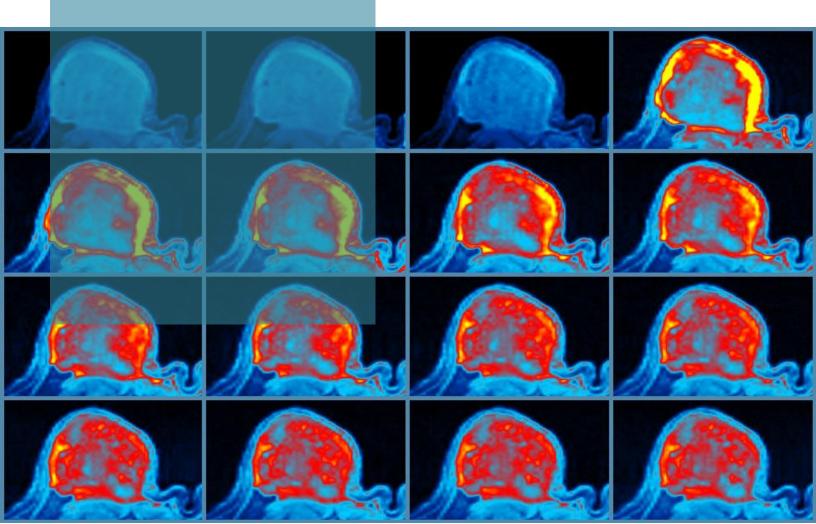
Activity Report 20<u>18</u>





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Report Production: Anna Llanes

Cover Image: © 2019, Pedro Ramos Cabrer

Activity Report 2018



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The Center

The Center for Cooperative Research in Biomaterials - CIC biomaGUNE, located in San Sebastian (Spain), was officially opened in December 2006. CIC biomaGUNE 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 create a new business sector based on biosciences.

CIC biomaGUNE currently comprises 11 international and dynamic research teams, which conduct highlevel research at the interface between chemistry, physics and biology, with particular emphasis on the properties and applications of nanostructures at the biomolecular level. The final aim of CIC biomaGUNE's research is to contribute to understanding the way in which biological systems interact with nanometersized materials, at the molecular level.

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 theranostic or multitherapeutic platforms. To carry out this ambitious program of research, the Center counts with a unique research infrastructure equipped with the most advanced nanoscience, biochemistry and molecular imaging facilities, including fully equipped research laboratories, Technological Platforms and the Molecular Imaging Facility, one of the biggest preclinical imaging research infrastructures in Europe.

CIC biomaGUNE celebrated its 10th anniversary in 2016. In the course of these ten years, with an average critical mass of around 120 researchers, 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) - which further confirms this recognition.

2018 AtaGlance

2018 At a Glance

CURRENT ORGANIZATION*



*Data from 31/12/2018

SCIENTIFIC OUTPUT

In 2018, 169 articles in high impact scientific journals have been published.



2018 At a Glance

FUNDING

Competitive public funding

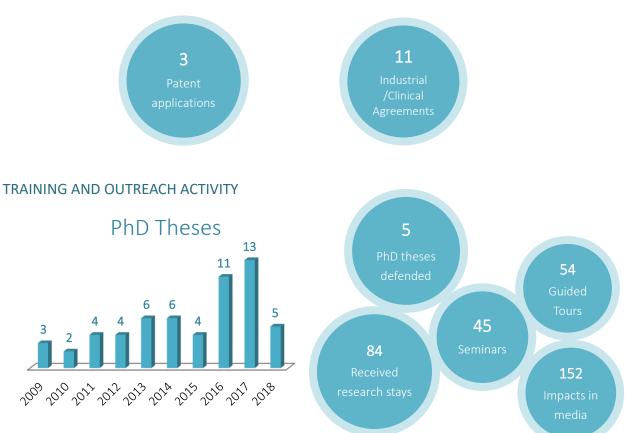
Private funding

36 new projects have been launched with a total contribution Income from private sources amounted **0.5 M €**. of **7.7 M€** from competitive funding.



TECHNOLOGY TRANSFER

During 2018, **3** new patent applications have been filed and **11** agreements have been established with industrial or clinical partners.



2018 At a Glance

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**.

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.

Awards/Recognitions

Wolfgang J. Parak received the 2018 Bioconjugate Chemistry Lectureship Award (American Chemical Society).

Maurizio Prato, Luis Liz-Marzán and Wolfgang Parak included in the 2018 list of Highly Cited Researchers (Clarivate Analytics), in the categories of Materials Science (Liz-Marzán) and Cross-Field (Prato and Parak).

The **Basque Government** recognizes the work carried out by **Niels Reichardt**, leader of the Glycotechnology laboratory at CIC biomaGUNE and co-founder of the spin-off Asparia Glycomics.

Enrique Moles National Chemistry Award awarded to **Luis Liz-Marzán** by the *Spanish Ministry of Science, Innovation and Universities*, in the category of Chemical Science and Technology for his numerous and significant contributions to the fields of Colloid Chemistry and Nanoscience.

Luis Liz-Marzán awarded his second ERC Advanced Grant for the project entitled "Four-Dimensional Monitoring of Tumour Growth by Surface Enhanced Raman Scattering".

Aitziber L. Cortajarena awarded with an ERC Proof of Concept Grant for the project entitled "Fluorescencebased nano-immunoassay IVD platform".

Academy Memberships/Fellowships

Maurizio Prato named corresponding member of the Venetian Institute of Sciences, Letters and Arts.

Luis Liz-Marzán elected as a new member of the Academia Europaea (The Academy of Europe).

Maurizio Prato named **ChemPubSoc Fellow**. This is the highest award given by the organization to recognize outstanding support and contributions towards the European joint publishing venture.

Best PhD thesis Awards

Guillermo González-Rubio received four prizes for his PhD thesis entitled "Synthesis and Assembly of Uniform Plasmonic Gold Nanostructures for Biomedical Applications". The thesis was carried out at Complutense University of Madrid and CIC biomaGUNE, under joint supervision of Andrés Guerrero-Martínez and Luis Liz-Marzán. It has not only received the Extraordinary thesis award from Complutense University, the Best doctoral thesis by the Specialized Group on Nanoscience and Molecular Materials and the Specialized Group of Coloids and Interfaces of the Spanish Royal Society of Chemistry, but it was also selected as the best thesis of the year in chemistry at all universities in Madrid by RSEQ.

Best Presentation/ Poster Awards

The work Entitled "In vivo imaging of a7 nicotinic receptors as a novel method to monitor neuroinflammation after cerebral ischemia" by Abraham Martin and 3 members of the Molecular Imaging Laboratory, was awarded the **best poster prize** in the cathegory *Neuroimaging / Disease Models* at **EMIM 2018**.

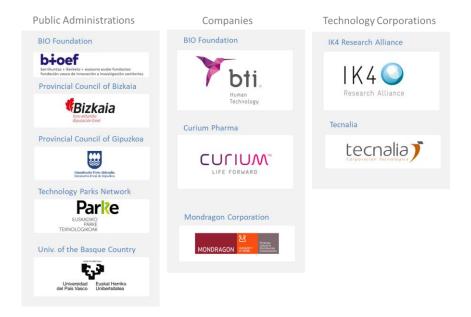
Best Oral Presentation and **Best Poster** in Radiopharmacy awarded to members of the Radiochemistry and Nuclear Imaging Group and the Radiochemistry Platform in the **37 Congreso de la Sociedad Española de Medicina Nuclear e Imagen Molecular** (SEMNIM 2018). **Jordi Llop** awarded for the Best oral presentation for his talk entitled "Marcaje de inhibidores de butirilcolinesterasa con carbono-11 y evaluación como biomarcadores para el diagnóstico precoz de la enfermedad de Alzheimer".

Best presentation/poster awards at the **International Workshop SAHMB** to **Ángel Martínez-Villacorta** (Best oral presentation) for his talk "*Polymeric Nanoparticles as hydrophobic carriers: from synthesis to in vivo evaluation*" and **Mathias Charconnet** for his poster "*Universal self-assembly process of differently shaped nanoparticles*".

Organization



GENERAL ASSEMBLY



INTERNATIONAL SCIENTIFIC ADVISORY BOARD

The scientific activity of CIC biomaGUNE is regularly assessed by the International Scientific Advisory Board (ISAB), composed of internationally distinguished scientists, who are active in CIC biomaGUNE's research fields. The ISAB is currently formed by the following members:



Peter Morris Sir Peter Mansfield Magnetic Resonance Centre University of Nottingham, UK



Monica Olvera de la Cruz Department of Chemistry Northwestern University, USA



Prof. Itamar Willner Institute of Chemistry The Hebrew University of Jerusalen, Israel



Prof. Peter Seeberger Max Plank Institute of Colloids and interfaces. Germany



Prof. Jon Dilworth Depart. of Inorganic Chemistry University of Oxford, UK



Prof. Samuel I. Stupp Institute for BioNanotechnology in Medicine Northwester University, USA



Prof. Patrick Couvreur Université Paris-Sud, France

Organization

2018 GROUP LEADERS

Glycotechnology

Niels Reichardt





Biosensing

Soft matter Nanotechnology Sergio E. Moya



FORMER GROUP LEADERS

Bionanoplasmonics

Computational

Biophysics

Ivan Coluzza

Luis Liz-Marzán Ikerbasque Professor



Molecular and **Functional Biomarkers** Jesús Ruiz Cabello Ikerbasque Professor Ikerbasque Professor





Theranostic Nanomedicine Juan C. Mareque-Rivas Ikerbasque Professor



Biosurfaces

Ralf Richter

2007 – Feb 2018

2011 – June 2018



Bioengineered Carbon Bionanotechnology Particles Wolfgang Parak

Radiochemistry and

Nuclear Imaging

Jordi Llop



Maurizio Prato **Ikerbasque Professor**



Biomolecular Nanotechnology Aitziber L. Cortajarena Ikerbasque Professor



Magnetic Resonance Imaging Pedro Ramos





Ikerbasque Professor



2018 RESEARCH ASSOCIATES

Bionanoplasmonics Javier Reguera Ikerbasque Fellow





Bionanoplasmonics

Isabel García-Martín





Biomarkers Susana Carregal CIBERES

Ikerbasque Fellow 2010 – Apr 2018



FORMER RESEARCH ASSOCIATES **Bioengineered Particles**

Abraham Martín Muñoz 2010 - Sept 2018



Bioengineered Particles Molecular & Functional

Mónica Carril

Experimental Molecular Imaging



RESEARCH SUPPORT

Molecular & Functional Imaging Facility

This integrated bioimaging structure offers state-ofthe-art preclinical imaging instrumentation in Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), Optical/Fluorescence and Ultrasound (US) Imaging. It includes a fully equipped radiochemistry laboratory with a biomedical cyclotron, advanced microscopy equipment, a dedicated animal housing facility for rodents which holds AAALAC accreditation, and complementary equipment including gamma spectrometry and autoradiography.

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).

Technological platforms

Each platform is managed by an expert platform manager, who provides technical and scientific support to the research activities at CIC biomaGUNE. The Platforms comprise the following state-of-the-art research infrastructures: Electron Microscopy, Nuclear Magnetic Resonance, Mass Spectrometry, Surface Analysis and Fabrication, Colloidal Nanofabrication and Optical Spectroscopy and Microscopy. All researchers have access to the platforms, upon training and supervision by the platform managers.

R&D&I Management Unit

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

FINANCIAL AND ECONOMIC MANAGEMENT AREA

Administration

Maintenance

This department is responsible for the management of finances, accounting,

administration, and the human resources of the Center.

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

Computing & Communications

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

Biosafety & Radioprotection

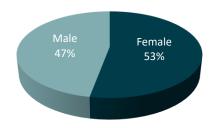
Dedicated to establish safe working conditions of all CIC biomaGUNE's personnel by promoting good laboratory practices. The service is also in charge of the appropriate operation of the Center's Radioactive Facility.

Organization

The table below provides the distribution of CIC biomaGUNE's personnel as per December 31, 2018

CIC biomaGUNE's P	ersonnel
Principal Investigators	11
Associate Researchers	4
Research Assistants	2
Platform Managers	9
Laboratory Technicians and Platform Specialists	26
Postdoctoral Researchers	19
PhD Students	28
Direction and Administration	16
IT and Maintenance	8
Biosafety and Radioprotection	1
Total	124

Gender Distribution





Argentina 1	Germany 7	Russia 1
China 1	India 2	Slovenia 1
Denmark 1	Italy 12	Spain 94
France 3	Lithuania 1	UK 1

Personnel from **12** countries

Organization

GROUP LEADER RECRUITMENTS

Jesús Ruiz-Cabello Osuna joined CIC biomaGUNE in January 2018 as Ikerbasque Research Professor and head of the Molecular and Functional Biomarkers group.

Prof. Ruiz-Cabello graduated in Chemistry from the Universidad de Granada in 1986, and obtained a PhD in Pharmaceutical Physical Chemistry from the Universidad Complutense de Madrid in 1990. Since January 2018 he is Ikerbasque Research Professor at CIC biomaGUNE. He has been Professor of Physical Chemistry at the Complutense University of Madrid (UCM) since 2010 and from February 2012 to February 2017 he held the position of Head of the Advanced Imaging Unit of the National Center for Cardiovascular Research (CNIC). Since 2008, he is also a member of CIBERES (Biomedical Research Networking Center of Respiratory Diseases, as head of one of the associated research groups, and since the end of 2015, he is the Scientific Deputy Director of CIBERES). He has directed several research initiatives in the EU and coordinated Marie Curie European networkwing projects. He has participated in more than 40 projects funded under competitive calls, 18 as Principal Investigator (3 of them EU grants), 4 as coordinator (1 EU grant) and co-authored more than 170 articles and book chapters. He is co-inventor of 6 patents, four of them European patents, and has been a founding partner of the technology-based company Numio Technologies. He has advanced knowledge on multimodal images and advanced skills in statistical analysis. The focus of his current research is pulmonary hypertension, in particular focusing on the identification of new (early) images and markers derived from system's biology, of use for the diagnosis and monitoring of new treatments for pulmonary hypertension. He is particularly interested in the role of pulmonary vascular remodeling, metabolic changes associated with cell growth, RV structure and function, and cardio-vascular coupling.

DEPARTURES

- Juan Mareque-Rivas, leader of the Theranostic Nanomedicine group (2011 2018), joined Swansea University in August 2016 as Co-Head of the new Department of Chemistry. He held this position as a secondary affiliation next to his position as Ikerbasque Research Professor and Group Leader of the Theranostic Nanomedicine Laboratory at CIC biomaGUNE, until June 2018, when he finalized his affiliation with CIC biomaGUNE, although he maintains a link with us, through a collaboration agreement.
- Ralf Richter, leader of the Biosurfaces group (2007 2018), joined the University of Leeds in October 2016 as a secondary affiliation next to his position as Group Leader of the Biosurfaces Laboratory at CIC biomaGUNE, until February 2018 when he finalized his activity at CIC biomaGUNE.
- Mónica Carril, Ikerbasque Fellow associated to the Glyconanoparticles Laboratory (2010 2015) and to the Bioengineered Particles Laboratory (2015 – April 2018) joined the Basque Centre for Biophysics as Ikerbasque Associate Researcher.
- Abraham Martín, responsible of the Experimental Molecular Imaging area (2010 September 2018) joined the Achucarro Basque Center for Neuroscience as Ikerbasque Research Fellow.

Funding

During 2018, **36** new projects (from competitive funding sources) have been launched with a total contribution of € **7,737,650**.

LIST OF FINANCED PROJECTS STARTING IN 2018



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Luis Liz-Marzán	ERC-AdG-2017	2,410,771.00	2018 - 2023	4DBIOSERS - Four-Dimensional Monitoring of Tumour Growth by Surface Enhanced Raman



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Maurizio Prato	H2020-SGA-FET- GRAPHENE-2017	400,000.00	2018 - 2020	GrapheneCore2 - Graphene Flagship Core 2
Luis Liz-Marzán	MSCA-IF-2017	158,121.60	2018 - 2020	NANOBIOME - Gradient nanocluster screening arrays for sers analytics of wound microbiome
Sergio Moya	H2020-MSCA-ITN- 2018	501,809.76	2018 - 2022	NanoCarb - Glyco-Nanoparticles for Applications in Advance Nanomedicine



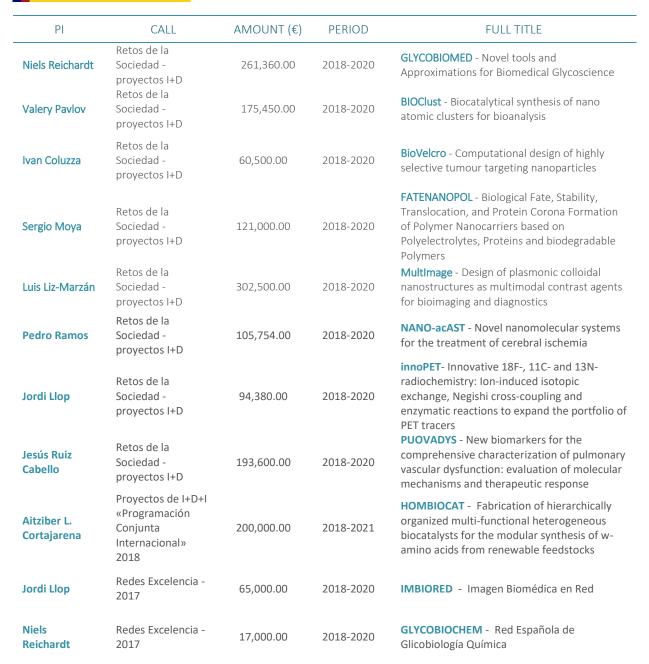
UNIDAD DE EXCELENCIA MARÍA DE MAEZTU 07/2018-06/2022

CALL	AMOUNT (€)	PERIOD
Apoyo a Centros de Excelencia "Severo Ochoa" y a Unidades de Excelencia "María de Maeztu	2,000,000.00	2018 - 2022

Funding









PI (Fellow)	CALL	AMOUNT (€)	PERIOD
Maurizio Prato (Alejandro Criado)	Juan de la Cierva – Incorporación Fellowship	64,000.00	2018-2020
Luis Liz-Marzán (Clara Garcia)	Juan de la Cierva – Formación Fellowship	50,000.00	2018-2020
Maurizio Prato (Donato Maria Mancino)	Ayudas para contratos predoctorales	92,750.00	2018-2022
Aitziber L. Cortajarena (Elena López)	Ayudas para contratos predoctorales	92,750.00	2018-2022
Javier Calvo (Dorleta Otaegui)	Personal Tecnico de Apoyo (PTA)	39,000.00	2018-2020
Luis Liz-Marzán (Javier Plou)	ayudas para la Formación del Profesorado Universitario (FPU)	49,266.00	2018-2021



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Niels Reichardt	Retos- Colaboracion 2017	159,776.00	2018-2021	Advanced Tools for Quantitative and Functional Glycomics



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Jesús Ruiz Cabello	Programa RED - Investigación	89,655.00	2017 - 2018	diBIOVADYS - Nuevos biomarcadores diagnósticos de disfunción vascular pulmonar
Luis Liz-Marzán	Programa RED- Infraestructura	100,000.00	2018-2019	BIOPRINT3D - Adquisición de una bioimpresora 3D
Carlos Sánchez Cano	Programa Fellows Gipuzkoa	46,961.55	2018 - 2019	NanoBioMeSi - Nano-materiales metálicos en muestras Biológicas; explorando interacciones entre Metales usando radiación de Sincrotrón

Funding



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Niels Reichardt	Elkartek 2018	1,641,866.02	2018-2019	biomaGUNE 2018 – Herramientas y Oportunidades paraq la glicociencia biomédica
Pedro Ramos Cabrer	Ayudas a proyectos de investigación y desarrollo en salud	7,500.00	2018	Vesículas extracelulares como vehículo de sncRNA al sistema nervioso central
Aitziber L. Cortajarena	Ayudas a proyectos de investigación y desarrollo en salud	11,646.00	2018	NKTPH - Papel de las células NK en el trasplante de precursores hematopoyéticos autólogo en el tratamiento de cáncer y enfermedades raras
Aitziber L. Cortajarena	Ayudas a proyectos de investigación y desarrollo en salud	8,271.00	2018	Medicina personalizada en tumores cerebrales : desarrollo y validación de estrategias terapéuticas basadas en la inhibición de la auto-renovación
Luis Liz-Marzán	Ayudas a proyectos de investigación y desarrollo en salud	35,054.00	2018	BACA 2018 - Bio-Reactor automatizado para células adherentes
Luis Liz-Marzán	Ayudas a proyectos de investigación y desarrollo en salud	26.961,00	2018	INDICATE 2018 - Desarrollo de un biosensor económico, sensible y rápido para detectar mutaciones en sangre asociadas a medicina personalizada
Niels Reichardt (Anna Ballesteros)	BIKAINTEK2018 - doctorado Industrial	64.160,12	2018 - 2022	GlycoNat - Desarrollo de metodología para el aislamiento de N-glicanos de fuentes naturales (in coll. With Asparia)
Sergio Moya	Ayudas Organización de Congresos	6.240,00	2018	1 st International Workshop in Self-assembly and Hierarchical Materials in Biomedicine: Drug Delivery, Tissue Engineering, Sensing and Safety Issues



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Pedro Ramos	La Marató 2017	133,312.50	2018 - 2021	Blood brain barrier disruption after subarachnoid hemorrhage: clinical relevance, role of hyperglycemia and effect of potentiating endogenous antioxidant mechanisms. A translational study



PI	CALL	AMOUNT (€)	PERIOD	FULL TITLE
Jordi Llop	Health Research Call 2017	29,150.00	2018 - 2021	HIDDENMETS - Erradicating prostate cancer metastasis before clinical manifestation

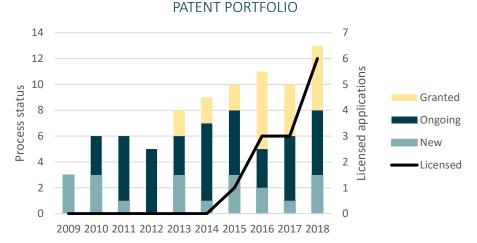
Technology Transfer

Knowledge & Technology Transfer

CIC biomaGUNE is making a substantial effort to promote the transfer to the market of research results produced at the Center. In this respect, an initiative has been launched to identify and support the development of those technologies with a clear market potential, namely the Development Unit (DU) initiative, within the R&D&I Management Unit. The DU acts as an antenna and incubator of ideas, with the main objective of identifying and transferring research results from the Center into the market, by protecting the results, encouraging their exploitation and strengthening patent licensing. Projects to be matured within the DU are initially evaluated by the scientific direction of the Center, on the basis of criteria that include the consistency of the initiative with the Center's activity and the benefit that the initiative can obtain from the infrastructure/resources of the center for its maturation. In addition, the R&D&I Management Unit works on establishing new contracts with companies, promoting cross-sectorial research and maximizing the transfer of knowledge and technology.

PATENTS

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



2018 Patent Applications

Method and apparatus for the cardiovascular assessment of a subject in need thereof

EP18382080.2 (13/02/2018)

J.M. Ruiz Cabello, A. J. Santos Oviedo

Vacuna multivalente para el tratamiento y prevención de la tuberculosis, listeriosis y neumonía P201830628 (22/06/2018)

I. García, M. Marradi, S. Penadés, C. Álvarez, R. Calderón, H. Terán, D. Salcines, E. Frande

Support coil

EP18382944.9 (19/12/2018)

M. Simon

Knowledge & Technology Transfer

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 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.

"The company is led by Dr. Juan Echevarria, co-inventor of the technology, who moved to *Asparia Glyomics* from the Glycotechnology laboratory. The standards and kit solutions offered by *Asparia Glycomics* find multiple applications in clinical glycomics research, biopharmaceutical glycan analysis and glycobiology in general.

The company started operating in October 2016 and has currently obtained ca. **117** k€ from direct sales and signed a distribution agreement with the multinational company Sigma.

The company also managed to obtain public funding in the form of **3** Torres Quevedo postdoctoral fellowships, **2** industrial PhD studentships (in collaboration with CIC biomaGUNE), **1** Hazitek grants from SPRI- Basque Government, **1** NEOTEC grant from the Spanish Government and **1** collaborative research project (Retos-Colaboración), also with CIC biomaGUNE. Additionally, Asparia's innovation has been recognized by the MBAe3-Gaztenpresa (Laboral Kutxa) award, has been finalist of EmprendedorXXI awards in the Basque Country and has passed the world final to access to the 2018 program of the prestigious MassChallenge Accelerator in Boston (MA). **The company has been certified as Innovative SME by the Spanish government**"

RESEARCH AGREEMENTS WITH COMPANIES

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 2018, besides several technical services provided to industry and the initiation of conversations with many companies, twelve collaboration agreements with industrial or clinical partners were signed:

Solmeglas (Spain) – Specialty nanoparticles distribution agreement.

Nanolike (France) – Design and tailor made synthesis of nanoparticles.

IIS Biodonostia (Spain) – Service provision in connection to the development of nanoparticle-based thermosensitive devices.

Policlínica de Gipuzkoa (Spain) - Collaborative clinical assay on the therapeutic effect of a pro-coagulant drug

Asparia Glycomics (Spain) – Extension of agreement for custom production of specialty chemicals.

Midatech Pharma España (Spain) – Extension of agreement for analytical services provision.

Curium Pharma Spain (Spain) – Grant of use and exploitation rights of the cyclotron and radio-pharmacy laboratories for the production of radio-labeled drugs.

Janssen Pharmaceutica NV (Belgium) – Pre-clinical evaluation of a radiotracer.

Nanovex Biotechnologies (Spain) - Specialty nanoparticles distribution agreement.

Biokit Research & Development (Spain) – Characterization of microparticle aggregation processes at single particle level.

INDICATE Solutions (Spain) – Service Provision.

INDEXED PUBLICATIONS

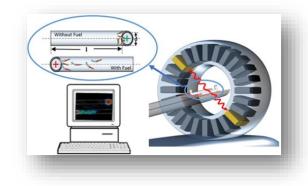


ARTICLES PUBLISHED IN JOURNALS WITH IMPACT FACTORS ABOVE 9.5 (30%)

JOURNAL	IMPACT FACTOR	Nº OF ARTICLES
Nature Reviews Materials	51.941	1
Nature	41.577	1
Science	41.058	2
Chemical Society Reviews	40.182	1
Nature Materials	39.235	1
Nature Nanotechnology	37.490	1
Nature Photonics	35.521	1
Energy & Environmental Science	30.067	1
Advanced Materials	21.950	2
Advanced Energy Materials	21.875	1
Accounts of Chemical Research	20.955	1
Nano Today	17.753	1
Journal of the American Chemical Society	14.357	4
Chem	14.104	1
ACS Nano	13.709	7
Advanced Functional Materials	13.325	4
Nano Energy	13.120	1
Nature Protocols	12.423	1
Nature Communications	12.353	2
Angewandte Chemie International Edition	12.102	8
Applied catalysis B-environmental	11.698	1
ACS Catalysis	11.384	2
EMBO Molecular Medicine	10.293	1
Chemistry of Materials	9.890	1
Small	9.589	1
PNAS	9.504	1
TOTAL		50

HIGHLIGHTS

Positron emission tomography (PET) as an imaging tool for the in vivo localization of artificial micromotors

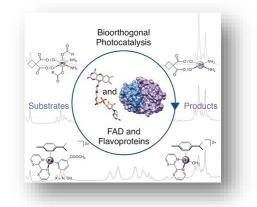


Medical Imaging for the Tracking of Micromotors Vilela, D; Cossío, U; Parmar, J; Martínez-Villacorta, AM; Gómez-Vallejo, V; Llop, J; Sánchez, S.

ACS Nano, 2018, 12, 1220-1227

Micro/nanomotors are useful tools for several biomedical applications, including targeted drug delivery and minimally invasive microsurgeries. However, major challenges such as in vivo imaging need to be addressed before they can be safely applied on a living body. Here, we show that positron emission tomography (PET), a molecular imaging technique widely used in medical imaging, can also be used to track a large population of tubular Au/PEDOT/Pt micromotors. Chemisorption of an iodine isotope onto the micromotor's Au surface rendered them detectable by PET, and we could track their movements in a tubular phantom over time frames of up to 15 min. In a second set of experiments, micromotors and the bubbles released during self-propulsion were optically tracked by video imaging and bright-field microscopy. The results from direct optical tracking agreed with those from PET tracking, demonstrating that PET is a suitable technique for the imaging of large populations of active micromotors in opaque environments, thus opening opportunities for the use of this mature imaging technology for the in vivo localization of artificial swimmers.

Flavins and flavoproteins: unconventional catalyzers of Pt IV and Ru II complexes: new opportunities for the design of chemically-and light-activated metal-based prodrugs



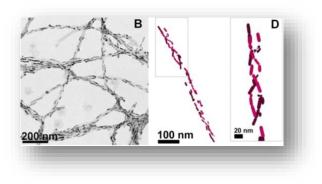
Bioorthogonal Catalytic Activation of Platinum and Ruthenium Anticancer Complexes by FAD and Flavoproteins

Alonso-de Castro, S; Cortajarena, AL; López-Gallego, F; Salassa, L.

Angew. Chem. Int. Ed. 2018, 57, 3143-3147

Recent advances in bioorthogonal catalysis promise to new chemical tools for performing deliver chemoselective transformations in complex biological environments. Herein, we report how FAD (flavin adenine dinucleotide), FMN (flavin mononucleotide), and four flavoproteins act as unconventional photocatalysts capable of converting PtIV and Rull complexes into potentially toxic PtII or Rull-OH2 species. In the presence of electron donors and low doses of visible light, the flavoproteins mini singlet oxygen generator (miniSOG) and NADH oxidase (NOX) catalytically activate PtIV prodrugs with bioorthogonal selectivity. In the presence of NADH, NOX catalyzes PtIV activation in the dark as well, indicating for the first time that flavoenzymes may contribute to initiating the activity of PtIV chemotherapeutic agents.

Gold nanorods for early stage detection of amyloids in Parkinson's and prion diseases



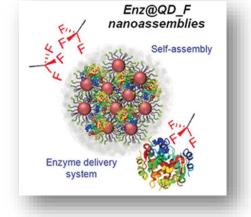
Detection of amyloid fibrils in Parkinson's disease using plasmonic chirality

Kumar, J; Eraña, H; López-Martínez, E; Claes, N; Martín, VF; Solís, DM; Bals, S; Cortajarena, AL; Castilla, J; Liz-Marzán, LM.

Proc. Natl. Acad. Sci. U. S. A., 2018, 201721690

This contribution reports on the application of gold nanorods to the detection of amyloids in Parkinson's and prion diseases. We found that gold nanorods show no interaction with monomeric proteins but adsorb onto helical protein fibrils. Chiral amyloid templates induce helical arrangement of nanorods, giving rise to intense optical activity at the plasmon resonance wavelengths. This report shows the use of protein fibrils as templates for chiral nanoparticle assembly and development of a biodetection technique. We show this effect on a model recombinant protein, α -synuclein (involved in Parkinson's disease), using CD, cryogenic transmission EM tomography, and theoretical simulations supporting the experimental findings. We additionally show application to identify patients with Parkinson's disease from human brain homogenates.

Hydrophobic fluorine interactions key elements for the encapsulation and release of enzymes



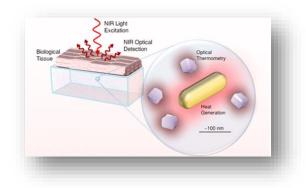
Taking advantage of hydrophobic fluorine interactions for self-assembled nanoclusters of quantum dots as delivery platform for enzymes

Carrillo-Carrión, C; Atabakhshi-Kashi, M; Carril, M; Khajeh, K; Parak, WJ.

Angew. Chem. Int. Ed. 2018, 57, 5033-5036

Self-assembly of nanoparticles provides unique opportunities as nanoplatforms for controlled delivery. By exploiting the important role of noncovalent hydrophobic interactions in the engineering of stable assemblies, nanoassemblies were formed by the selfassembly of fluorinated quantum dots in aqueous medium through fluorine-fluorine interactions. These nanoassemblies encapsulated different enzymes (laccase and α -galactosidase) with encapsulation efficiencies of ≥74 %. Importantly, the encapsulated enzymes maintained their catalytic activity, following Michaelis–Menten kinetics. Under an acidic environment the nanoassemblies were slowly disassembled, thus allowing the release of encapsulated enzymes. The effective release of the assayed enzymes demonstrated the feasibility of this nanoplatform to be used in pH-mediated enzyme delivery. In addition, the as-synthesized nanoassemblies, having a diameter of about 50 nm, presented high colloidal stability and fluorescence emission, which make them a promising multifunctional nanoplatform.

Plasmonic nanothermometers

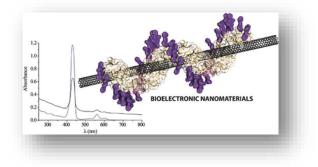


Subtissue Plasmonic Heating Monitored with CaF₂:Nd³⁺,Y³⁺ Nanothermometers in the Second Biological Window

Quintanilla, M; Zhang, Y; Liz-Marzán, LM. *Chem. Mater.*, **2018**, *30*, 2819-2828

Measuring temperature in biological environments is an ambitious goal toward supporting medical treatment and diagnosis. Minimally invasive techniques based on optical probes require very specific properties that are difficult to combine within a single material. These include high chemical stability in aqueous environments, optical signal stability, low toxicity, high emission intensity, and, essential, working at wavelengths within the biological transparency windows so as to minimize invasiveness while maximizing penetration depth. We propose CaF₂:Nd³⁺,Y³⁺ as a candidate for thermometry based on an intraband ratiometric approach, fully working within the biological windows (excitation at 808 nm; emission around 1050 nm). We optimized the thermal probes through the addition of Y³⁺ as a dopant to improve both emission intensity and thermal sensitivity. To define the conditions under which the proposed technique can be applied, gold nanorods were used to optically generate subtissue hot areas, while the resulting temperature variation was monitored with the new nanothermometers.

Biomolecules as efficient scaffolds to organize photoactive and electroactive moieties: a promising strategy for the fabrication of the next-generation of bioelectronic nanomaterials

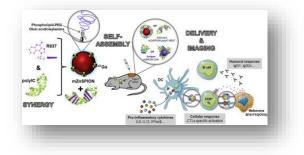


TowardBioelectronicNanomaterials:PhotoconductivityinProtein–PorphyrinHybridsWrapped around SWCNT

López-Andarias, J; Mejías, SH; Sakurai, T; Matsuda, W; Seki, S; Feixas, F; Osuna, S; Atienza, C; Martín, N; Cortajarena, AL

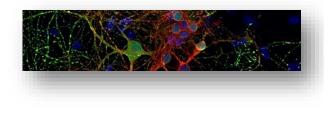
Adv. Funct. Mater., 2018, 28, 1704031

The development of sophisticated ordered functional materials is one of the important challenges in current science. One of the keys to enhance the properties of these materials is the control of the organization and morphology at different scales. This work presents a novel bioinspired methodology to achieve highly ordered donor/acceptor bio-nanohybrids using a designed repeat protein as scaffold, endowed with photoactive and electron donating porphyrin (P) units, to efficiently wrap around electron accepting single wall carbon nanotubes (SWCNT). A systematic experimental and theoretical study to evaluate the effect of the length of the protein reveals that longer proteins wrap around the SWCNT in a more efficient manner due to the stronger supramolecular interaction existing between the inner concave surface of the protein and the convex surface of the SWCNT. Finally, the new bio-nanohybrids show remarkable enhancement а on the photoconductivity values by flash-photolysis microwave conductivity (FP-TRMC technique) demonstrating that the major charge carriers of electrons are injected into the SWCNTs and move along the 1D-structures.



Magnetic nanoparticles for cancer immunotherapy

Graphene carpets: Better communication for neurons



Effective cancer immunotherapy in mice by polyICimiquimod complexes and engineered magnetic nanoparticles

Bocanegra Gondan, AI; Ruiz-de-Angulo, A; Zabaleta, A; Gómez Blanco, N; Cobaleda-Siles, BM; García-Granda, MJ; Padro, D; Llop, J; Arnaiz, B; Gato, M; Escors, D; Mareque-Rivas, JC.

Biomaterials 2018, 170, 95-115

Encouraging results are emerging from systems that exploit Toll like receptor (TLR) signaling, nanotechnology, checkpoint inhibition and molecular imaging for cancer immunotherapy. A major remaining challenge is developing effective, durable and tumourspecific immune responses without systemic toxicity. Here, we report a simple and versatile system based on synergistic activation of immune responses and direct cancer cell killing by combined TLR ligation using polyIC as TLR3 and imiquimod (R837) as TLR7 agonist, in combination with the model antigen ovalbumin (OVA) and phospholipid micelles loaded with zinc-doped iron oxide magnetic nanoparticles (MNPs). The combination of TLR agonists triggered a strong innate immune response in the lymph nodes (LNs) without systemic release of pro-inflammatory cytokines. Overall, we show this synergistic TLR agonists and their combination with MNPs and immune checkpoint blockade to have considerable potential for preclinical and clinical development of vaccines for cancer immunotherapy.

Single-layer graphene modulates neuronal communication and augments membrane ion currents

Pampaloni NP, Lottner M, Giugliano M, Matruglio A, D'Amico F, Prato M, Garrido JA, Ballerini L, Scaini D *Nature Nanotechnology* **2018**, *13*, 755–764

The use of graphene-based materials to engineer sophisticated biosensing interfaces that can adapt to the central nervous system requires a detailed understanding of how such materials behave in a biological context. Graphene's peculiar properties can cause various cellular changes, but the underlying mechanisms remain unclear. Here, we show that singlelayer graphene increases neuronal firing by altering membrane-associated functions in cultured cells. Graphene tunes the distribution of extracellular ions at the interface with neurons, a key regulator of neuronal excitability. The resulting biophysical changes in the membrane include stronger potassium ion currents, with a shift in the fraction of neuronal firing phenotypes from adapting to tonically firing. By using experimental and theoretical approaches, we hypothesize that the graphene-ion interactions that are maximized when single-layer graphene is deposited on electrically insulating substrates are crucial to these effects.

Spectrometry

Quantification of glycosyl hydrolase activity by Mass Carbon nanotubes scaffolds as neural prostheses



Measuring Bacterial Glycosyl Hydrolase Activity with a Soluble Capture Probe by Mass Spectrometry Serna, S; Ercibengoa, M; Marimón, JM; Reichardt, N. Anal. Chem. 2018, 90, 12536-12543

A solution-phase enzymatic assay has been developed to track bacterial glycosyl hydrolase activity by surfaceassisted MALDI-TOF mass spectrometry. Lactose was equipped with an azide-functionalized linker and was supplemented to bacterial cultures as an artificial substrate for bacterial β-galactosidase enzyme. The azide linked glycoside probe was then covalently captured on an alkyne-functionalized indium tin oxide sample plate via a bio-orthogonal copper-catalyzed azide alkyne cycloaddition (CuAAC). The noncovalent immobilization of the alkyne capture tag via hydrophobic interactions on the ITO-sample plate allowed the analysis of the probe conjugate by surfacebased mass spectrometry. The ratio of digested to nondigested lactose probe was then employed as a measure for bacterial hydrolase activity, which correlated well with bacterial growth measured by optical density. In addition, we established in a proof of concept experiment that the setup was well suited to identify antibiotic susceptibility of bacterial strains with a performance comparable to current state-of-the-art methods. While the proof of concept version is limited to the identification of a single enzyme activity, we envisage that the use of multiple substrate probes in a multiplexed version will allow the guantification of various glycosyl hydrolase activities with clinical relevance in a single experiment.

3D conductive scaffolds based on Carbon Nanotubes and Polypyrrole as Neural Prostheses with high biocompatibility

Alegret, N; Dominguez-Alfaro, A; Gonzalez-Dominguez, JM; Arnaiz, B; Cossío, U; Bosi, S; Vázquez, E; Ramos-Cabrer, P; Mecerreyes, D; Prato, M.

ACS Appl. Mater. Interfaces 2018, 10, 43904–43914

Here, we construct three-dimensional (3D) porous and conductive composites, where C8-D1A astrocytic cells were incubated to study their biocompatibility. The manufactured scaffolds are composed exclusively of carbon nanotubes (CNTs), a most promising material to interface with neuronal tissue, and polypyrrole (PPy), a conjugated polymer demonstrated to reduce gliosis, improve adaptability, and increase charge-transfer efficiency in brain-machine interfaces. We developed a new and easy strategy, based on the vapor phase polymerization (VPP) technique, where the monomer vapor is polymerized inside a sucrose sacrificial template containing CNT and an oxidizing agent. After removing the sucrose template, a 3D porous scaffold was obtained and its physical, chemical, and electrical properties were evaluated. The obtained scaffold showed very low density, high and homogeneous porosity, electrical conductivity, and Young's Modulus similar to the in vivo tissue. Its high biocompatibility was demonstrated even after 6 days of incubation, thus paving the way for the development of new conductive 3D scaffolds potentially useful in the field of electroactive tissues.

COVER PAGES



Colloidal Design of Plasmonic Sensors Based on Surface Enhanced Raman Scattering Hamon, C.; Liz-Marzán, LM J. Colloid Interface Sci. 2018, 512, 834-843



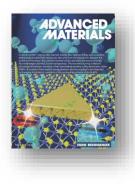
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Cortajarena, AL; López-Gallego, F; Salassa, L. *Angew. Chem. Int. Ed.* **2018**, *57*, 2980



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Tunable Fano Resonance and Plasmon-Exciton Coupling in Single Au Nanotriangles on Monolayer WS2 at Room Temperature

Wang, M; Krasnok, A; Zhang, T; Scarabelli, L; Liu, H; Wu, Z; Liz-Marzán, LM; Terrones, M; Alù, A; Zheng, Y. *Adv. Mater.* **2018**, *30*, 1705779





Microwave-induced MicroRN covalent functionalization of few-layer graphene of Chiral with arynes under solventfree conditions Marzán,

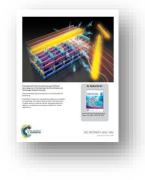
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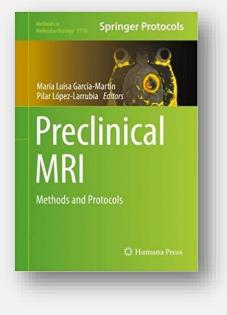
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Environmentally responsive plasmonic nanoassemblies for biosensing

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PhD PROGRAMS

The objective of CIC biomaGUNE's PhD Program is to a 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.

CIC biomaGUNE has agreements with several universities (which are the degree-grating bodies) to enroll PhD students in different PhD programs.

Additionally, CIC biomaGUNE principal researchers are PhD Program Professors in the following Doctoral programs from the **University of the Basque Country (UPV/EHU)**, CIC biomaGUNE participates in the following Doctoral programs:

- Synthetic and Industrial Chemistry
- Applied Chemistry and Polymeric Materials
- Molecular Biology and Biomedicine
- Medicine and 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 2018, 26 PhD theses were co-directed with the following institutions:

- POLYMAT
- DIPC
- CIC bioGUNE
- CIC nanoGUNE
- IIS BioCruces
- IIS BIODONOSTIA
- TECNALIA
- GAIKER
- CIDETEC
- Achucarro Basque Center for Neuroscience

Industrial PhD Scheme

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

PhD THESES

During 2018, 5 students obtained their PhD at CIC biomaGUNE.



Stavros Azinas Mechanical and structural studies of internal lipid-containing

Supervisor: Ralf Richter and Nicola G.A. Abrescia

Date: 12/06/2018

bacteriophage PRD1



Silvia Alonso de Castro Bioorthogonal photocatalytic activation of metal-based anticancer prodrugs Supervisor: Luca Salassa

Date: 26/10/2018



Julie Pham

Synthesis, screening and use of parasitic O-glycans and mimetics for improved C-type lectin receptor targeting Supervisors: Niels C. Reichardt and Jesús Jiménez Barbero

Date: 21/11/2018



Unai Cossío

Radiolabelling and preclinical evaluation of nanoparticles as drug delivery systems: Application to infectious pulmonary diseases **Supervisors: Jordi Llop and Iraida Loinaz**

Date: 11/12/201



Ane Escobar

Functionalized mesoporous titania film coatings for bone implants with antibacterial and enhanced osseointegrative properties Supervisors: Sergio Moya and Marek Grzelczak

Date: 14/12/2018

MASTER & VOCATIONAL TRAINING PROGRAMS

Master Students

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

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

- Molecular Biology and Biomedicine
- Nanoscience
- Chemistry and Polymers

Vocational Training Program

CIC biomaGUNE has agreements with **CPES**, **CESA**, **BHIP**, **Don Bosco** 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.

Every year several training placements take place at different laboratories of the Center.

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

RESEARCH SECONDMENTS & SUMMER INTERNSHIPS

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 2018, our researchers performed **11** secondments at collaborating partners and we hosted **84** stays of visiting researchers.

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. CIC biomaGUNE regularly hosts students from the University of the Basque Country, Autonomous University of Barcelona, and University of Navarra.

	2015	2016	2017	2018	TOTAL
Research stays from CIC biomaGUNE	30	30	19	11	90
Research stays to CIC biomaGUNE	59	105	92	84	340
 Visiting Professors/Sabbaticals 	1	4	1	2	8
 Erasmus placements 	1	7	7	2	17
 Summer placements 	2	5	6	6	19
 Vocational Training 	4	7	5	3	19

SEMINARS

CIC biomaGUNE runs an annual program of scientific seminars, which includes: i) **International seminars** delivered by internationally recognized researchers of varying scientific backgrounds and fields, ii) **PhD seminars** delivered by PhD students of the Center, and iii) **Training seminars** delivered by CIC biomaGUNE's PIs or Platform Managers, aimed at strengthening the technical training program and soft skills training. Altogether, these programs contribute to the career development of our researchers. During 2018, **45** seminars have been delivered.

CIC biomaGUNE Seminars

17/01/2018 Harnessing the Mycobacterium tuberculosis cell surface's physiology to generate better antiinfective tools Rafael Prados-Rosales - CIC bioGUNE

25/01/2018 Multimetallic Nanomaterials by Design Sara Skrabalak - University in Bloomington

30/01/2018 From academia to industry and back **Helmuth Möhwald** - MPI Golm

01/02/2018 Biomimetic Nanocomposites Nicholas Kotov - University of Michigan

09/02/2018 Career development outside academia. Women in Science day Alba Centeno Perez & Africa G. Barrientos -Graphenea & Midatech Pharma

15/02/2018 Development of implantable bone-forming devices: From regenerative medicine to human neoplasia modelling in xenografts Ander Abarrategi - Francis Crick Institute, London 22/02/2018 High resolution cryoEM structure of flexible

filamentous plant viruses Mikel Valle - CIC bioGUNE

08/03/2018

Surface-Enhanced Raman Spectroscopy and Imaging with Molecularly Functionalized Noble Metal Nanoparticles: From Experimental Precision Plasmonics to iSERS Microscopy and Chemical Energy Conversion Sebastian Schlücker - University Duisburg-Essen

20/03/2018 Optimizing the use of molecular imaging in early drug development Mats Bergstrom - GSK

22/03/2018 Sugars, Natural Products and Algal Blooms Rob Field - John Innes Center, Norwich

13/04/2018 Role of conformational dynamics in the design of novel function and nanohybrid materials Silvia Osuna - University of Girona & ICREA

19/04/2018

Interfacing Nanomaterials with Biology: From CRISPR delivery to Antimicrobials Vincent M. Rotello - University of Massachusetts Amherst

03/05/2018

Machine learning in atomistic simulations: from reaction pathways to phase diagrams **Christoph Dellago** - University of Vienna

17/05/2018

Photoswitchable Organometallics Zoraida Freixa - University of the Basque Country (UPV/EHU)

18/05/2018

Development of a Myeloid-Specific Targeted Nanotherapy for Immune Pathologies Jordi Cano Ochando - Instituto de Salud Carlos III

23/05/2018

New synthetic pharmapolymers for applications in pharmacy and medicine and/or tailor-made polymeric nanoparticles **Ulrich S. Schubert** - Friedrich-Schiller-Universität Jena

30/05/2018 Plasmonics: enhancing Biomedical Diagnostics and Therapeutics Naomi Halas - Rice University

31/05/2018 Modular Objects for Nano-Immuno-Oncology Patrizio Giacomini - Regina Elena National Cancer Institute. Rome.

01/06/2018

Differences in post-T cell receptor metabolic response of naive versus memory human CD4+ T cells Catherine Thornton - Swansea University

07/06/2018

Polymer-based nanoparticle libraries for targeted anti-inflammatory strategies **Stephanie Schubert** - Friedrich-Schiller-University Jena - Jena Center for Soft Matter (JCSM)

21/06/2018 Optoacustic imaging: clinical and preclinical application in oncology Isabel Quirós - University of Oviedo

02/07/2018 Putting Nanomaterials to Work for Biomedical and Energy Research Younan Xia - Georgia Institute of Technology

03/07/2018 Investigating the Heterogeneous Nucleation in Nanocrystal Growth with an Isocyanide Probe by Surface-Enhanced Raman Scattering Dong Qin - Georgia Institute of Technology

09/07/2018 Multivalent binding in cellular processes: targeting, recognition and activation Jure Dobnikar - University of Cambridge

24/07/2018

Understanding in vivo degradation of mesoporous silica therapeutic vectors through in situ ellipsometry Elisa Bindini - Laboratoire de Chimie de la Matière Condensée de Paris (LCMCP), Sorbonne Université.

27/07/2018

Polymer-Assisted Metal Deposition: An Interfacial Chemical Approach for Soft Electrodes and Devices **Zijian Zheng** - Hong Kong Polytechnic University

23/08/2018

Integrating supramolecular chemistry with engineering principles for the design of new functional biomaterials

Alvaro Mata - School of Engineering and Materials Science of the Queen Mary University of London

14/09/2018

Exploring the Energy Landscape for Protein Folding and Function: The Convergences of Structural Models and Sequence Coevolution Information José N. Onuchic - Rice University

27/09/2018

The circle of life of magnetic nanoparticles: Synthesis, aggregation, biomedical applications and biotransformations Lucía Gutierrez - University of Zaragoza

04/10/2018

Fast-setting protein- and polysaccharide-based bioinks for tissue engineering, 3D in vitro tissue/tumour models, and biofabrication of patient-specific implants **Miguel de Oliveira** - University of Minho, Braga, portugal

25/10/2018

Multimodal imaging for the optimisation of cell therapy Mangala Srinivas - Radboud University Medical Center (RadboudUMC) 31/10/2018 Dark and bright interlayer plasmons in colloidal nanoparticle multilayers Stephanie Reich - Freie Universität Berlin

08/11/2018

Addressing Oncology Questions with Gold Nanostars and SERS Laura Fabris - Rutgers University

27/11/2018

Biomaterials with optoregulated functions Aránzazu del Campo - INM-Leibniz Institute for New Materials

12/12/2018

Altered glycosylation in Cancer - targeting tumor heterogeneity and therapeutic implications. **Celso Reis** - Ipatimup Institute of Molecular Pathology and Immunology of the University of Porto

19/12/2018 Novel Photonic Architectures by Nanoimprinting Unconventional Materials Agustín Mihi - ICMAB-CSIC

CIC biomaGUNE PhD Seminars

16/07/2018 Mechanical and structural studies of internal lipidcontaining bacteriophage PRD1 Stavros Azinas - CIC biomaGUNE

05/11/2018

Bioorthogonal photocatalytic activation of metalbased anticancer prodrugs Silvia Alonso de Castro - CIC biomaGUNE

20/11/2018

Synthesis, screening and use of parasitic O-glycans and mimetics for improved C-type lectin receptor targeting Julie Pham - CIC biomaGUNE

30/11/2018

Radiolabelling and preclinical evaluation of nanoparticles as drug delivery systems: Application to infectious pulmonary diseases **Unai Cossio** - CIC biomaGUNE

18/12/2018

Functionalized mesoporous titania film coatings for bone implants with antibacterial and enhanced osseointegrative properties. Ane Escobar - CIC biomaGUNE

CIC biomaGUNE PhD Trainig

20/03/2018 The start-up route to exploit your research results Marcos Simón - CIC biomaGUNE

20/03/2018 Life after the PhD: How to apply for grants Anna Llanes-Pallàs - CIC biomaGUNE 29/05/2018 Cellular decision making Tahereh KashkouliNejad Kouhi - CIC biomaGUNE

19/06/2018 Radiochemistry: the key step in Nuclear Imaging Vanessa Gómez-Vallejo - CIC biomaGUNE

ORGANIZATION OF 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 2018:

11-13 July 2018

Immunoshape International Symposium on Glycoimmunology



The International Symposium on Glycoimmunology is an international scientific meeting aimed at providing a forum for scientists from chemistry, immunology and glycobiology to discuss recent advances in the understanding and the opportunities for shaping glycan mediated immune responses.

Keynote lectures from world leaders addressing major topics in glycoimmunology provided the framework for a large number of **short lectures** and **flash presentations** together with a **poster session** showcasing recent achievements from major European research groups active in the field.

This symposium gave especially younger pre-doctoral and early postdoctoral investigators the opportunity to discuss their research with a large audience of specialists.

The following topics were covered in the program: Glycoconjugate vaccines, Glycan based immunotherapy, Host pathogen interactions, Synthesis of glycan antigens and Glycomimetics.

CIC biomaGUNE Organizers: Niels Reichardt and Cristina Díez.

8-10 October 2018

International Workshop on Self-Assembly and Hierarchical Materials in Biomedicine: Drug Delivery, Tissue Engineering, Sensing and Safety Issues



The "Self assembly and Hierarchical Materials in biomedicine: Drug Delivery, Tissue Engineering, Sensing and Safety Issues" conference aimed at bringing a comprehensive view in the field of hybrid materials in biomedicine. The conference adressed the design of hierarchical and self assembled materials and their application in drug delivery, sensing and tissue engineering covering from the material science aspects to clinical perspectives.

The program covered: Molecular Self-Assembly, Hybrid Materials, Drug delivery, Sensors, Tissue Engineering, Safety issues.

Keynote and invited lectures were complemented with poster sessions and contributed presentations covering all aspects of the conference. The event attracted >70 researchers from 16 different countries.

CIC biomaGUNE Organizers: Sergio Moya (chair), Patrizia Andreozzi and Julia Cope

Additionally, our researchers chaired or co-organized a number of international symposia as listed below:

Wolfwang Parak, co-organizer of "Colloidal Nanoparticles for Biomedical Applications" of the **SPIE Photonics West meeting**, San Francisco, California, USA, 27 January-2 February 2018

Abraham Martín and Mónical Carril, organizers of the 2nd young Spanish ESMI Group Meeting (ySMIN2018), Madrid, 26 February 2018.

Jesús Ruiz-Cabello, organizer and chair, 2nd Meeting of Research in Pulmonary Hypertension, Madrid, 2 February 2018.

Luis Liz-Marzán and Wolfgang Parak, co-chairs of the "Solubility of colloids in different solvents" symposium at the 255th ACS National Meeting, New Orleans, USA, 18-22 March 2018

Jordi Llop, Pedro Ramos, Abraham Martín and Jesús Ruiz-Cabello local organizers of the European Molecular Imaging Meeting (EMIM), San Sebastian, Spain, March 20-23, 2018

Jesús Ruiz-Cabello, co-organizer of the 1st Spanish Conference on Biomedical applications of nanomaterial (SBAN), Madrid, 7-8 June 2018

Jesús Ruiz-Cabello, organizer and chair, Annual Groups meeting of Ciberes, Madrid, 27-29 June 2018

Luis Liz-Marzán and Wolfgang Parak, co-chairs of the "Heating with Colloidal Nanoparticles: Physical Mechanisms and Applications in Life Science" symposium at the 256th ACS National Meeting, Boston, USA, 19-23 August 2018

Luis Liz Marzán, co-chair of the Beilstein Meeting on Nanomedicine 2018, Berlin, 16-18 Sept 2018

Luis Liz-Marzán, co-organizer of Conferencia Española de Nanofotónica, CEN2018, San Sebastian, 3-5 Oct 2018

Maurizio Prato, co-organizer, Conference "Solar driven chemistry: towards new catalytic solutions for a sustainable world". Roma, Italy, 18-19 Oct 2018

One of the strategic objectives of CIC biomaGUNE is the communication and dissemination of knowledge within and beyond the academic community. During **2018** the following outreach events have been organized:

INTERNATIONAL DAY OF WOMEN AND GIRLS IN SCIENCE

On February 8th and 9th 2018 **CIC biomaGUNE** in collaboration with the **Materials Physicis Center** (CFM, CSIC-UPV/EHU), **CIC nanoGUNE** and **Donostia International Physics Center** (DIPC) commemorated this day celebrating a series of events that aimed 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 adolescents. The activites organized included: Activites for 5th elementary grade students, a seminar by two women scientists on **Career development outside academia** who gave their view on switching career from academia to industry, prospects, and outcomes, and finally the participation by Aitziber L. Cortajarena on the Donostia City of Women researchers Colloquium.



MIKROFOOD – MICROSOPIC PHOTOGRAPHY EXHIBITION

What does milk or tomato look like on a small scale? Our researchers have tried to capture the complexity of each day's meals through photographs taken under a microscope. The project "Mikro Food": food under the microscope, is born from an idea of **Patrizia Andreozzi** (Soft Matter Nanotechnology Laboratory).

To date, 3 editions of the Photography Exhibition have taken place:

- December 2017 until the January2018 in Vitoria-Gasteiz,
- February March 2018 Malandrino Bar
- May-July 2018, Garraxi Restaurant

PINT OF SCIENCE

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

For the 4th consecutive year CIC biomaGUNE researchers took active part in the organization of the Pint of Science event in San Sebastián. The organizing team was led by CIC biomaGUNE's postdoctoral researchers **Susana Carregal** and **Dorleta Jimenez de Aberasturi**.





INSPIRA

The **INSPIRA project** is a pioneering project in Euskadi 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 aim to:

- 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.

The school whose students receive mentoring from CIC biomaGUNE scientists is: **Deutsche Schule San Alberto Magno**, where 5th elementary grade students receive mentoring from the hand of **Irantzu Llarena**.

SCIENCE, I WANT TO BE A SCIENTIST

Jordi Llop, leader of the Radiochemistry and Nuclear Imaging Lab contributed in the book <u>CIENCIA, y yo quiero ser científico</u> with the chapter - <u>Y yo quiero ser...Alquimista (Radioquímico)</u>

In this chapter, he takes us into the world of the philosopher's stone of the 21st century: explaining what a cyclotron is and how it transmutes matter, what radiochemistry consists of and how it can help to understand how we function, when and why we get sick and even how to find a possible cure.



inspire

CIC NETWORK

CIC biomaGUNE is involved in the production of the CIC NETWORK magazine, the science magazine of the Cooperative Research Centers. To date 18 issues have been published, the most recent one in July 2018.



"Donostia WeekINN" INNOVATION WEEK

In the frame of the Donostia Week INN 2018 and in collaboration with Fomento, CIC biomaGUNE co-organized an activity to bring science closer to society and share scientific knowledge in a funny, entertaining and rigorous way.

On Thursday, October 25, at 6:30 p.m., in Dabadaba, Jordi Llop head of the Radiochemistry & Imaging Laboratory from CIC biomaGUNE, together with researchers from Biodonostia and Polymat discussed about clinical image and early detection of Alzheimer's, the improvement of the recycling of the plastic waste that we generate and will challenge us to ask what we want about health research.

CIC biomaGUNE participated also with guided school visits at the Center complemented with discussions with researchers about research techniques, future technologies, applications and visits to laboratories.

NAUKAS

Susana Carregal and **Dorleta Jiménez de Aberasturi**, CIC biomaGUNE postdoctoral researchers, participate this Saturday 15th of September at the NAUKAS Outreach event that will take place in Bilbao. If you wish to enjoy their science with plenty of humor do not miss their talk about Local heating and good vibrations (calentamiento local y buenas vibraciones).

Bizitza salbatu nahian

Bizitza salbatu nahian is a project promoted by the center Tolosako Inmakulada Lanbide Ikastola with the participation of CIC biomaGUNE and Onkologikoa whose objective is to relieve the stress of oncological patients.

This project aims to inform about the PET test (Positron Emission Tomography, is a non-invasive diagnostic and in vivo research technique, capable of measuring the metabolic activity of the human body that is used in cancer patients). For this purpose, the students of Radiodiagnosis and Nuclear Medicine have recorded a video, where the process of the test is explained in a clear and detailed manner.



Vanessa Gómez-Vallejo Radiochemistry platform manager at CIC biomaGUNE and supervisor of the project from Eneko Galarraga, during the presentation of the innitiative at Onkologikoa.





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**, **Irantzu Llarena** and **Vanessa Gómez** with the support from other Platform Managers as well as PhDs, Postdocs and Principal Investigators.



	2015	2016	2017	2018	TOTAL
Undegraduate and Highschool visits	7	7	12	9	35
Guided Visits at the Molecular Imaging Facility	23	38	40	45	146

MEDIA

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



Facilities

Facilities

Research Facilities

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

CIC biomaGUNE's state-of-the art facilities are depicted in the images below. In the first row the Technological Platforms are presented, whereas the second row shows the instruments of the Molecular Imaging Facility.



MOLECULAR & FUNCTIONAL IMAGING FACILITY

Housed within 900 m², the Molecular and Functional Imaging Facility at CIC biomaGUNE is an integrated bioimaging structure that offers state-of-the-art preclinical imaging instrumentation in Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), Optical/Fluorescence and Ultrasound (US) Imaging. It includes a fully equipped radiochemistry laboratory with a biomedical cyclotron, advanced microscopy equipment, a dedicated animal housing facility for rodents which holds AAALAC accreditation, and complementary equipment including gamma spectrometry and autoradiography. 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). The infrastructure has been designed, built and equipped to tackle longitudinal and multimodal pre-clinical projects and to develop applications in the area of Preclinical Molecular and Functional Imaging and Nanomedicine.

Nuclear Imaging: Equipped with a hybrid PET-CT (eXplore Vista-CT) and full ring SPECT-CT (eXplore speCZT CT 120), the latter offering the possibility of multi-isotope studies with energy discrimination. An additional trimodal PET-SPECT-CT system has been acquired within 2018 and will be installed at the beginning of 2019.

Magnetic Resonance Imaging: 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).

Radiochemistry Platform: 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 $[^{18}F]$ F⁻, $[^{18}F]$ F², $[^{13}N]$ -NH⁴⁺⁻, $[^{15}O]$ -O₂ $[^{11}C]$ -CO₂ and $[^{11}C]$ -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 adio-HPLC, radio-GC, radio-TLC, and gamma spectrometry.

Facilities

Pre-Clinical Image Analytics: The Image Analytics service takes care of processing all the outcoming multimodal images obtained within the Molecular Imaging Unit (PET, SPECT, CT, MRI and Optical Imaging).

Working on different operating systems, we carry out co-registration, segmentation, and quantification of multimodal images. Moreover, we also work with Matlab, FSL and IDL in the development of analysis and processing algorithms. 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.

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)**, 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 work stations and a data storage system in the Terabyte scale enable image reconstruction, processing, quantification and archiving.

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) – 500 MHz NMR: 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 – SEM-EDX, TEM – 120 keV and 200 keV: 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 – MALDI-TOF, ICP-MS: 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 techniques.

Surface analysis and Fabrication – XPS, 3 x AFM, sputtering: Focuses on the analysis of materials at the surface level, including spectroscopic and microscopic techniques especially suited to surfaces. The platform offers also a deposition service of thin layers for controlled manufacture at the nanoscale.

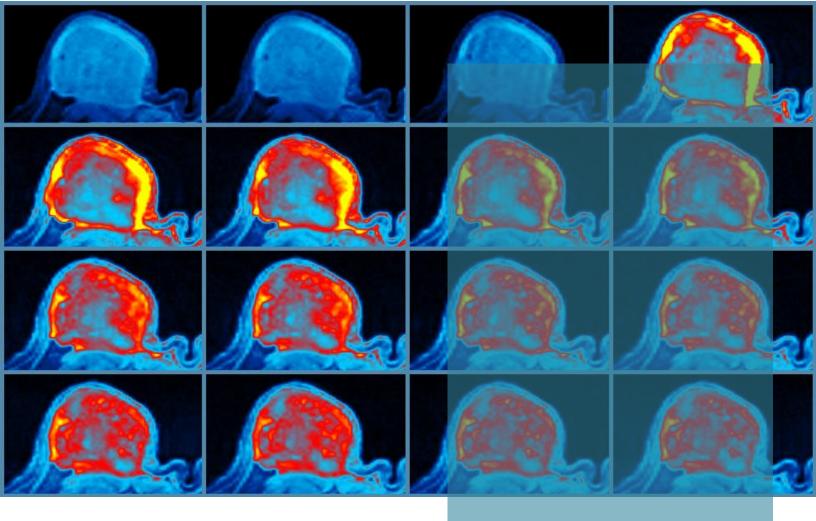
Colloidal Nanofabrication: Within the priority area of biofunctional nanomaterials and nanomedicine, colloidal synthesis plays an essential role. This platform provides knowledge, training and service for the manufacture of nanoparticles with a wide variety of compositions and morphologies.

Optical Spectroscopy & Imaging – 2 x Confocal, Confocal-Raman, UV-VIS-NIR, Flow Cytometer, Cell Observer, CD, DLS, DCS, ITC, TGA, SPR: Offers a wide variety of techniques for the spectroscopic characterization of biomaterials and biosurfaces. Also included are optical microscopy techniques (confocal, Raman, etc.) that allow to investigate the interaction of nanomaterials with cellular systems of diverse complexity.



Supported by:





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