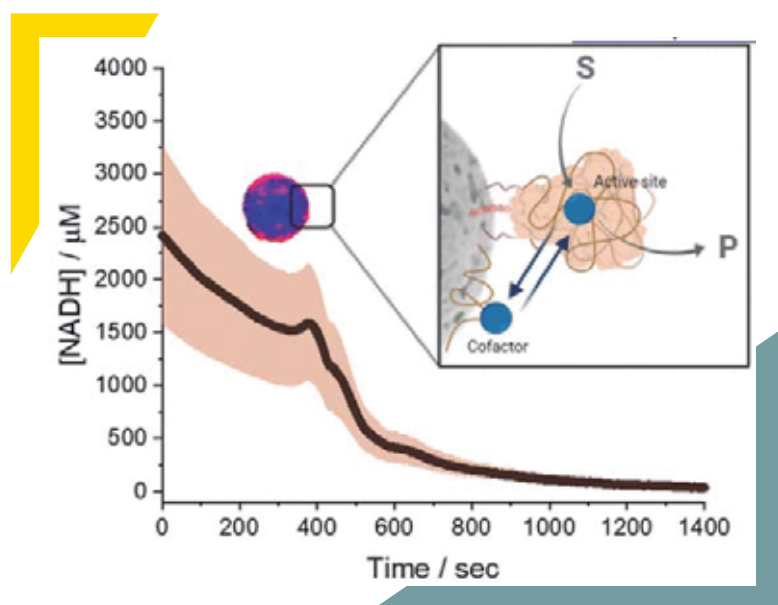
SCIENTIFIC OUTPUT



In 2021, **146 research articles** have been published in international scientific journals with an **average impact factor** of **9.28** and received **10,826** citations.

From these articles, **47%** were led by **CIC biomaGUNE researchers**, **59%** include **international** collaboration, **54%** **national** collaboration, and **23%** **internal** collaboration.

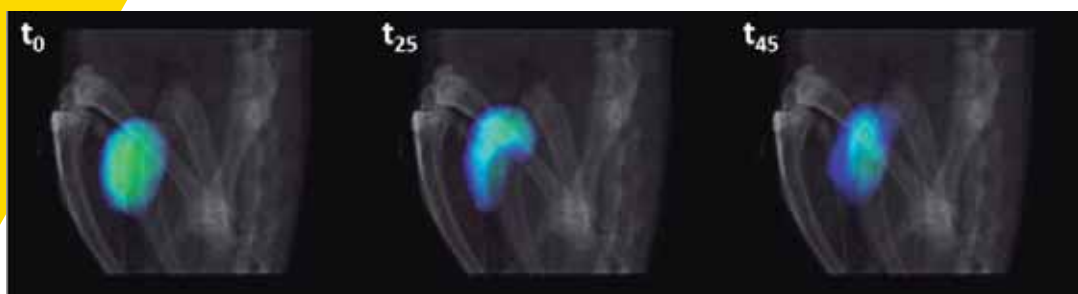
Highlights



Intraparticle Kinetics Unveil Crowding and Enzyme Distribution Effects on the Performance of Cofactor-Dependent Heterogeneous Biocatalysts

Diamanti, E; Santiago-Arcos, J; Grajales-Hernández, D; Czarniewicz, N; Comino, N; Llarena, I; Di Silvio, D; Cortajarena, AL; López-Gallego, F.
ACS Catal., 2021, 11, 15051-15067
DOI: 10.1021/acscatal.1c03760

Multidimensional kinetic analysis of immobilized enzymes is essential to understand the enzyme functionality at the interface with solid materials. However, spatiotemporal kinetic characterization of heterogeneous biocatalysts on a microscopic level and under operando conditions has been rarely approached. As a case study, we selected self-sufficient heterogeneous biocatalysts where His-tagged cofactor-dependent enzymes (dehydrogenases, transaminases, and oxidases) are co-immobilized with their corresponding phosphorylated cofactors [nicotinamide adenine dinucleotide phosphate (NAD(P)H), pyridoxal phosphate (PLP), and flavin adenine dinucleotide (FAD)] on porous agarose microbeads coated with cationic polymers. These self-sufficient systems do not require the addition of exogenous cofactors to function, thus avoiding the extensive use of expensive cofactors. To comprehend the microscopic kinetics and thermodynamics of self-sufficient systems, we performed fluorescence recovery after photobleaching measurements, time-lapse fluorescence microscopy, and image analytics at both single-particle and intraparticle levels. These studies reveal a thermodynamic equilibrium that rules out the reversible interactions between the adsorbed phosphorylated cofactors and the polycations within the pores of the carriers, enabling the confined cofactors to access the active sites of the immobilized enzymes. Furthermore, this work unveils the relationship between the apparent Michaelis-Menten kinetic parameters and the enzyme density in the confined space, eliciting a negative effect of molecular crowding on the performance of some enzymes. Finally, we demonstrate that the intraparticle apparent enzyme kinetics are significantly affected by the enzyme spatial organization. Hence, multiscale characterization of immobilized enzymes serves as an instrumental tool to better understand the in operando functionality of enzymes within confined spaces.

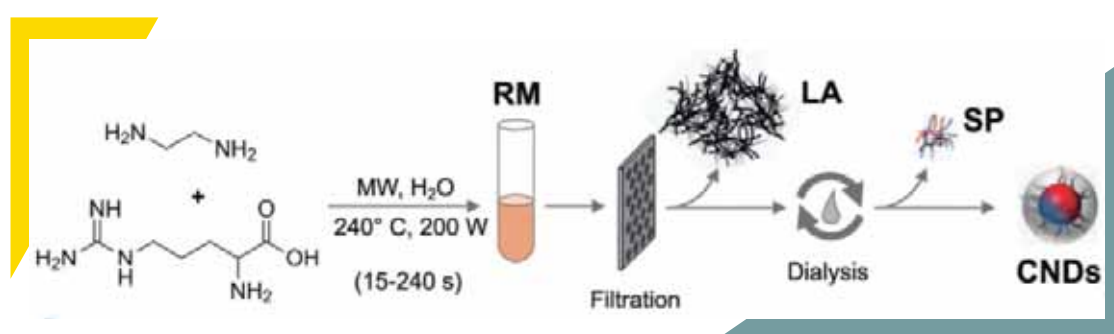


Swarming behavior and *in vivo* monitoring of enzymatic nanomotors within the bladder

Hortelao, AC; Simó, C; Guix, M; Guallar-Garrido, S; Julián, E; Vilela, D; Rejc, L; Ramos-Cabrer, P; Cossío, U; Gómez-Vallejo, V; Patiño, T; Llop, J; Sánchez, S

Sci. Robot. 2021, 6, eabd2823. DOI: 10.1126/scirobotics.abd2823

Enzyme-powered nanomotors are an exciting technology for biomedical applications due to their ability to navigate within biological environments using endogenous fuels. However, limited studies into their collective behavior and demonstrations of tracking enzyme nanomotors *in vivo* have hindered progress toward their clinical translation. Here, we report the swarming behavior of urease-powered nanomotors and its tracking using positron emission tomography (PET), both *in vitro* and *in vivo*. For that, mesoporous silica nanoparticles containing urease enzymes and gold nanoparticles were used as nanomotors. To image them, nanomotors were radiolabeled with either ^{124}I on gold nanoparticles or ^{18}F -labeled prosthetic group to urease. *In vitro* experiments showed enhanced fluid mixing and collective migration of nanomotors, demonstrating higher capability to swim across complex paths inside microfabricated phantoms, compared with inactive nanomotors. *In vivo* intravenous administration in mice confirmed their biocompatibility at the administered dose and the suitability of PET to quantitatively track nanomotors *in vivo*. Furthermore, nanomotors were administered directly into the bladder of mice by intravesical injection. When injected with the fuel, urea, a homogeneous distribution was observed even after the entrance of fresh urine. By contrast, control experiments using nonmotile nanomotors (i.e., without fuel or without urease) resulted in sustained phase separation, indicating that the nanomotors' self-propulsion promotes convection and mixing in living reservoirs. Active collective dynamics, together with the medical imaging tracking, constitute a key milestone and a step forward in the field of biomedical nanorobotics, paving the way toward their use in theranostic applications.

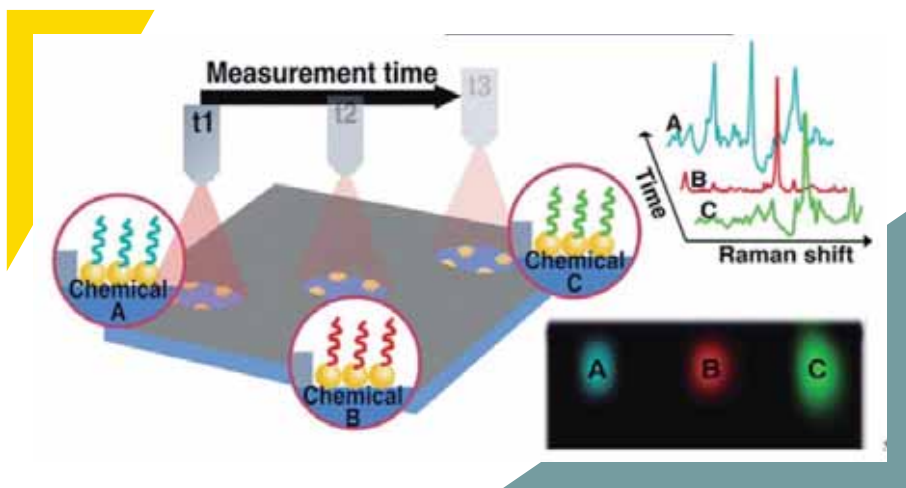


Snapshots into carbon dots formation through a combined spectroscopic approach

Rigodanza, F; Burian, M; Arcudi, F; Đorđević, L; Amenitsch, H; Prato, M.

Nat. Commun. 2021, 12, 2640. DOI: 10.1038/s41467-021-22902-w

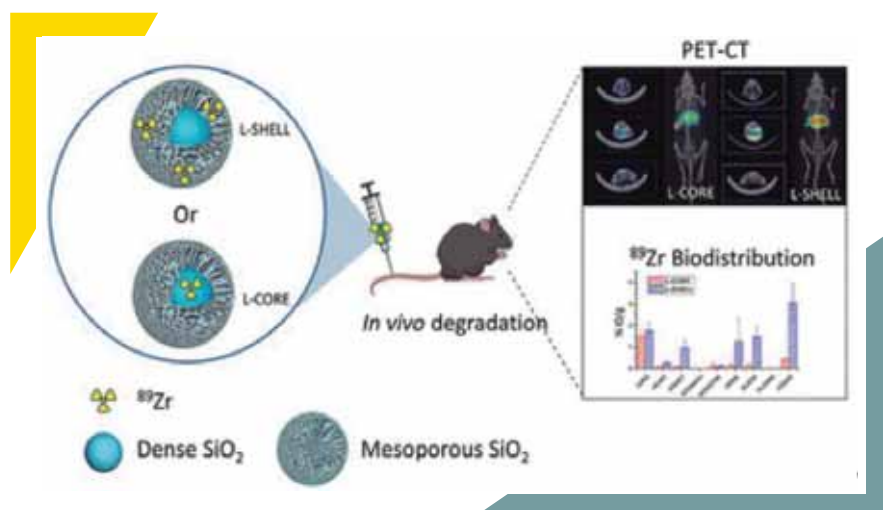
The design of novel carbon dots with ad hoc properties requires a comprehensive understanding of their formation mechanism, which is a complex task considering the number of variables involved, such as reaction time, structure of precursors or synthetic protocol employed. Herein, we systematically investigated the formation of carbon nanodots by tracking structural, chemical and photophysical features during the hydrothermal synthesis. We demonstrate that the formation of carbon nanodots consists of 4 consecutive steps: (i) aggregation of small organic molecules, (ii) formation of a dense core with an extended shell, (iii) collapse of the shell and (iv) aromatization of the core. In addition, we provide examples of routes towards tuning the core-shell design, synthesizing five novel carbon dots that all consist of an electron-dense core covered by an amine rich ligand shell.



Preventing Memory Effects in Surface-Enhanced Raman Scattering Substrates by Polymer Coating and Laser-Activated Deprotection

Plou, J; Charconnet, M; García, I; Calvo, J; Liz-Marzán, LM.
ACS Nano 2021, 15, 8984-8995.
 DOI: 10.1021/acsnano.1c01878

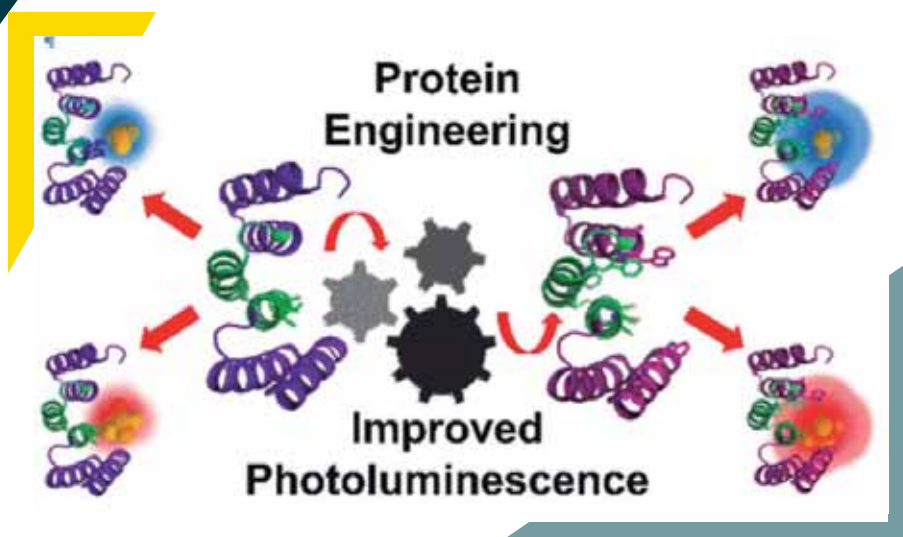
The development of continuous monitoring systems requires in situ sensors that are capable of screening multiple chemical species and providing real-time information. Such in situ measurements, in which the sample is analyzed at the point of interest, are hindered by underlying problems derived from the recording of successive measurements within complex environments. In this context, surface-enhanced Raman scattering (SERS) spectroscopy appears as a noninvasive technology with the ability of identifying low concentrations of chemical species as well as resolving dynamic processes under different conditions. To this aim, the technique requires the use of a plasmonic substrate, typically made of nanostructured metals such as gold or silver, to enhance the Raman signal of adsorbed molecules (the analyte). However, a common source of uncertainty in real-time SERS measurements originates from the irreversible adsorption of (analyte) molecules onto the plasmonic substrate, which may interfere in subsequent measurements. This so-called “SERS memory effect” leads to measurements that do not accurately reflect varying conditions of the sample over time. We introduce herein the design of plasmonic substrates involving a nonpermeable poly(lactic-co-glycolic acid) (PLGA) thin layer on top of the plasmonic nanostructure, toward controlling the adsorption of molecules at different times. The polymeric layer can be locally degraded by irradiation with the same laser used for SERS measurements (albeit at a higher fluence), thereby creating a micrometer-sized window on the plasmonic substrate available to molecules present in solution at a selected measurement time. Using SERS substrates coated with such thermolabile polymer layers, we demonstrate the possibility of performing over 10,000 consecutive measurements per substrate as well as accurate continuous monitoring of analytes in microfluidic channels and biological systems.



In Vivo Tracking of the Degradation of Mesoporous Silica through Zr-89 Radio-Labeled Core-Shell Nanoparticles

Bindini, E; Ramirez, MdA; Rios, X; Cossío, U; Simó, C; Gomez-Vallejo, V; Soler-Illia, G; Llop, J; Moya, SE.
Small, 2021, 17, 2101519.
 DOI: 10.1002/smll.202101519

While mesoporous silica nanoparticles (MSNs) are extensively studied as high-potential drug delivery platforms, the successful clinical translation of these nanocarriers strongly depends on their biodistribution, biodegradation, and elimination patterns *in vivo*. Here, a novel method is reported to follow the *in vivo* degradation of MSNs by tracking a radioactive label embedded in the silica structure. Core-shell silica nanoparticles (NPs) with a dense core and a mesoporous shell are labeled with low quantities of the positron emitter ⁸⁹Zr, either in the dense core or in the mesoporous shell. *In vivo* positron emission tomography imaging and ex vivo organ measurements reveal a remarkable difference in the ⁸⁹Zr biodistribution between the shell-labeled and the core-labeled NPs. Release of the radiotracer from shell-labeled NPs is used as a probe of the extent of silica dissolution, and a prompt release of the radioisotope is observed, with partial excretion already in the first 2 h post injection, and a slower accumulation in bones over time. On the other hand, when ⁸⁹Zr is embedded in the nanoparticle core, the biodistribution remains largely unchanged during the first 6 h. These findings indicate that MSNs have fast, hour-scale, degradation kinetics *in vivo*.

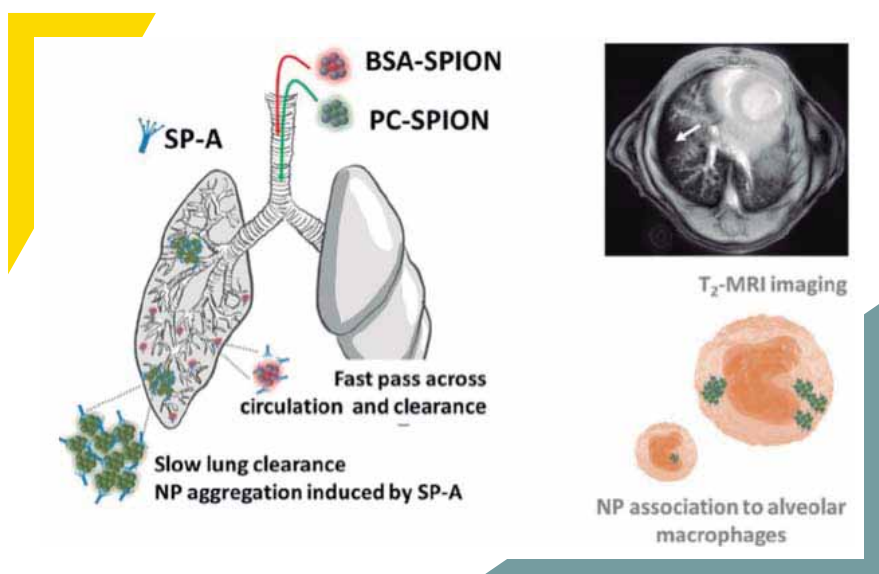


Boosting the Photoluminescent Properties of Protein-Stabilized Gold Nanoclusters through Protein Engineering

Aires, A; Sousaraei, A; Möller, M; Cabanillas-Gonzalez, J; Cortajarena, AL.

Nano Letters, 2021, 21, 9347–9353.
DOI: 10.1021/acs.nanolett.1c03768

This work reports on the use of protein engineering as a versatile tool to rationally design metal-binding proteins for the synthesis of highly photoluminescent protein-stabilized gold nanoclusters (Prot-AuNCs). The use of a single repeat protein scaffold allowed the incorporation of a set of designed metal-binding sites to understand the effect of the metal-coordinating residues and the protein environment on the photoluminescent (PL) properties of gold nanoclusters (AuNCs). The resulting Prot-AuNCs, synthesized by two sustainable procedures, showed size-tunable color emission and outstanding PL properties. In a second stage, tryptophan (Trp) residues were introduced at specific positions to provide an electron-rich protein environment and favor energy transfer from Trps to AuNCs. This modification resulted in improved PL properties relevant for future applications in sensing, biological labeling, catalysis, and optics.

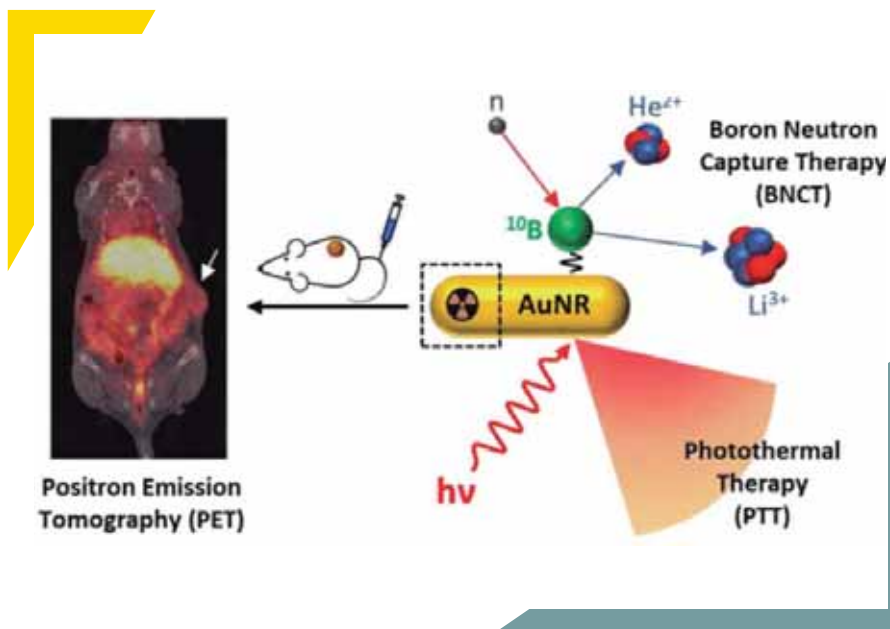


Delayed alveolar clearance of nanoparticles through control of coating composition and interaction with lung surfactant protein A

Carregal-Romero, S; Groult, H; Cañadas, O; A-Gonzalez, N; Lechuga-Vieco, AV; García-Fojeda, B; Herranz, F; Pellico, J; Hidalgo, A; Casals, C; Ruiz-Cabello, J.

Mater. Sci. Eng. C, 2021, 112551.
DOI: 10.1016/j.msec.2021.112551

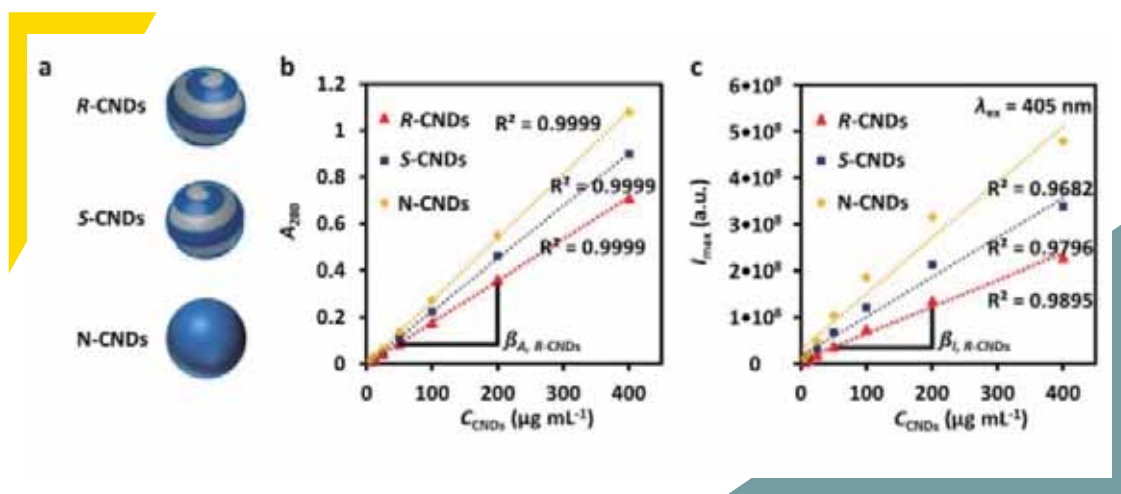
The coating composition of nanomedicines is one of the main features in determining the medicines' fate, clearance, and immunoresponse in the body. To highlight the coatings' impact in pulmonary administration, two micellar superparamagnetic iron oxide nanoparticles (SPION) were compared. These nanoparticles are similar in size and charge but have different coatings: either phosphatidylcholine (PC-SPION) or bovine serum albumin (BSA-SPION). The aim of the study was to increase the understanding of the nano-bio interaction with the cellular and non-cellular components of the lung and underline valuable coatings either for local lung-targeted drug delivery in theranostic application or patient-friendly route systemic administration. PC-SPION and BSA-SPION were deposited in the alveoli by in vivo instillation and, despite the complexity of imaging the lung, SPION were macroscopically visualized by MRI. Impressively, PC-SPION were retained within the lungs for at least a week, while BSA-SPION were cleared more rapidly. The different lung residence times were confirmed by histological analysis and supported by a flow cytometry analysis of the SPION interactions with different myeloid cell populations. To further comprehend the way in which these nanoformulations interact with lung components at the molecular level, we used fluorescence spectroscopy, turbidity measurements, and dynamic light scattering to evaluate the interactions of the two SPION with surfactant protein A (SP-A), a key protein in setting up the nanoparticle behavior in the alveolar fluid. We found that SP-A induced aggregation of PC-SPION, but not BSA-SPION, which likely caused PC-SPION retention in the lung without inducing inflammation. In conclusion, the two SPION show different outcomes from interaction with SP-A leading to distinctive fate in the lung. PC-SPION hold great promise as imaging and theranostic agents when prolonged pulmonary drug delivery is required.



In Vivo Evaluation of Multifunctional Gold Nanorods for Boron Neutron Capture and Photothermal Therapies

Pulagam, KR; Henriksen-Lacey, M; Uribe, KB; Renero-Lecuna, C; Kumar, J; Charalampopoulou, A; Facchetti, A; Protti, N; Gomez-Vallejo, V; Baz, Z; Kumar, V; Sanchez-Iglesias, A; Altieri, S; Cossio, U; Di Silvio, D; Martinez-Villacorta, AM; de Angulo, AR; Rejc, L; Liz-Marzan, LM; Llop, J
ACS Appl. Mater. Interfaces, 2021, 13, 49589-49601
 DOI: 10.1021/acsami.0c17575

The incidence and mortality of cancer demand more innovative approaches and combination therapies to increase treatment efficacy and decrease off-target side effects. We describe a boron-rich nanoparticle composite with potential applications in both boron neutron capture therapy (BNCT) and photothermal therapy (PTT). Our strategy is based on gold nanorods (AuNRs) stabilized with polyethylene glycol and functionalized with the water-soluble complex cobalt bis(dicarbollide) ($[3,3'\text{-Co}(1,2\text{-C}_2\text{B}_9\text{H}_{11})_2]^-$), commonly known as COSAN. Radiolabeling with the positron emitter copper-64 (^{64}Cu) enabled *in vivo* tracking using positron emission tomography imaging. ^{64}Cu -labeled multifunctionalized AuNRs proved to be radiochemically stable and capable of being accumulated in the tumor after intravenous administration in a mouse xenograft model of gastrointestinal cancer. The resulting multifunctional AuNRs showed high biocompatibility and the capacity to induce local heating under external stimulation and trigger cell death in heterogeneous cancer spheroids as well as the capacity to decrease cell viability under neutron irradiation in cancer cells. These results position our nanoconjugates as suitable candidates for combined BNCT/PTT therapies.



Influence of the chirality of carbon nanodots on their interaction with proteins and cells

Yan, HJ; Cacioppo, M; Megahed, S; Arcudi, F; Dordevic, L; Zhu, DC; Schulz, F; Prato, M; Parak, WJ; Feliu, N
Nat. Commun., 2021, 12, 7208 DOI: 10.1038/s41467-021-27406-1

Carbon nanodots with opposite chirality possess the same major physicochemical properties such as optical features, hydrodynamic diameter, and colloidal stability. Here, a detailed analysis about the comparison of the concentration of both carbon nanodots is carried out, putting a threshold to when differences in biological behavior may be related to chirality and may exclude effects based merely on differences in exposure concentrations due to uncertainties in concentration determination. The present study approaches this comparative analysis evaluating two basic biological phenomena, the protein adsorption and cell internalization. We find how a meticulous concentration error estimation enables the evaluation of the differences in biological effects related to chirality.



Mechanistic Insights into the Light-Driven Catalysis of an Immobilized Lipase on Plasmonic Nanomaterials

de Barros, HR; García, I; Kuttner, C; Zeballos, N; Camargo, PHC; de Torresi, SIC; López-Gallego, F; Liz-Marzán, LM.

ACS Catalysis, 2021, 11, 414. DOI: 10.1021/acscatal.0c04919

The use of light as an external stimulus to control the enzyme activity is an emerging strategy that enables accurate, remote, and noninvasive biotransformations. In this context, immobilization of enzymes on plasmonic nanoparticles offers an opportunity to create light-responsive biocatalytic materials. Nevertheless, a fundamental and mechanistic understanding of the effects of localized surface plasmon resonance (LSPR) excitation on enzyme regulation remains elusive. We herein investigate the plasmonic effects on biocatalysis using Au nanospheres (AuNSp) and nanostars (AuNST) as model plasmonic nanoparticles, lipase from *Candida antarctica* fraction B (CALB) as a proof-of-concept enzyme, and 808 nm as near-infrared light excitation. Our data show that LSPR excitation enables an enhancement of 58% in the enzyme activity for CALB adsorbed on AuNST, compared with the dark conditions. This work shows how photothermal heating over the LSPR excitation enhances the CALB activity through favoring product release in the last step of the enzyme mechanism. We propose that the results reported herein shed important mechanistic and kinetic insights into the field of plasmonic biocatalysis and may inspire the rational development of plasmonic nanomaterial-enzyme hybrids with tailored activities under external light irradiation.

Cover Pages



Grafting density induced reentrant disorder-order-disorder transition in planar di-block copolymer brushes

Capone, B; Likos, CN; Coluzza, I.

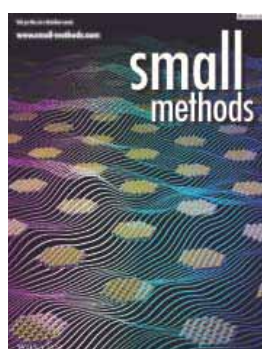
Soft Matter, 2021, 17, 4719-4729



3D Printable Conducting and Biocompatible PEDOT-graft-PLA Copolymers by Direct Ink Writing

Dominguez-Alfaro, A; Gabirondo, E; Alegret, N; De León-Almazán, CM; Hernandez, R; Vallejo-Illarramendi, A; Prato, M; Mecerreyes, D.

Macromol. Rapid Commun. 2021, 42, 2170047



Mechanically Tunable Lattice-Plasmon Resonances by Templated Self-Assembled Superlattices for Multi-Wavelength Surface-Enhanced Raman Spectroscopy

Charconnet, M; Kuttner, C; Plou, J; Garcia-Pomar, JL; Mihi, A; Liz-Marzán, LM; Seifert, A.

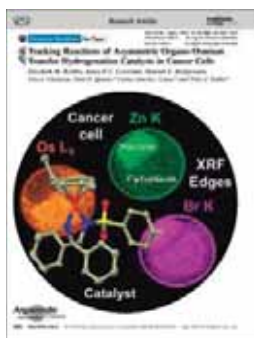
Small Methods. 2021, 5, 2100453



Novel Core-Shell Polyamine Phosphate Nanoparticles Self-Assembled from PEGylated Poly(allylamine hydrochloride) with Low Toxicity and Increased *In Vivo* Circulation Time

Andreozzi, P; Simó, C; Moretti, P; Porcel, JM; Lüdtkke, TU; Ramirez, MdA; Tamberi, L; Marradi, M; Amenitsch, H; Llop, J; Ortore, MG; Moya, SE.

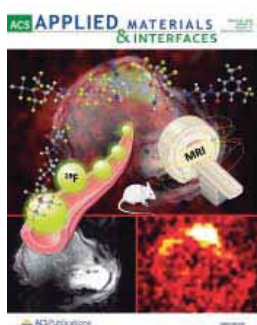
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Tracking Reactions of Asymmetric Organo-Osmium Transfer Hydrogenation Catalysts in Cancer Cells

Bolitho, EM; Coverdale, JPC; Bridgewater, HE; Clarkson, GJ; Quinn, PD; Sánchez-Cano, C; Sadler, PJ.

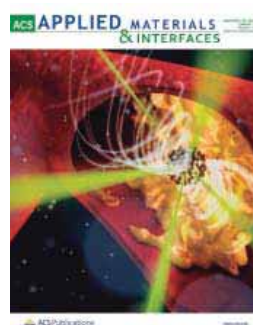
Angew. Chem. Int. Ed. 2021, 60, 6462-6472



Fluorine Labeling of Nanoparticles and *In Vivo* F-19 Magnetic Resonance Imaging

Arango, JM; Padró, D; Blanco, J; López-Fernández, S; Castellnou, P; Villa-Valverde, P; Ruiz-Cabello, J; Martín, A; Carril, M.

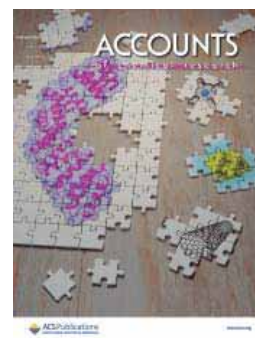
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HAP-Multitag, a PET and Positive MRI Contrast Nanotracer for the Longitudinal Characterization of Vascular Calcifications in Atherosclerosis

Pellico, J; Fernández-Barahona, I; Ruiz-Cabello, J; Gutiérrez, L; Muñoz-Hernando, M; Sánchez-Guisado, MJ; Aiestaran-Zelaia, I; Martínez-Parra, L; Rodríguez, I; Bentzon, J; Herranz, F.

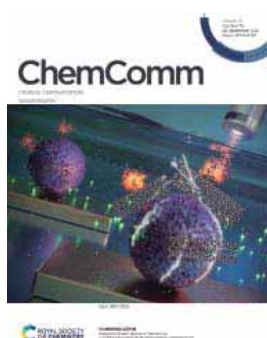
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Engineered Repeat Protein Hybrids: The New Horizon for Biologic Medicines and Diagnostic Tools

Uribe, KB; Guisasaola, E; Aires, A; López-Martínez, E; Guedes, G; Sasselli, IR; Cortajarena, AL.

Acc. Chem. Res. 2021, 54, 4166-4177



Electrochemiluminescent immunoassay enhancement driven by carbon nanotubes

Rebecani, S; Wetzl, C; Zamolo, V; Criado, A; Valenti, G; Paolucci, F; Prato, M.

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Turning the Light on Phenols: New Opportunities in Organic Synthesis

Bartolomei, B; Gentile, G; Rosso, C; Filippini, G; Prato, M.

Eur. J. Chem 2021, 27, 16062-16070



Plasmonic metal-organic frameworks

Zheng, G; Pastoriza-Santos, I; Pérez-Juste, J; Liz-Marzán, LM.

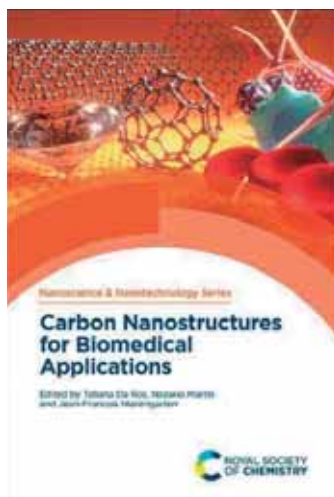
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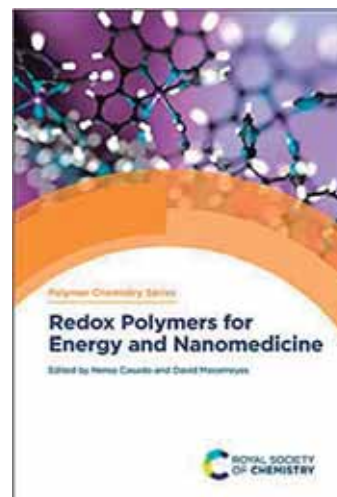
CHAPTER 8 Biomedical applications of carbon nanotubes

Mancino, D; Alegret N.
Handbook of Carbon-Based Nanomaterials, Elsevier, 2021, pp. 365-398
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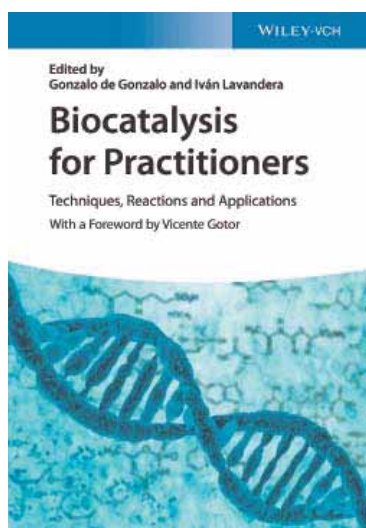
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Peña, B; Alegret, N; Laughter, M; Taylor, MRG; Mestroni, L; Prato, M.
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CHAPTER 10 Conductive Polymers Building 3D Scaffolds for Tissue Engineering

Alegret, N; Domínguez-Alfaro, A; Mecerreyes, D.
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ISBN: 978-1-78801-871-5



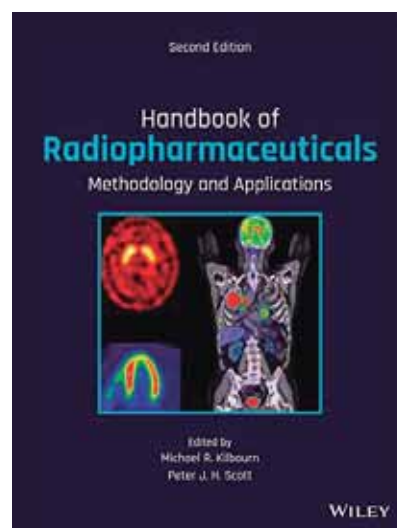
CHAPTER 3 Immobilization Techniques for the Preparation of Supported Biocatalysts: Making Better Biocatalysts Through Protein Immobilization

Rocha-Martín, J; Betancor, L; López-Gallego, F.
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Cells and Materials for Disease Modeling and Regenerative Medicine

Abarrategi, A; Lanceros-Mendez, S.
2021, MDPI
Reprint of the Special Issue Cells and Materials for Disease Modeling and Regenerative Medicine that was published in IJMS)
ISBN: 978-3-0365-0262-5



CHAPTER 6 Synthesis of ¹³N- and ¹⁵O-labeled Radiopharmaceuticals.

Pulagam KR, Gómez-Vallejo V, López-Gallego F, Rejc L, Llop J;
Handbook of Radiopharmaceuticals: Methodology and Applications Wiley-VCH, 2021, pp. 109 - 142
ISBN: 978-1-119-50054-4

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- ✓ Bolitho, EM; Sanchez-Cano, C; Shi, H; Quinn, PD; Harkiolaki, M; Imberti, C; Sadler, PJ Single-Cell Chemistry of Photoactivatable Platinum Anticancer Complexes. *J. Am. Chem. Soc.* 2021, 143, 20224-20240
- ✓ Uribe, KB; Chemello, K; Larrea-Sebal, A; Benito-Vicente, A; Galicia-García, U; Bourane, S; Jaafar, AK; Lambert, G; Martín, C A Systematic Approach to Assess the Activity and Classification of PCSK9 Variants. *Int. J. Mol. Sci.* 2021, 22, 13602-13617
- ✓ Gomez, IJ; Alegret, N; Domínguez-Alfaro, A; Sulleiro, MV Recent Advances on 2D Materials towards 3D Printing. *Chemistry* 2021, 3, 1314-1343
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- ✓ Yan, HJ; Cacioppo, M; Megahed, S; Arcudi, F; Dordevic, L; Zhu, DC; Schulz, F; Prato, M; Parak, WJ; Feliu, N Influence of the chirality of carbon nanodots on their interaction with proteins and cells. *Nat. Commun.* 2021, 12, 7208
- ✓ Larrea-Sebal, A; Benito-Vicente, A; Fernández-Higuero, JA; Jebari-Benslaiman, S; Galicia-García, U; Uribe, KB; Cenarro, A; Ostolaza, H; Civeira, F; Arrasate, S; González-Díaz, H; Martín, C MLb-LDLr A Machine Learning Model for Predicting the Pathogenicity of LDLr Missense Variants. *Jacc-basic Transl Sc* 2021, 6, 815-827
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TRAINING



In 2021 there have **63** active **PhD tesis, 9** of them defended during the year. Our researchers performed **12** secondments at collaborating institutions, and we hosted **97** stays of visiting researchers. The Center has organized **34** seminars, **3** workshops/conferences and our researchers have participated as co-organizers of **5** international conferences.



Postdoctoral Program

Postdoctoral researchers are hired at CIC biomaGUNE for periods of 1-5 years. During this time, postdoctoral researchers broaden and deepen their research skills and boost their career perspectives so they can become independent research scientists. Researchers gain training-through-research, by means of individual personalized projects under the guidance of a group leader and receive hands-on-training for developing scientific skills and transferrable skills.

PhD Program

The objective of CIC biomaGUNE's PhD Program is to provide PhD students with top quality multidisciplinary training at the interface between biology, chemistry, nanobiotechnology and materials science. The students benefit from international training and are exposed to different research areas. The training program offers weekly lectures by leading scientists, technical training courses on a broad range of scientific techniques and instrumentation, opportunities for short stays at renowned international research institutions, as well as complementary training in soft skills to prepare doctoral candidates to become highly qualified, autonomous and skilled professionals. The joint training of PhD candidates fosters closer ties and cooperation between research groups and researchers of the institutions involved.

In partnership with the **University of the Basque Country (UPV/EHU)**, CIC biomaGUNE participates in the following Doctoral programs:

- ✓ Synthetic & Industrial Chemistry
- ✓ Applied Chemistry & Polymeric Materials
- ✓ Molecular Biology & Biomedicine
- ✓ Medicine & Surgery
- ✓ Biomedical Research

Co-supervised PhD Scheme

Since 2016, CIC biomaGUNE is running a program of co-supervised (and co-funded) PhD theses, in collaboration with other research institutions, technology centers and enterprises in the Basque Country. In 2021, 29 PhD theses were co-directed with the following institutions:

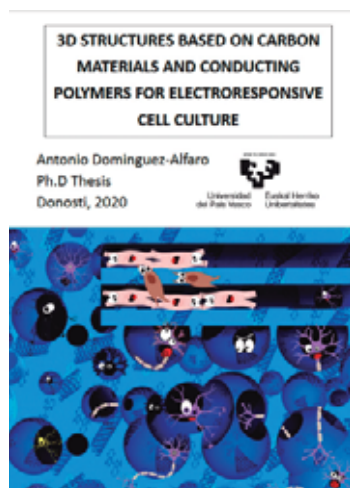
- ✓ UPV-EHU
- ✓ POLYMAT- Basque Center for Macromolecular Design & Engineering
- ✓ ACHUCARRO - Basque Center for Neuroscience
- ✓ BIOFISIKA- Basque Center for Biophysics
- ✓ DIPC – Donostia International Physics Center
- ✓ CIC bioGUNE
- ✓ CIC nanoGUNE
- ✓ IIS BIOCRUCES
- ✓ IIS BIODONOSTIA
- ✓ TECNALIA
- ✓ GAIKER
- ✓ CIDETEC

Industrial PhD Scheme

CIC biomaGUNE has agreements with industrial partners, to conduct industrially oriented PhD research projects.

Completed PhD Theses

During 2021, 9 students obtained their PhD at CIC biomaGUNE.



Antonio Domínguez-Alfaro

3D structures based on carbon materials and conducting polymers for electroresponsive cell cultures

Supervisors:

Prof. David Mecerreyes (POLYMAT) & Prof. Maurizio Prato (CIC biomaGUNE)

Defense Date: 13/01/2021



Rafael López Moreno

Estudio de la diversidad y estabilidad de diferentes priones recombinantes infecciosos para dilucidar los mecanismos moleculares que rigen el fenómeno de cepa

Supervisors:

Prof. Jokin Castilla (CIC bioGUNE) & Dr. Niels C. Reichardt (CIC biomaGUNE)

Defense Date: 28/05/2021



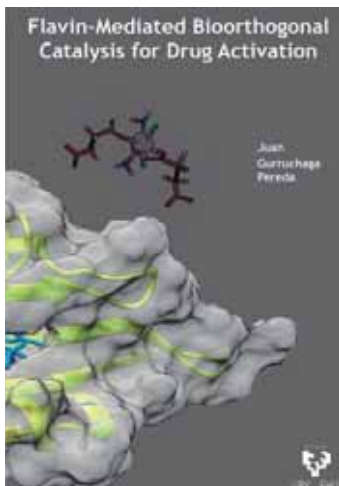
Mathias Charconnet

Self-assembly and optical properties of gold nanoparticle superlattices for surface-enhanced Raman spectroscopy

Supervisors:

Prof. Andreas Seifert (CIC nanoGUNE) & Prof. Luis M. Liz-Marzán (CIC biomaGUNE)

Defense Date: 07/06/2021



Juan Gurruchaga

Flavin-mediated Bioorthogonal Catalysis for Drug Activation

Supervisors:

Dr. Luca Salassa (DIPC) & Prof. Aitziber L. Cortajarena (CIC biomaGUNE)

Defense Date: 07/10/2021



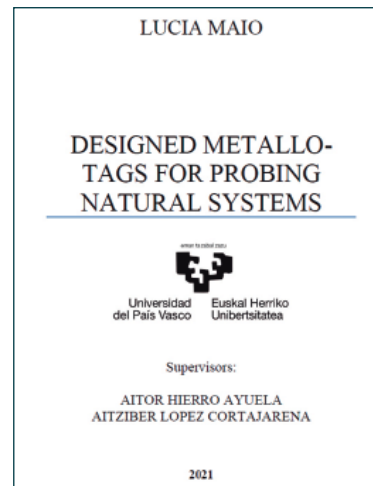
María de los Ángeles Ramírez

Diseño, síntesis y caracterización de nanopartículas de sílice mesoporosa como sistemas de liberación controlada y sus potenciales aplicaciones biomédicas

Supervisors:

Dr. Galo Soler-Illia (UNSAM) & Dr. Sergio Moya (CIC biomaGUNE)

Defense Date: 08/10/2021



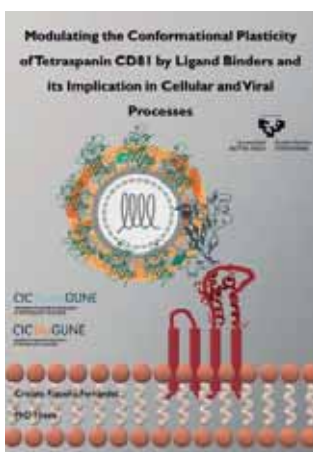
Lucía Maio

Designed Metallo-Tags for Probing Natural Systems

Supervisors:

Dr. Aitor Hierro (CIC bioGUNE) & Prof. Aitziber L. Cortajarena (CIC biomaGUNE)

Defense Date: 26/11/2021



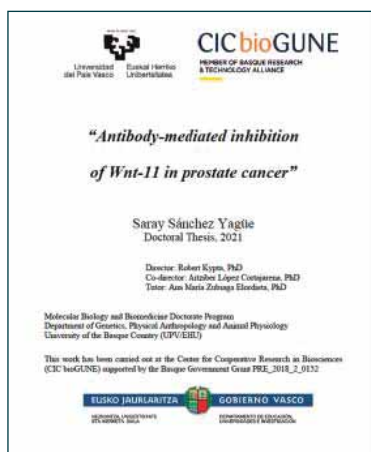
Cristina Risueño

Modulating the conformational plasticity of tetraspanin CD81 by ligand-binders and its implication in cellular and viral processes

Supervisors:

Dr. Nicola Abrescia (CIC bioGUNE) & Dr. Ivan Coluzza (CIC biomaGUNE)

Defense Date: 01/12/2021



Saray Sánchez Yagüe

Antibody-mediated inhibition of Wnt-11 in prostate cancer

Supervisors:

Prof. Aitziber L. Cortajarena (CIC biomaGUNE) & Dr. Robert Kypta (CIC bioGUNE)

Defense Date: 13/12/2021



Rosanna Passannante

Pharmacokinetic evaluation of new drugs with potential application in Duchenne muscular dystrophy using Positron Emission Tomography and complementary techniques

Supervisors:

Dr. Jordi Llop (CIC biomaGUNE) & Prof. Jesús María Aizpurua (UPV-EHU)

Defense Date: 21/12/2021

Training Initiatives for Undergraduate Students

MASTER'S FELLOWSHIP PROGRAM

CIC biomaGUNE has agreements with several universities (which are the degree-grating bodies) in different Master's programs.

Additionally, in partnership with the **University of the Basque Country (UPV/EHU)**, CIC biomaGUNE researchers participate in the following MSc courses by providing lectures and direction of master thesis:

- ✓ Molecular Biology & Biomedicine
- ✓ Nanoscience
- ✓ Chemistry & Polymers

In 2019, the **Master's Fellowship Program** was launched with the support of the Maria de Maeztu grant. The program aims at offering scholarships to highly qualified master students to carry out their Master's Project. Since then **5 fellowships have been granted**.

SUMMER RESEARCH PROGRAM

During the summer period, undergraduate students with a background in Chemistry, Biology and Materials Science are hosted at CIC biomaGUNE's laboratories. The undergraduates work alongside pre- and post-doctoral researchers and receive high level training while working on a research project, but also by attending weekly group meetings and seminars. At the end of the traineeship, the students are required to prepare a short report and a presentation summarizing their research and results.

In 2019, the **Summer Research Program** was launched with the support of the Maria de Maeztu grant. The program aims at offering scholarships to highly qualified students in their second and third years of study, to carry out research stays at CIC biomaGUNE during summer. **Since 2019 13 fellowships have been granted**. Unfortunately, due to the coronavirus outbreak, it was not possible to host any summer fellows in 2020.

VOCATIONAL TRAINING PROGRAM

CIC biomaGUNE has agreements with **CPES, CESA, BHIP, Don Bosco, CEBANC** and **Colegio Inmakulada Ikastetxea**, Centers for Intermediate and Superior level vocational training in the fields of Chemistry or Biosciences to host training internships of students.

Several training placements take place every year at different laboratories of the Center.

Selected undergraduates are mentored and supervised by postdoctoral researchers or PhD students and receive hands-on training.

Research Secondments

In the framework of different national and international projects, CIC biomaGUNE has established collaborations with international institutions to **second** and **host research stays of PhD students and postdoctoral researchers**. During 2021, our researchers performed 12 secondments at collaborating partners and we hosted **97** stays of visiting researchers.

	2017	2018	2019	2020	2021
Research stays from CIC biomaGUNE	19	11	23	16	12
Research stays to CIC biomaGUNE	92	84	110	86*	97
• Experienced Researchers Visiting Professors	1	2	12	10	7
• Erasmus placements	7	2	8	1	6
• Summer placements	6	6	15		17
• Vocational Training	5	3	5	8	6

* Many of the visits in 2020 were interrupted due to the pandemic situation

Seminars and Internal Training

CIC biomaGUNE runs an annual program of scientific seminars, which includes:

- ✓ **International seminars** delivered by internationally recognized researchers of varying scientific backgrounds and fields.
- ✓ **Postdoctoral seminars** delivered by selected postdoctoral fellows to share progress in each of our laboratories to the rest of the Center.
- ✓ **PhD seminars** delivered by PhD students of the Center.
- ✓ **Training seminars** delivered by CIC biomaGUNE's PIs or Platform Managers, aimed at strengthening the technical training program and soft skills training.

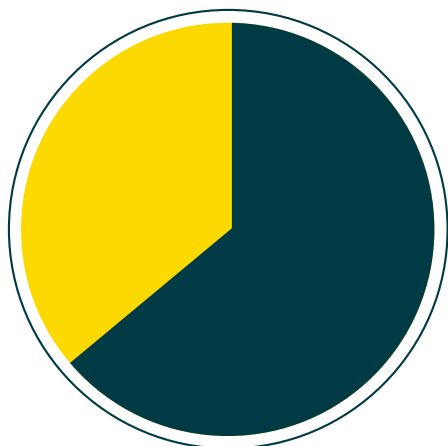
These actions aim at discussing recent developments, fostering internal and external interactions and paving the way toward future collaborations and contributing to the career development of our researchers. Altogether, these programs contribute to the career development of our researchers. During 2021, **34** Seminars and **114** Internal Scientific & Technology Trainings have been delivered with a total of **1566** participants reached.

Training Type	Number of events
CIC biomaGUNE Seminar	25
PhD Seminar	1
Postdoctoral Seminar	2
Soft Skills Seminar	5
Christmas Lecture	1
Internal Scientific & Technology Trainings	114

INVITED SPEAKERS

34

36%



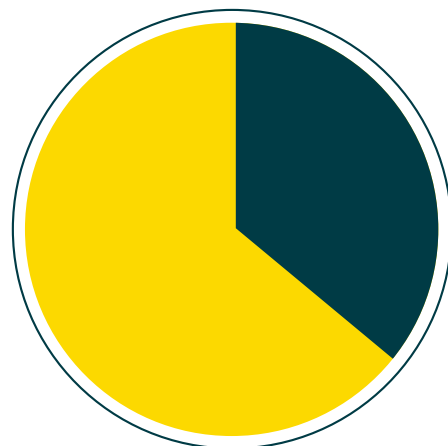
64%



TRAINING PARTICIPANTS

1566

61%



39%



13/01/2021

RNA-processing in health and disease: new experimental and therapeutic approaches

Dr. Lorea Blázquez

Biodonostia

03/03/2021

Cellular senescence, the Achilles heel of ageing and disease

Dr. Sofia Ferreira

University of Edinburgh

05/05/2021

Stabilizing and Functionalizing Inorganic Nanocrystals via Metal-Ligand Coordination Interactions

Prof. Hedi Mattoussi

Florida State University

27/01/2021

Biological Fate of Soft Nanomaterials: A Physico-Chemical and Translocation Study

Dr. Marta Martínez-Moro

CIC biomaGUNE

10/03/2021

Custom hydrophilic polymer materials

Dr. Alberto Gallardo

Institut de Ciència y Tecnologia de Polímeros-CSIC

26/05/2021

Imaging and targeting (pre) metastatic niches: implications for cancer immunotherapy

Dr. Marisol Soengas

Spanish National Cancer Research Center (CNIO)

10/02/2021

3D structures based on carbon materials and conducting polymers for electroresponsive cell culture

Dr. Antonio Domínguez-Alfaro

CIC biomaGUNE

24/03/2021

Organ on chip: Microfluidic devices to mimic the tissue microenvironment and some possible applications in cancer

Prof. Ignacio Ochoa-Garrido

University of Zaragoza

02/06/2021

Self-assembly and optical properties of gold nanoparticle superlattices for surface-enhanced Raman spectroscopy

Mathias Charconnet

CIC biomaGUNE

24/02/2021

Using polyoxometalates as multifunctional coatings, scaffolds and supramolecular self-assembly tools

Dr. Scott G. Mitchell

Instituto de Nanociencia y Materiales de Aragón (INMA-CSIC)

21/04/2021

Nanomaterials and molecular imaging for the non-invasive diagnosis of cardiovascular diseases

Dr. Fernando Herranz

Institute of Medicinal Chemistry (IQM-CSIC)

16/06/2021

Protein-hybrid nanomaterials for biomedical applications

Dr. Antonio Aires

CIC biomaGUNE

28/04/2021

Applications of Oligosaccharides in Nanomedicine strategies

Dr. Hugo Groult

La Rochelle University

23/06/2021

Diffuse myocardial fibrosis in chronic heart failure: A problem yet to be solved

Dr. Arantxa González-Miqueo

CIMA Universidad de Navarra

30/06/2021

Cross-grating phase microscopy for nanophotonics and biology

Prof. Guillaume Baffou

Institut Fresnel, CNRS

02/07/2021

Chiral sensing with semiconductor nanophotonics

Dr. Alberto G. Curto

Eindhoven University of Technology

07/07/2021

Chemical precision tools to understand protein O-glycosylation

Dr. Ben Schumann

The Francis Crick Institute

14/07/2021

From nanoparticle heat generation to temperature determination: a day in the Bionanoplasmonics Lab

Dr. Carlos Renero Lecuna

CIC biomaGUNE

21/07/2021

Evaluation of global and local induced temperature therapeutic profiles in magnetic and photo-thermal nanoparticles for biomedical applications

Dr. Ana Espinosa

IMDEA Nanociencia

28/07/2021

Novel Approaches for the treatment of Heart Failure

Prof. Beatriz Pelacho

CIMA Universidad de Navarra

04/08/2021

Brief course on entrepreneurship

Prof. Nicholas Kotov

University of Michigan

08/09/2021

Plasmonics for Trace Detection and Imaging

Prof. Zachary D. Schultz

The Ohio State University

15/09/2021

Multimodal molecular and functional imaging in pulmonary hypertension

Dr. Jesús Ruiz-Cabello

CIC biomaGUNE

05/10/2021

The start-up route to exploit your research results

Marcos Simón

CIC biomaGUNE

13/10/2021

Integrating graphene into enzyme-based amperometric biosensors

Dr. Alessandro Silvestri

CIC biomaGUNE

02/11/2021

Water purification

Jorge Nicolás

Merck Live Science

03/11/2021

Nanoparticle-based imaging agents for molecular imaging and particle tracking applications

Dr. Juan Pellico-Saez

King's College London

09/11/2021

Fluorescence microscopy: techniques and applications in

CIC biomaGUNE

Dr. Irantzu Llarena

CIC biomaGUNE

10/11/2021

Plasmonic Nanoparticle-MOF nanohybrids for Sensing Applications

Prof. Isabel Pastoriza-Santos

University of Vigo

17/11/2021

Hybrid nanoparticles protected by fluorinated ligands: features and potentialities

Prof. Lucia Pasquato

University of Trieste

24/11/2021

Ancestral proteins: Evolution meets Biotechnology

Prof. Raul Perez-Jimenez

CIC nanoGUNE

29/11/2021

Protocol of prevention and action against workplace, sexual, and gender-based harassment

Sortzen

01/12/2021

Heteroplasmy of wild type mitochondrial DNA variants in mice causes metabolic heart disease with pulmonary hypertension and frailty

Dr. Ana Victoria Lechuga-Vieco

University of Oxford

16/12/2021

Advanced therapies and precision diagnostics for the postpandemic era

Dr. Asís Palazón

CIC bioGUNE

Scientific Workshops/Conferences

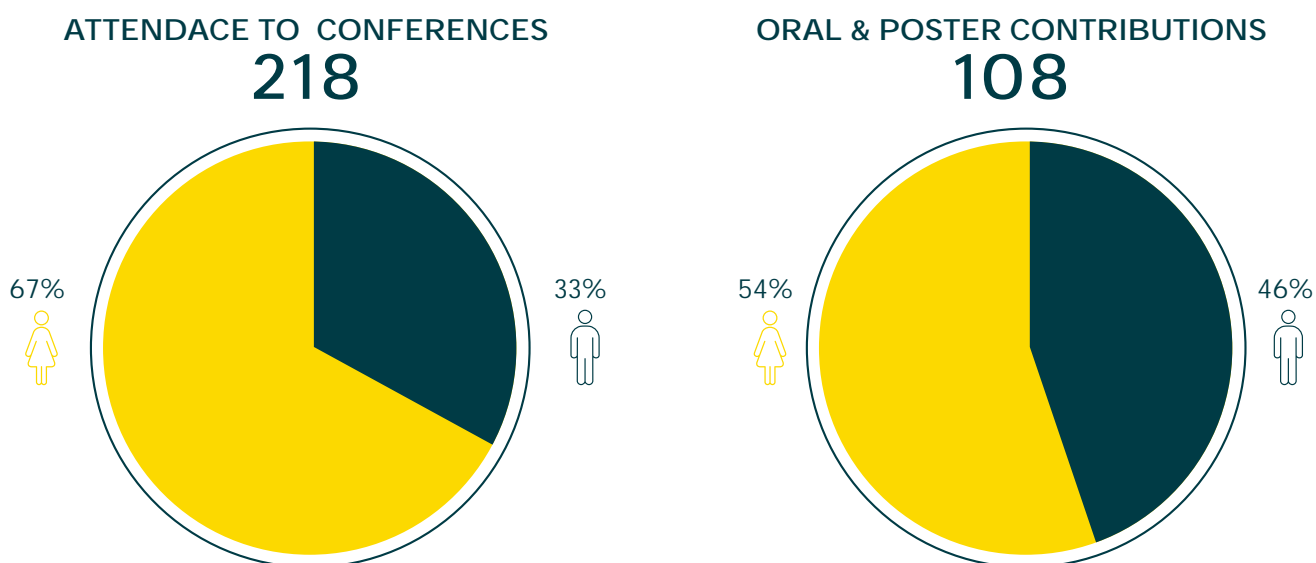
CIC biomaGUNE seeks to enhance its national and international visibility and reputation by organizing conferences, workshops and seminars that share knowledge about the latest research and advances in the field of biomaterials. The following events have been organized during 2021:

- ✓ **3rd CIC biomaGUNE PhD Day**, Organizer: **CIC biomaGUNE Research Associates**, Donostia-San Sebastián, **October 14-15**.
- ✓ **3rd Glycobasque Meeting**, Organizer: **Niels Reichardt**, Donostia-San Sebastián, **November 11-12**.
- ✓ **15th CIC biomaGUNE Anniversary**, Organizer: **CIC biomaGUNE**, Donostia-San Sebastián, **December 14**.

Our researchers have also chaired or co-organized a number of international symposia as listed below:

- ✓ **"5th Annual Meeting of Research in Pulmonary Hypertension"**, CIC biomaGUNE organizer: **Jesús Ruiz Cabello**, Madrid, **February 28**.
- ✓ Symposia in the **ACS Spring National Meeting**, CIC biomaGUNE organizer: **Wolfgang Parak**, Online, **April 5-16**.
- ✓ **NanoTech Poland 2021**, CIC biomaGUNE member of the international advisory board: **Luis M. Liz-Marzán**, Online, **June 9-11**.
- ✓ **Nanomaterials in Medicine, Nanotoxicology and Nanoregulation** symposium in the XIX BMRS Meeting of the Brazilian Materials Society, CIC biomaGUNE co-organizer: **Sergio Moya**, Online, **August 30-September 3**.
- ✓ Symposia in the **ACS Fall National Meeting**, CIC biomaGUNE organizer: **Wolfgang Parak**, Online, **August 22-26**.

The participation of CIC biomaGUNE personnel to events is summarized below:



OUTREACH



One of the strategic objectives of CIC biomaGUNE is the communication and dissemination of knowledge within and beyond the academic community.

Our commitment toward dissemination and outreach has been strengthened, in particular to promote STEAM careers in young girls and visibility of women in science, (see detailed list of activities at: <https://www.cicbiomagune.es/outreach>).

During **2021**, **44** outreach activities were organized including open-doors/visits by high-school and university students, **19** of these activities aimed to promote STEAM careers in young girls and improve visibility of women in science.

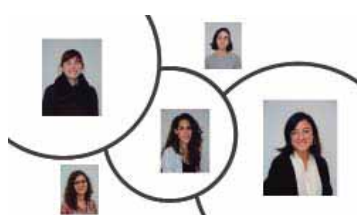
Activities include the active participation in the following annual events: International Day of Women and Girls in Science – Emakumeak Zientzian (together with 17 Basque research Centers), Pint of Science, Inspira, Innovation Week, among others.

EMAKUMEAK ZIENTZIAN



Since 2017 CIC biomaGUNE participates together with CIC nanoGUNE, the Materials Physics Centre (CFM CSIC-UPV/EHU), the Donostia International Physics Center (DIPC), Biodonostia, UPV-EHU, Tecnun-School of Engineering, CEIT, POLYMAT, Eureka Science Museum and Elhuyar in the **EMAKUMEAK ZIENTZIAN** event on the occasion of the celebration on February 11 of the “International Day of Women and Girls in Science”. These organizations have come together to commemorate this day celebrating a series of events that aim to make visible the activity of women in science, break with the typically male roles attributed to scientific-technical activities and encourage the choice of scientific careers among girls and teenagers. The activities organized included: Activities for **5th elementary grade** students, colloquiums about **past and present women scientists**, **women and science exhibition**, practical workshops for retired women, seminars by women scientists on **Career development outside academia** who gave their view on switching career from academia to industry, prospects, and outcomes, **YouTube videos** on laboratory experiments, etc.

INTERNATIONAL DAY OF WOMEN AND GIRLS IN SCIENCE



Women researchers from CIC biomaGUNE participate every year in the ‘Women and Girls in Science’ campaign organized by the Basque Technology Park Network on the occasion of the celebration on February 11 of the “International Day of Women and Girls in Science”. This campaign aims to make visible the female talent working in companies and centers of the Technology Parks of the Basque Country.

PINT OF SCIENCE



This initiative brings Science to local pubs, thereby breaking down the barriers that separate science from society.

CIC biomaGUNE researchers have taken active part in the organization of the Pint of Science event in San Sebastián during 5 editions.

INSPIRA



The **INSPIRA project** is a pioneering project in the Basque Country for the promotion of the scientific-technological vocation (STEAM: Science, Technology, Engineering, Arts and Maths) among girls.

The mentors accompany students during a period of two months with the following aims:

- Provide new references of nearby women technologists.
- For boys and girls to discover the STEAM professions.
- Raise awareness of the need for the development of the country to occur between men and women.
- Sensitize and guide on the career in technology.
- Make visible and value women technologists.

ENCOUNTER OF SCIENTIFIC LIVES



CIC biomaGUNE participates in the "Encuentro de Vidas Científicas" organized by Eureka! Zientzia Museoa, located in the Gipuzkoa Science Park. This activity is directed to 4th elementary grade and bachelor students with the aim of boosting scientific vocations. The objective is to create a space where students can speak, ask questions and exchange opinions directly with various professionals from different scientific and technological fields. Thus, students who have in mind to study science related studies, are able to find out about future employment opportunities, ask questions about what it means to enrol to certain studies, detect possible difficulties to be encountered, etc.

"Donostia WeekINN" INNOVATION WEEK



CIC biomaGUNE participates since 2016 at the Innovation Week, Donostia WeekINN, an initiative of the San Sebastián city council, whose objectives are:

- To raise awareness about the importance of innovation.
- To train and bring knowledge, share, learn, etc.
- To recognize and make visible different organizations from the city that have an orientation towards Innovation.

Open Days & Visits

CIC biomaGUNE regularly receives visits from high-school and university students who come to have a closer look at our activity. These visits typically include a lecture about biomaterials in the context of life sciences, an open discussion with CIC biomaGUNE researchers, and a guided tour to six technical facilities/laboratories (Nanoparticle synthesis platform, Confocal Microscopy, Radiochemistry platform, Molecular Imaging Facility, Scanning Electron Microscopy, Atomic Force Microscopy). The program of visits is run by **Ana Sánchez-Iglesias, Marco Möller, Daniel Padró** and **Vanessa Gómez** with the support from other Platform Managers as well as PhDs, Postdocs and Principal Investigators. Unfortunately, this activity has been severely hindered by the pandemic situation in 2020 and 2021.

UNDEGRADUATE & HIGHSCHOOL VISITS

2015	7
2016	7
2017	12
2018	9
2019	9
2020	4
2021	1






Communications

CIC biomaGUNE is committed to disseminating research results and other news, not only to the scientific community but also to the general public. Our presence at social media has remained with an increase of the number of followers/connections.

MEDIA RELATIONS

Modality	Impacts
Written Media	71
Online Media	209
Specialized Online Media	105
Radio	15
Tv	7
Total Media Appearances	407

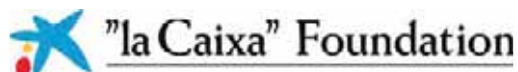
WEB & SOCIAL MEDIA

Modality	2021	2020	2019
 Web visits	55,142	60,447	36,715
 Twitter Followers	2,726	2,047	1,827
 LinkedIn Followers	3,368	2,643	1,755
 Facebook Followers	235	208	165
 Facebook Likes	208	184	151

ACCREDITATIONS



FUNDING



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Report Production: Anna Llanes-Pallàs, Naiara Laespada, Luis M. Liz-Marzán, Aitziber L. Cortajarena


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Picture Credits: Paula Vazquez Aristizabal, Winner of the 1st Prize of the 2021 CIC biomaGUNE Scientific Photocontest.

Description: melanoma cell spheroid.

Activity REPORT 2021

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BASQUE RESEARCH
& TECHNOLOGY ALLIANCE

 EXCELENCIA
MARIA
DE MAEZTU
07/2018 - 06/2022