



BBN

Annual Report

2016

*ciber-bbn*

Centro de Investigación Biomédica en Red  
Bioingeniería, Biomateriales y Nanomedicina

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## Scientific Director's Presentation

I shall now sum up what 2016 has meant for the CIBER-BBN, although you will find plenty more detailed information on this in the following pages.

The number of scientific publications in 2016 would seem to have dropped back in respect of previous years, a reduction which could be attributed to the economic situation and lower resources, mainly in the numbers of contracted staff, the main asset of a research centre. We nevertheless go on keeping high quality standards in our scientific production, with over 70% of the production in first quartile journals and almost 28% in the first decile.

We should also stress the improvement in indicators as regards communication and visibility of our work for society. The number of appearances in the media and social networks, press releases, etc. has considerably improved as compared with previous years.

In 2016 a large number of intramural projects were started to describe the research work done by our thematic area, and which are being undertaken on a collaborative basis. After the evaluation by the ANEP, 30 projects were classified as excellence projects, and 39 as projects of recognised activity. Each project focusses on solving a clinical problem, cancer and neurological diseases being the pathologies most tackled by our researchers.

We are extremely satisfied with the increase in applications for competitive financing projects, on both national and international scales. The projects applied for by CIBER, either by several groups going in for these as CIBER or by contracted researchers, have exceeded the ones presented in 2015 by 60%. The success rate has also consequently improved. At present CIBER-BBN researchers are taking part in several H2020 projects as partners or coordinators.

We are aware that we have to provide a response to the great challenge which we have been set, of bringing the results of our research closer to society and clinical practice, improving our indicators as regards transfer and translation. We continue to work to this end with the aim of improving the flow of our results into industry and supporting measures that include, amongst others, the co-financing of projects with companies.

In the scope of clinical cooperation, three clinical forums have been arranged in the framework of the latest sessions. These were of great interest due to the stimulus that was meant by bringing together medical doctors and the researchers who develop technologies.

In 2016 NANBIOSIS became established as a unique scientific infrastructure. The internal management of competitive access has been consolidated, awareness of this has been heightened in the professional biomedical sector nationwide and internationally, and its online positioning has improved.

In 2016 the criteria for annual assessment of research groups have furthermore been modified and simplified. As a result of this, no group has been put forward for discontinuity after the 2015 assessment.

We would like to welcome two new groups (led by José Miguel López Higuera from the Universidad de Cantabria and by Jesús Martínez de la Fuente from the Instituto de Ciencia de Materiales de Aragón), which joined CIBER-BBN from late 2016, enriching the bioengineering and nanomedicine programmes.

We are also pleased about the institutional reinforcement of the CIBER model, through the creation of the new thematic areas with which there are doubtlessly many interests in common and with which we expect to establish cooperation links in the near future.

As Scientific Director I am persuaded that the CIBER project is an ambitious, stimulating endeavour, able to create some extraordinary scientific achievements through cooperation. I would like to take this opportunity to thank all the researchers for their work, patience and persistence, in their daily efforts to overcome new challenges and ensure the progress of science, in spite of the difficulties involved.

With my best regards,

**Ramón Martínez Máñez,**

Scientific Director





# 2

## Organisation



# Organisational Structure

CIBER-BBN is one of the thematic areas forming the Centro de Investigación Biomédica en Red (CIBER), a Spanish research consortium in the field of biomedical research with enormous scientific capacity, set up under the Instituto de Salud Carlos III (ISCIII) – Ministry of the Economy and Competitiveness. In 2016 it was made up of 8 thematic areas, which were extended to 11 in 2017.

The area of Bioengineering, Biomaterials and Nanomedicine consists of 45 research groups and retains its independence as regards scientific management. Its organisational structure is based on its research groups and its activity revolves around its Research Programmes and Transversal Programmes, with a coordinator for each Programme belonging to the Steering Committee. Scientific decisions are made by the Scientific Director, advised by the aforementioned Steering Committee and the External Scientific Committee.

The senior administrative bodies of the CIBER-BBN are the Governing Body and the Permanent Commission, common for all areas of CIBER research. The Governing Body is made up of three representatives of the ISCIII and one institutional representative of each of the centres in the consortium. It is presided over by the Director of the ISCIII and meets every six months. The Permanent Commission is an executive committee formed of the ISCIII and 8 members of the Governing Body, who can be renewed annually. Both the operation and the purposes of the governing, support and advisory bodies are established in the statutes of the CIBER.

The Steering Committee is presided over by the Scientific Director and formed by the coordinators of the programmes and the CIBER manager.

## Steering Committee Members

NAME	POST
Ramón Martínez-Mañez	Scientific Director
José Becerra Rata	Deputy Scientific Director
Jordi Aguiló Llobet	Coordinator of Bioengineering and Medical Imaging
Julio San Román del Barrio	Coordinator of Biomaterials and Advanced Therapies
M. Pilar Marco Colás	Coordinator of Nanomedicine
Jaume Veciana Miró	Coordinator of Platforms / ICTS
Simó Schwartz Navarro	Coordinator of Industrial Transfer
Ramón Mangues Bafalluy	Coordinator of Clinical Translation
Raimon Jané Campos	Coordinator of Training
Jesús Santamaría Ramiro	Coordinator of the Strategic Plan
Manuel Sánchez Delgado	Manager

Attached to Scientific Director: Begoña Pérez Magallón

Contact <http://www.ciber-bbn.es/en/about-us/contact>

## External Scientific Advisory Committee

The External Advisory Scientific Committee is a body for scientific support and assessment, made up of internationally significant researchers of special relevance in the field of health sciences who are prominent for their professional or scientific careers, in line with the centre's objectives.

NAME	INSTITUTION
Niilo Saranummi	VTT Technical Research Centre, Finland
Leif Sörnmo	Biomedical Engineering Department, University of Lund, Sweden
Begoña Castro	Scientific Director of HistoCell, Spain
Matthias Epple	Centre for Medical Biotechnology, Universität Duisburg-Essen, Alemania
Abhay Pandit	Centre for Research in Medical Devices (CÚRAM) National University of Ireland - Galway, Ireland
Patrick Boisseau	Business development in NanoMedicine at CEA-Leti, Chair of the Executive Board of European Technology Platform on Nanomedicine, Francia
Wolfgang Parak	Philipps Universität Marburg, Germany
Alberto A. Gabizon	Shaare Zedek Medical Center, Oncology Institute The Hebrew University of Jerusalem, Israel
Joan Bigorra	Director of Innovation of the Hospital Clinic de Barcelona, Spain
Pilar Calvo	Head of Pharmaceutical Development of PHARMAMAR, Spain

## Medical Advisory Committee

NAME	POST
Joan Bigorra Llosas	Director of Innovation at the Hospital Clinic de Barcelona
Arcadi García Alberola	Head of the Arrhythmia Section of the Cardiology Service at the Hospital Universitario Virgen de la Arrixaca de Murcia
Enrique Gómez Barrena	Specialist Doctor in the Traumatology and Orthopaedics Area at the Hospital Universitario La Paz, Madrid
M <sup>a</sup> José Martí Doménech	Neurology Service of the Hospital Clínic, Barcelona
José M. Ruíz Moreno	Specialist Doctor in the Ophthalmology Area of the Complejo Universitario Hospitalario de Albacete
Josep Taberner Caturla	Coordinator of Onco-Haematology at the Hospital Vall d'Hebrón, Barcelona

## Scientific Management

Name	Programmes
Theodora Tsapikouni	Bioengineering and Medical Imaging
Aída Castellanos Páez	Biomaterials and Advanced Therapies
Johanna Katharina Scheper	Nanomedicine
Nerea Argarate Madariaga	Nanomedicine
Fernando Santos Benito	Industrial Transfer
Jesús M. Izco Zaratiegui	Equipment Platforms (ICTS NANBIOSIS)

## Technical Unit

See list of personnel: <http://www.ciber-bbn.es/en/about-us/structure/head-office>



# Directory of Groups and Institutions

Group Leader	Institution	Centre	Centre Prov.
Aguiló Llobet, Jordi	Universidad Autónoma de Barcelona	Centro Nacional de Microelectrónica	Barcelona
Albericio Palomera, Fernando	Universidad de Barcelona	Facultad de Química	Barcelona
Arús Caralto, Carles	Universidad Autónoma de Barcelona	Facultat de Biociències	Barcelona
Becerra Ratia, José	Universidad de Málaga	Facultad de Ciencias	Málaga
Bellón Caneiro, Juan Manuel	Universidad de Alcalá	Facultad de Medicina	Madrid
Blanco Fernández, Jerónimo	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Calonge Cano, Margarita	Universidad de Valladolid	Instituto de Oftalmobiología Aplicada	Valladolid
Engel López, Elisabeth	Fundación Instituto de Bioingeniería de Cataluña	Instituto de Bioingeniería de Cataluña	Barcelona
Eritja Casadella, Ramon	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Farré Ventura, Ramon	Universidad de Barcelona	Facultad de Medicina	Barcelona
Fernández Jover, Eduardo	Universidad Miguel Hernández	Instituto de Bioingeniería	Alicante
Gómez Ramírez, Rafael	Universidad de Alcalá	Facultad de Farmacia	Madrid
Gómez Ribelles, José Luis	Universidad Politécnica de Valencia	Centro de Biomateriales e Ingeniería Tisular	Valencia
González Martín, María Luisa	Universidad de Extremadura	Facultad de Ciencias	Badajoz
Jané Campos, Raimon	Fundación Instituto de Bioingeniería de Cataluña	Instituto de Bioingeniería de Cataluña	Barcelona
Laguna Lasasosa, Pablo	Universidad de Zaragoza	Instituto de Investigación en Ingeniería	Zaragoza
Lechuga Gómez, Laura María	Agencia Estatal Consejo Superior de Investigaciones Científicas	Institut Català de Nanociència i Nanotecnologia	Barcelona
Leiva Hidalgo, Alberto	Instituto de Investigación del Hospital de la Santa Creu i Sant Pau	Instituto de investigación del Hospital de la Santa Creu i Sant Pau	Barcelona
Liz Marzán, Luis Manuel	CIC biomaGUNE	CIC BiomaGUNE	Guipúzcoa
Mangues Bafalluy, Ramon	Instituto de Investigación del Hospital de la Santa Creu i Sant Pau	Instituto de investigación del Hospital de la Santa Creu i Sant Pau	Barcelona
Marco Colas, María Pilar	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Martínez Barca, Miguel Ángel	Universidad de Zaragoza	Instituto de Investigación en Ingeniería	Zaragoza
Martínez Mañez, Ramón	Universidad Politécnica de Valencia	Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico	Valencia
Muñoz Fernández, M <sup>a</sup> Ángeles	Servicio Madrileño de Salud	Hospital Gregorio Marañón	Madrid
Pavía Segura, Javier	Universidad de Barcelona	Hospital Clínic de Barcelona	Barcelona
Pedraz Muñoz, José Luis	Universidad del País Vasco	Facultad de Farmacia	Álava



Group Leader	Institution	Centre	Centre Prov.
Peris Serra, José Luis	Asociación Instituto de Biomecánica de Valencia	Instituto de Biomecánica de Valencia	Valencia
Pozo Guerrero, Francisco del	Universidad Politécnica de Madrid	ETSI Telecomunicación	Madrid
Raya Chamorro, Ángel	Centro de Medicina Regenerativa de Barcelona	Centro de Medicina Regenerativa de Barcelona	Barcelona
Ritort Farran, Félix	Universidad de Barcelona	Facultad de Física	Barcelona
Roa Romero, Laura María	Universidad de Sevilla	Escuela Superior de Ingenieros	Sevilla
Rodríguez Cabello, José Carlos	Universidad de Valladolid	Centro de Investigación Científica y Desarrollo Tecnológico	Valladolid
Ruiz Romero, Cristina	Servicio Gallego de Salud	Complejo Hospitalario Universitario A Coruña	A Coruña
Samitier Martí, Josep	Fundación Instituto de Bioingeniería de Cataluña	Instituto de Bioingeniería de Cataluña	Barcelona
San Román del Barrio, Julio	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Ciencia y Tecnología de Polímeros	Madrid
Santamaría Ramiro, Jesús	Universidad de Zaragoza	Universidad de Zaragoza	Zaragoza
Santos Lleó, Andrés	Universidad Politécnica de Madrid	ETSI Telecomunicación	Madrid
Sanz Carrasco, Fausto	Universidad de Barcelona	Facultad de Química	Barcelona
Schwartz Navarro, Simó	Fundación Hospital Universitario Vall d' Hebron - Institut de Recerca (VHIR)	Hospital Vall d'Hebrón	Barcelona
Solans Marsá, Concepción	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Trepast Guixer, Xavier	Fundación Instituto de Bioingeniería de Cataluña	Instituto de Bioingeniería de Cataluña	Barcelona
Vallet Regí, María	Universidad Complutense de Madrid	Facultad de Farmacia	Madrid
Veciana Miró, Jaume	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Ciencias de Materiales de Barcelona	Barcelona
Vilaboa Díaz, Nuria	Servicio Madrileño de Salud	Hospital La Paz	Madrid
Villaverde Corrales, Antonio	Universidad Autónoma de Barcelona	Instituto de Biotecnología y Biomedicina	Barcelona



# Budget

INCOME				
ISCIII TRANSFER	GRANTS PROJECTS	RENDERED SERVICES	OTHER INCOMES	TOTAL
3.960.160,00	879.444,36	227.127,26	24.000,00	5.090.731,62

GASTOS				
PROJECT	INVENTORIABLE	PROVISIONS AND OTHER ACTIVITY EXPENSES	PERSONNEL	TOTAL
Scientific Management, Scientific Secretariat, Communication	0,00	90.922,00	64.195,54	155.117,54
Groups	77.191,76	319.234,23	1.084.193,43	1.480.619,42
Training and Capacity Building	0,00	22.577,70	1.608.948,07	1.631.525,77
Programmes	1.090,95	21.905,28	168.288,84	191.285,07
Platforms	19.616,57	64.361,39	58.815,00	142.792,96
Transfer	1.156,67	114.411,52	111.494,26	227.062,45
Intramural Projects	0,00	10.332,51	0,00	10.332,51
External Projects	1.295,99	448.252,34	606.915,32	1.056.463,65
<b>TOTAL</b>	<b>100.351,94</b>	<b>1.091.996,97</b>	<b>3.702.850,46</b>	<b>4.895.199,37</b>

# Personnel

Personnel contracted during the year as of 31 December itemised by categories:

	MEN	WOMEN	Overall Total
Diploma holders	-	1	1
Doctors	24	43	67
Graduates	17	23	40
Technical staff	1	10	11
<b>TOTAL</b>	<b>42</b>	<b>77</b>	<b>119</b>

# Significant activities

## Projects

### NATIONAL

#### Funding agency: Instituto de Salud Carlos III

- *Molecular links between diabetes and neurodegenerative disorders. PIE14/00061.*
- Cohort study. Search for biomarkers for early detection of Alzheimer's disease in the cohort of the Vallecas project.

#### Funding agency: Ministerio de Economía y Competitividad

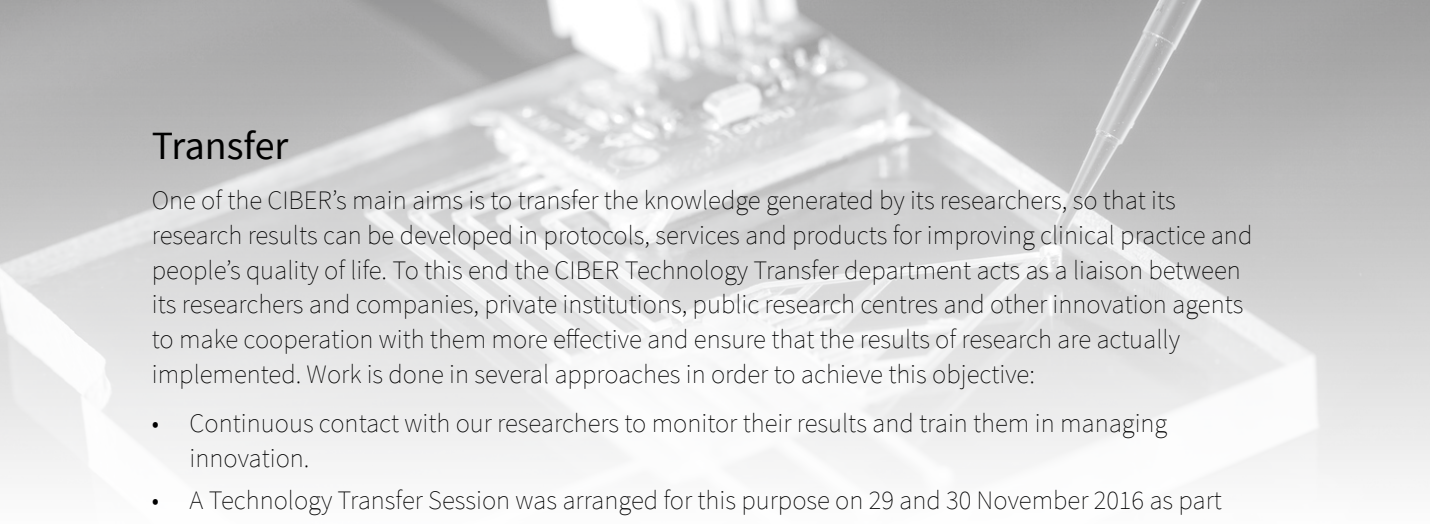
- 3 grants for contracts of Technical Support Personnel. PTA-2013-8426-I; PTA-2013-8849-I; PTA2014-09466-I.
- Consolidation of the model for management and promotion of NANBIOSIS. PRONANBIOSIS. SAF2015-69388-REDI.
- ANSHEART. The autonomic nervous system as modulator of cardiac function: integral research by signal processing and computational modelling. TIN2013-41998-R.
- TERARMET: Development of therapies for treatment of rare congenital metabolic diseases. RTC-2014-2207-01.
- TERET. New treatments for retinal degenerative diseases. RTC-2014-2038-01.
- *Nanoconductance of electron transfer proteins of the respiratory chain. Direct measurement at the single molecular level and therapeutic regulation in cancer stem cells. nanoET-leukemia. CTQ2015-66194-R.*
- Juan de la Cierva Grant for Training. FJCI-2015-27201.
- Development of systems of bioprinting and biodyes for three-dimensional regeneration of cartilage and bone. RTC-2016-5451-1.
- Development of a new bioadhesive for pterygium surgery. BIOTAPE. RTC-2016-4770-1.
- Purchase, installation and adjustment of the equipment for production and characterisation for complementing units: U3-Peptide Synthesis, U18-Nanotoxicology and U20- In vivo Experimentation. FICTS1420-02-20.

#### Other Funding agencies

- Ministry of Education, Culture and Sport: 2 Mobility grants José Castillejo. JC201500370; CAS16/00127.
- Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria: Optimisation of the cow's dry period by means of protein nanoparticles. RTA2012-00028-C02-02.
- Regional Ministry for Education, Research, Culture and Sport. Generalitat Valenciana. Subsidy for contracting predoctoral research staff. ACIF/2016/023.

### INTERNATIONAL PROJECTS EU

- Benzimidazol and Triazol Research group for Nanomedicine and Innovation on Chagas disease. BERENICE (FP7).
- Neurological recordings with Graphene. NEUROGRAPHENE (H2020). 9140.
- Graphene-based disruptive technologies. GrapheneCore1 (FP7) 696656.
- Diabetes Reversing Implants with enhanced Viability and long-term Efficacy Project. DRIVE (H2020). 645991-2.
- E-MEDIVIP: E-learning platform for medical informatics to improve vocational and ICT practice. 2015-1-TR01-KA202-022634 E. Erasmus+.
- Remote assessment of disease and relapse in central nervous system disorders. RADAR-CNS (IMI2). In cooperation with the CIBERSAM.



## Transfer

One of the CIBER's main aims is to transfer the knowledge generated by its researchers, so that its research results can be developed in protocols, services and products for improving clinical practice and people's quality of life. To this end the CIBER Technology Transfer department acts as a liaison between its researchers and companies, private institutions, public research centres and other innovation agents to make cooperation with them more effective and ensure that the results of research are actually implemented. Work is done in several approaches in order to achieve this objective:

- Continuous contact with our researchers to monitor their results and train them in managing innovation.
- A Technology Transfer Session was arranged for this purpose on 29 and 30 November 2016 as part of the 30th anniversary of ISCIII. At this event experts in different areas shared their knowledge on industrial property, company creation, licencing processes, venture capital, grants for internationalisation, etc..
- Protection of the results of research and management of cooperation with other agents, as is vouched for by the application for patents and signing licence contracts, amongst other agreements.
- In 2016 eleven new patent applications and a registration of software were thus submitted at the CIBER. Seven inventions are also in the patentability study and one in the drafting stage, and these are expected to be submitted in early 2017.
- Eight licence contracts have also been signed and in 2016 different negotiations that are expected to end successfully in the first quarter of 2017 were also got under way.
- Specifically in the area of Bioengineering, Biomaterials and Nanomedicine, three new patent applications have been submitted and one invention is in the patentability study stage. Four licence contracts have been signed with companies for marketing technologies in the BBN area.
- Presentation of the results of research and technological capacities of our groups in technology transfer sessions. Amongst many other measures, and merely as an example of this, CIBER had a stand attended by members of institutions at BIOSPAIN 2016 (28-30 September, Bilbao).
- Support for creating technology-based companies derived from CIBER groups.
- Other activities involving innovation, public-private cooperation and industrial and intellectual property.
- In the CIBERBBN area contracts with consultants for furthering transfer and translation of results have been signed.



## Dissemination

In 2016 the CIBER'S Communication Department carried out different dissemination and disclosure action in order to raise awareness about the Centre, as well as to spread knowledge about the research work done by the groups in its eight thematic areas.

The main highlights of the Communication work done by CIBER-BBN in 2016 are as follows:

- **The CIBER-BBN in the media:**

67 CIBER press releases were issued in this period, 6 of these from the CIBER-BBN and 2 in cooperation between several CIBER areas.

Date	Title	Researcher/s
21/03/2016	Diseñan nuevos nanodispositivos de liberación controlada de fármacos para terapias contra el cáncer de mama	Ramón Martínez-Mañez
03/05/2016	Diseñan un nuevo implante para la regeneración del cartilago articular	José Luis Gómez Ribelles
04/05/2016	Desarrollan una superficie para implantes óseos que favorece la regeneración y disminuye el riesgo de infecciones	María Luisa González
28/09/2016	Idean un nuevo sistema que permite la detección de cocaína a muy bajas concentraciones	Ramón Martínez Máñez
28/06/2016	Los teléfonos inteligentes y la tecnología 'wearable' pueden revolucionar la asistencia médica y la calidad de vida de personas con trastornos mentales	Josep Maria Haro (CIBERSAM) / Jordi Aguiló
15/11/2016	Desarrollan un dispositivo de cultivo en 3D de los tumores que permite comprender mejor su funcionamiento	José Ayuso / Eduardo Fernández / Ignacio Ochoa
28/11/2016	Desarrollan nanosistemas inteligentes para el tratamiento del neuroblastoma	María Vallet
16/11/2016	El CIBER acerca su investigación a la sociedad de la mano de la improvisación teatral en #ImproCiencia	Empar Lurbe (CIBEROBN) / Elisabet Prats

There were also 671 appearances in the media

2016	News	Audience
CIBER-BBN	671	62.941.600

- **CIBER Newsletter**

This year 5 CIBER newsletters were published and disseminated, including relevant content about the CIBER-BBN and other thematic areas. The digital newsletters were sent to roughly 4000 subscribers.

<http://www.ciberisciii.es/en/press/newsletter>

- **CIBER-BBN Newsletter**

In 2016 the CIBER-BBN newsletter was started up as a new tool for communication about this area. Every month, the newsletter contains an interview of a researcher and gives the news on the CIBER-BBN for that period <http://www.ciber-bbn.es/en/press/ciber-bbn-newsletter>. At present the newsletters are sent via e-mail to all the members of the area.

- **CIBER-BBN Web page**

In 2016 the CIBER-BBN web page published 75 news items and 39 events on the agenda.

Statistics for visits to the web page in 2016							
	No. of visits to pages	Sessions*	Users	Page/session	Average duration of the session	% rebound**	% new sessions
CIBER-BBN	104.892	36.743	21.657	2,85	2:17	59,45	57,62

(\*) Sessions: a session is a set of interactions taking place on this website in a certain period. For example, a single session may involve several pages being viewed.

(\*\*) Rebound: the rebound percentage is the percentage of sessions of a single page, i.e. the sessions in which the user has left the site on the entry page without interacting with this.

- **Social Networks**

Main indicators of the presence of CIBER-BBN on Twitter:

	Followers		Updates		Klout (Influence)	
	January	December	January	December	January	December
CIBER-BBN	2112	2559	1168	1455	46	46

- **CIBER-BBN Annual Report**

The CIBER Communication area coordinated the content of the CIBER-BBN Report 2015 in Spanish/English in cooperation with the CIBER-BBN, drawing up and disseminating 2 reports in interactive (flipbook) format and pdf. These reports were distributed over the web page and through Twitter account: <http://www.ciberisciii.es/en/press/annual-report>

- **CIBER Science Week #ImproCiencia**

The #ImproCiencia dissemination event, which was held on 16 November in Madrid, combined science and theatre improvisation to give a light-hearted explanation of the biomedical research work done by the CIBER in its eight thematic areas. At this event Elisabet Prats presented some of the properties of Graphene and its applications for research at the CIBER-BBN.



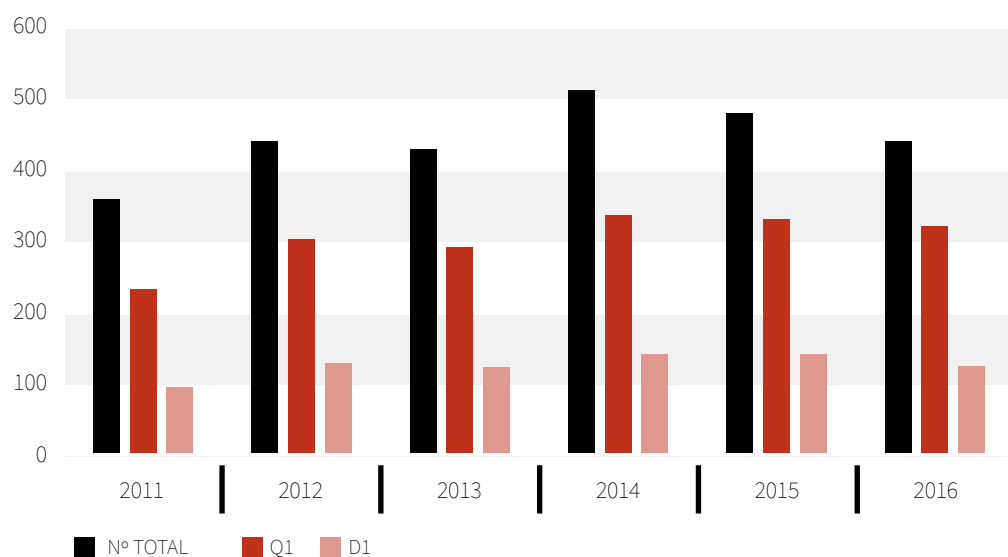
# Scientific Production

The evolution undergone by CIBER-BBN publications can be seen from the following tables, in which the data from 2010 to 2016 is analysed. The publications per group for this year are also itemised, as well as the interCIBER and intraCIBER cooperation work.

## Publications

Publications per year						
CIBER-BBN	2011	2012	2013	2014	2015	2016
Nº Totales	362	450	439	524	491	450
Q1	237	308	297	343	338	327
D1	95	130	124	142	142	125

### EVOLUTION OF CIBER-BBN PUBLICATIONS 2011-2016



## Most relevant publications of the CIBER-BBN in 2016 according to the Impact Factor

Publication	Impact Factor
Bodelon G., Montes-Garcia V., Lopez-Puente V., Hill E.H., Hamon C., Sanz-Ortiz M.N. et al. Detection and imaging of quorum sensing in Pseudomonas aeruginosa biofilm communities by surface-enhanced resonance Raman scattering. Nature Materials. 2016;15(11):1203-1211.	38,891
Aragones A.C., Haworth N.L., Darwish N., Ciampi S., Bloomfield N.J., Wallace G.G. et al. Electrostatic catalysis of a Diels-Alder reaction. Nature. 2016;531(7592):88-91.	38,138
Aznar E., Oroval M., Pascual L., Murguia J.R., Martinez-Manez R., Sancenon F. Gated Materials for On-Command Release of Guest Molecules. Chemical Reviews. 2016;116(2):561-718.	37,369
Sunyer R., Conte V., Escribano J., Elosegui-Artola A., Labernadie A., Valon L. et al. Collective cell durotaxis emerges from long-range intercellular force transmission. Science. 2016;353(6304):1157-1161.	34,661
Paradis-Bas M., Tulla-Puche J., Albericio F. The road to the synthesis of "difficult peptides". Chemical Society Reviews. 2016;45(3):631-654.	34,090
Grimaldi N., Andrade F., Segovia N., Ferrer-Tasies L., Sala S., Veciana J. et al. Lipid-based nanovesicles for nanomedicine. Chemical Society Reviews. 2016;45(23):6520-6545.	34,090
Palao-Suay R., Gomez-Mascaraque L.G., Aguilar M.R., Vazquez-Lasa B., Roman J.S. Self-assembling polymer systems for advanced treatment of cancer and inflammation. Progress in Polymer Science. 2016;53:207-248.	27,184
Gonzalez-Rubio G., Guerrero-Martinez A., Liz-Marzan L.M. Reshaping, Fragmentation, and Assembly of Gold Nanoparticles Assisted by Pulse Lasers. Accounts of Chemical Research. 2016;49(4):678-686.	22,003
Leonardi F., Casalini S., Zhang Q., Galindo S., Gutierrez D., Mas-Torrent M. Electrolyte-Gated Organic Field-Effect Transistor Based on a Solution Sheared Organic Semiconductor Blend. Advanced Materials. 2016;28(46):10311-10316.	18,960
Elosegui-Artola A., Oria R., Chen Y., Kosmalska A., Perez-Gonzalez C., Castro N. et al. Mechanical regulation of a molecular clutch defines force transmission and transduction in response to matrix rigidity. Nature Cell Biology. 2016;18(5):540-548.	18,699

## Publications per group

Group leader	TOTAL PUBLICATIONS	Q1	D1
Aguiló Llobet, Jordi	6	6	1
Albericio Palomera, Fernando	26	15	6
Arús Caralto, Carles	8	5	0
Becerra Ratia, José	7	6	3
Bellón Caneiro, Juan Manuel	7	3	0
Blanco Fernández, Jerónimo	4	4	0
Calonge Cano, Margarita	9	6	1
Engel López, Elisabeth	10	6	3
Eritja Casadella, Ramon	11	6	3
Farré Ventura, Ramon	20	13	2
Fernández Jover, Eduardo	10	8	3



Group leader	TOTAL PUBLICATIONS	Q1	D1
Gómez Ramírez, Rafael	14	10	0
Gómez Ribelles, José Luis	25	16	4
González Martín, María Luisa	8	6	1
Jané Campos, Raimon	15	14	2
Laguna Lasaos, Pablo	12	4	1
Lechuga Gómez, Laura María	9	9	6
Leiva Hidalgo, Alberto	9	2	2
Liz Marzán, Luis Manuel	24	22	15
Mangues Bafalluy, Ramon	9	9	2
Marco Colas, María Pilar	8	7	3
Martínez Barca, Miguel Ángel	26	20	4
Martínez Mañez, Ramón	26	20	10
Muñoz Fernández, María Ángeles	9	8	0
Pavía Segura, Javier	5	4	1
Pedraz Muñoz, José Luis	11	7	1
Peris Serra, José Luis	5	1	1
Pozo Guerrero, Francisco del	9	6	2
Raya Chamorro, Ángel	6	5	3
Ritort Farran, Félix	3	3	1
Roa Romero, Laura María	1	1	0
Rodríguez Cabello, José Carlos	11	8	4
Ruiz Romero, Cristina	2	0	0
Samitier Martí, Josep	3	3	0
San Román del Barrio, Julio	16	10	2
Santamaría Ramiro, Jesús	24	20	12
Santos Lleó, Andrés	7	4	1
Sanz Carrasco, Fausto	9	7	4
Schwartz Navarro, Simó	11	11	4
Solans Marsá, Concepción	9	4	1
Trepat Guixer, Xavier	7	7	5
Vallet Regí, María	21	14	6
Veciana Miró, Jaume	21	20	12
Vilaboa Díaz, Nuria	9	8	2
Villaverde Corrales, Antonio	13	11	4

## COLLABORATION WORK

Collaboration	2015	2016
IntraCIBER publications	67	55
InterCIBER publications	39	30

## Patents

### APPLIED FOR

#### **National**

- Connection device for microfluidic circuits.
- Procedure for exfoliation and transfer of graphene from a silicon carbide substrate doped into another substrate.

#### **European**

- Procedure for preparation of polymeric materials based on lactide, materials obtained by means of this procedure and their uses.

#### **International**

#### **PCT**

- Use of an adrenomedullin inhibitor for manufacturing a medication useful in preventing and treatment of diseases which reduce bone density.
- Compounds and their uses as haptens for detection of S. Aureus.
- Microfluidic chip, microfluidic device, procedures and associated uses.
- Microfluidic device and system for studying cell cultures.

#### **NATIONAL/REGIONAL EUROPEAN STAGE**

- Intelligent bioimpedance sensor for biomedical applications.
- Bioreactor for cell co-culture.

#### **NATIONAL PHASE U.S.A.**

- Bioreactor for cell co-culture.

#### **VALIDATION IN GERMANY, SPAIN, FRANCE, ITALY AND THE UNITED KINGDOM**

- A 1,4,5-trisubstituted 1,2,3-triazole mimetic of RGD or/and OGP10-14, procedure for obtaining this and its usages.

### GRANTED

#### **National**

- Method for surface chemical activation of a solid silicon-based support by means of direct covalent anchorage of at least one biomolecule of nucleic acids.
- Bioactive glasses, bioactive glass scaffolds and bioactive glass scaffolds seeded with cells: methods for preparation and its uses.

#### **European**

- A 1,4,5-trisubstituted 1,2,3-triazole mimetic of RGD or/and OGP10-14, procedure for obtaining this and its usages.



# 3

Scientific  
Programmes

# Bioengineering and Medical Imaging

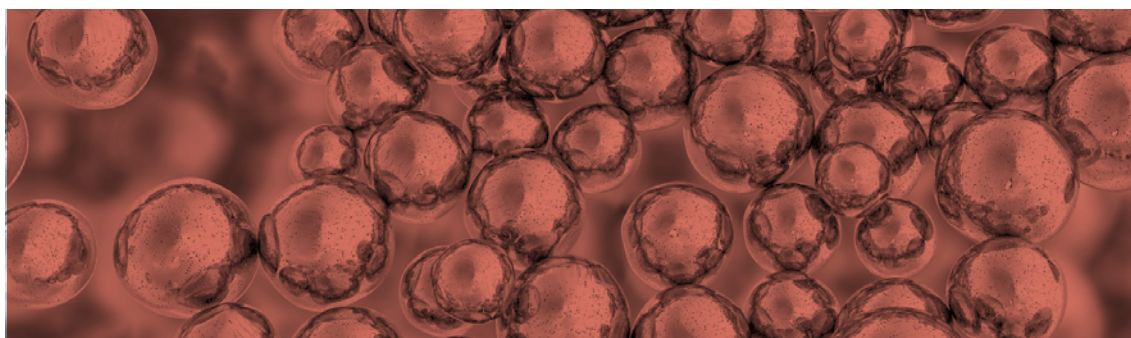
Coordinator: **Jordi Aguiló Llobet**

The scientific work done by the 10 research groups forming part of the Bioengineering and Medical Imaging programme resulted in roughly 80 publications (70% in Q1 and 23% in D1). Some of the programme's research lines furthermore exceeded the CIBER limits and obtained merits and financing through external competitive calls. Some of these that deserve mention are listed below:

- **Research into a personalised biomarker for depression and stress** (intramural project DEANS, PI: Raquel Bailón). The GBIO groups, led by Jordi Aguiló at the Universidad Autònoma de Barcelona and the BSICOS group, led by Pablo Laguna at the Universidad de Zaragoza, along with Josep María Haro's group from the CIBERSAM are taking part in the European project IMI2 RADAR-CNS: Remote Assessment of Disease and Relapse – Central Nervous System, which is being coordinated by King's College of London and Janssen Pharmaceutica NV. The project began in April 2016 and will last for 5 years.
- **Search for biomarkers for early detection of Alzheimer's disease in the Vallecas project cohort.** The groups led by Javier Pavía and Francisco del Pozo are taking part along with Ramón Martínez-Máñez's group in this project, to last 3 years, coordinated by the Fundación CIEN.
- **GRAFENO.** The CIBER-BBN, through researcher Rosa Villa of the Centro Nacional de Microelectrónica, is taking part in the CORE1, the new work package of the Graphene Flagship engaged in Biomedical Technologies, which is coordinated by Prof. Kostas Kostarelos, from the University of Manchester. Dr Villa's team presented their work in this field in the World Mobile Congress, attracting a great deal of interest from the visitors and the media. During the #ImproCiencia dissemination event organised by the CIBER, Elisabet Prats, from the same group, gave a monologue format presentation explaining how they are using graphene to measure the electrical activity of the brain in the Neurographene project, in which the CIBER-BBN is taking part along with the IDIBAPS and the company g.tec
- **Lab on a chip.** This other line of work by Rosa Villa and Jordi Gràcia-Sancho's group, from the CIBEREHD group at the Hospital Clínic-IDIBAPS about a microfluidic camera which simulates hepatic microcirculation, was recognised in the Awards for the Best Ideas of *Medical Journal* in November 2016. The same technology was awarded a prize in the 2016 edition of the Caixa Impulse competition and receives financing for the creation of a platform of services for in vitro studies and diagnoses of the cell functioning in vascular systems (liver, kidney, cardiovascular and others), pharmacology, toxicity and personalised medicine.

Apart from this Raimon Jané, head of the Biomedical Signals and Systems Group of the CIBER-BBN at the Instituto de Bioingeniería de Cataluña (IBEC) and the Universitat Politècnica de Catalunya, was re-elected president of the Sociedad Española de Ingeniería Biomédica (SEIB) for coming period 2016-2020.

Lastly, one should mention that the Photonic Engineering Group programme of the Universidad de Cantabria, led by José Miguel López-Higuera, joined the programme, as was officially announced in December 2016.





# Biomaterials and Advanced Therapies

Coordinator: **Julio San Román del Barrio**

In 2016, one European patent and one national patent were applied for. Three patents previously applied for (one European and two Spanish) were extended to PCT. One European patent previously extended to PCT was validated over the year in France, Germany, Italy, UK and Spain. One European patent and two Spanish patents have been licensed to companies.

The scientific production of articles, reviews, editorials and letters comes to around 170 publications, around 70% of which were in the first quartile and 21% in the first decile.

Financing has been achieved for several multidisciplinary research projects, stressing the cooperation of several groups in the excellence network *Research Network for the Development of Biofunctionalized Titanium Implants* (BIOIMPLANT) led by the Biomaterials Centre of the Universidad Politécnica de Valencia, whose Principal Investigator is José Luis Gómez Ribelles, and in which the groups of George Altankov from the IBEC, Marisa González from the Universidad de Extremadura, José Carlos Rodríguez from the BIOFORGE-UVA, and Nuria Vilaboa from the IDIPAZ are cooperating.

Financing has also been achieved for the RETOS - Colaboración Project *Systems of 3D bioprinting and biodyes for three-dimensional regeneration of cartilage and bone*, in which the Biomaterials Group of the ICTP-CSIC whose PI is Julio San Román, and NANBIOSIS-ICTS are cooperating. The project is coordinated by the BIOIBÉRICA company and the REGEMAT 3D company is also cooperating in this.

As regards high-impact scientific results, it should be mentioned that members of the research group led by Ángel Raya at the CMRB are coordinating a study which is proving that it is possible to convert skin cells of megakaryocytes with the same functions as the ones found in the human body, able to produce platelets, the cell types responsible for normal coagulation in the blood. This study has been published in the prestigious journal *Cell Reports*.

Dr María Vallet, who leads the Group for Investigation of Intelligent Biomaterials of the Universidad Complutense de Madrid, has obtained an *ERC Advanced Grant* for developing a polyvalent mesoporous nanosystem for treatment of bone diseases. Dr Vallet is considered to be one of the 300 researchers most cited in the world of science and materials engineering according to the list drawn up by MSE Supplies (ranking based on the Elsevier Scopus database), and also the Fundación Lilly has acknowledged her scientific career with the Prize for a Distinguished Career in the Speciality of Chemistry.

In 2016 the company *BeOnChip* was set up, as a derivative of the GEMM-I3A group of the Universidad de Zaragoza, which internationally markets microfluidic devices for cell culture in biomimetic atmospheres.

Also in this research group, María Virumbrales obtained the prize for best oral communication at the Congreso Nacional de Jóvenes Investigadores en Biomedicina (Valencia, 28-29 November).

This scientific programme continues to cooperate another year as Interested Party of the CAT-EMA (Comité de Terapias Avanzadas de la Agencia Española del Medicamento). We should stress the participation of CIBER-BBN in the IMI-EMA consultation on advanced therapies which was made during the second quarter of 2016, and whose results were discussed at the *IMI Stakeholder Forum* (Brussels, 29 September) giving ideas for the new IMI2 calls.

It has continued to cooperate with the CIBER-BBN initiative *Young Scientist Forum on Biomaterials* in the framework of its Annual Sessions.

# Nanomedicine

Coordinator: **M. Pilar Marco Colás**

In 2016 the new intramural projects of the CIBER-BBN for the 2016-2018 call started. 25 of the 69 accepted projects belonging to the nanomedicine programme, 10 of which were classified as excellence projects.

As one of the principal investigators of the Nanomedicine programme, Luis Manuel Liz Marzán is one of the most cited scientists in the world (published by Clarivate Analytics) along with María Vallet Regí (MSE Supplies). Laura M. Lechuga was awarded the Physics Prize of the Real Sociedad Española de Física (RSEF)-Fundación BBVA 2016 and was chosen as one of the 12 members that the journal QUO selected for its Spanish Selection for Science 2016. Our Scientific Director, Ramón Martínez-Máñez, has been given the prize for Research Excellence 2016 by the Real Sociedad Española de Química (RSEQ). Simó Schwartz has been appointed president of the European Society for Nanomedicine (ESNAM) and member of the executive board of the International Society of Nanomedicine (ISN) and of the advisory board of the Nanomedicine Characterisation Laboratory (EU-NCL). Lastly, Josep Samitier has been appointed president of the Associació Catalana d'Entitats de Recerca (ACER).

The researchers in the CIBER-BBN Nanomedicine Programme have continued with the externally financed projects obtained such as the TERARMET (Public-Private RETOS Project), PENTRI (Proyecto Marató of TV3 television station) and the LIPOCELL project of the transfer programme coordinated by Nora Ventosa. We should mention that funds were obtained for carrying out projects in public financing calls, on both Spanish and international scales. The following research projects which have obtained external financing could thus be highlighted:

- SMART-4 FABRY (Smart multifunctional GLA-nanoformulation for Fabry Disease), a project focussing on the development of nanoformulations to encapsulate the GLA enzyme for treatment of Fabry's Disease. This project is coordinated by the CIBER, its principal investigator and coordinator being Dr Nora Ventosa. This project, approved in 2016, was got under way in January 2017 and will last until December 2020. It has the participation of nine partners as well as the CIBER.
- The NanoET-Leukemia Project (Nanoconductance of electron transfer proteins of the respiratory chain. Direct measurement at the single molecular level and therapeutic regulation in cancer stem cells) is led by two contracted CIBER researchers, Dr Marina Inés Giannotti and Dr Anna Lagunas. On the national level financing has been obtained in the RETOS call for R+D+i (CTQ2015-66194-R).
- Furthermore, in the RETOS Colaboración call by MINECO [Ministry of the Economy and Competitiveness], the group in the nanomedicine programme of Jose Luis Pedraz has obtained external financing in two projects: Bioprinting and Biodyes for three-dimensional regeneration of cartilage and bone (RTC-2016-5451-a) and BIOTAPE (Development of a new bioadhesive for Pterygium surgery, RTC-2016-4770-1).

Lastly, the Caixaimpulse programme has selected two projects coordinated by CIBER-BBN researchers. The first of these is the ISCHEMSURG project, led by Mónica Mir, a CIBER researcher in Josep Samitier's research group and the second project is that of Pseudomonas aeruginosa diagnosis, to be led by Miriam Corredor from Pilar Marco's group in the IQAC-CSIC.

The group from the Instituto de Ciencia de Materiales de Aragón led by Jesús Martínez de la Fuente joined the Nanomedicine programme in late 2016 as a result of the call made by the Instituto de Salud Carlos III.

The following events and congresses concerning the Nanomedicine area were attended:

- CLINAM 2016 (European Foundation for Clinical Nanomedicine). Basel (Switzerland), 26–29 June 2016.
- Biospain 2016 (8th International Meeting on Biotechnology). Bilbao, 28–30 September 2016.
- Annual Meeting of the ETPN (European Technology Platform of Nanomedicine). Heraklion (Greece), 12–14 October 2016.

The scientific production of the programme consists of almost 240 publications (articles, reviews, editorials and letters), 84% of these in the first quartile and 35% in the first decile.



4

Transversal  
Programmes

# Industrial Transfer Programme

Coordinator: **Simó Schwartz Navarro**

In 2016 two Spanish patents, one European patent and four PCT extensions were applied for and three patents went into national stages, being validated in several countries. The grant of two Spanish and one European patents has been received and four licence contracts have been signed.

Five CIBER-BBN transfer projects were undertaken, with the support of the five companies financing these. Another of these projects has ended, due to reaching the end of the planned performance period, obtaining the results set at the start. The company and the groups of the CIBER-BBN continue to develop the technology of this last project, extending their cooperation by means of two projects with external financing. A new call for transfer projects is made, the start of two new projects being planned after signing the required R+D contracts with the companies.

Service provision contracts have been signed with seven consultancy companies for boosting technology transfer. These consultants have met the research groups of the CIBER-BBN to get to know their technologies, which they have valued for their transfer potential. Contacts have been made with some companies and investors to find out their interest in our technologies by means of cooperation and/or investment in our projects, creation of spin-off companies or acquisition of licences for our patents. As a result of this strategic action a project was submitted for the FIPSE (Fundación para la Innovación y la Prospectiva de Salud en España) call. Contacts with companies for possible cooperation in projects are also open.

# Translational Research Programme

Coordinator: **Ramón Mangues Bafalluy**

Aware of the fact that bringing our technologies closer to the clinical world is a task where there is still room for improvement, encounters with clinical staff have been held in the framework of the CIBER-BBN 2016 sessions to promote knowledge of the problems being faced by doctors. Three thematic forums were specifically arranged: on cancer, infections in implants and neurological diseases. In a first part of each forum, three doctors specialising in each field set forth their vision from the standpoint of clinical practice. Later on there was a chance to organise individualised debates at round tables between researchers and doctors which were highly enriching for both groups.

Cooperative projects in respiratory pathologies continued to be developed along with CIBERES and SEPAR, and work has started on defining a new cooperation call to be launched in 2017 by CIBER-BBN, CIBERER and CIBERES.

CIBER-BBN has gone on being an Interested Party in the Committee for Advanced Therapies (CAT) of the European Medicines Agency (EMA).

The call for intramural projects decided in 2016 passed 69 new cooperative projects, each of these focussing on solving a specific clinical problem. The pathologies which are tackled by cooperative research done in the framework of these projects are: cancer (24 projects), arthrosis, arthritis and bone regeneration (9), neurological and mental diseases (9), infectious diseases (6), ophthalmology (5), cardiovascular diseases (5), kidney diseases (3), ulcer healing (2), diabetes (2), implants (2), respiratory diseases (1) and rare diseases (1).



# Training and Qualification Programme

Coordinator: **Raimon Jané Campos**

The CIBER-BBN training programme sets out to increase the research skills of the staff in the groups by improving the professional competence of the technical and research staff as a factor for change, transforming the attitudes, knowledge and skills in accordance with the needs arising during the performance of their research activity.

The main initiatives in the CIBER-BBN training programme are support for initiation to research and aid for mobility.

## Training support for initiation to research

The aim of these “launching” grants is to cover the transitory period from the final stage of master studies until the resolution is published in public calls for pre-doctorate grants or other career paths which mean employment opportunities for recently qualified persons.

A single call was held in 2016, in the month of April. Unlike 2015, when two calls were issued over the year, in 2016, even though only a single call was made, the usual duration of 12 months for each of the grants was recovered. The number of applications was very high due to the interest that these grants arouse in the research groups. A total number of 14 grants were given for candidates with best academic records and in view of the suitability of their proposals for the priority lines of research of the CIBER-BBN.

### NO. OF “INITIATION TO RESEARCH” GRANTS ISSUED

2011	2012	2013	2014	2015	2016
19	12	15	37	18	14

## Aid for mobility

The purpose of this training programme is to encourage short stays at other research groups in order to facilitate transfer of experience and technology and to boost cooperation between different groups of the CIBER-BBN. These stays have to involve priority and strategic lines of work for our thematic area.

In 2016 there were two mobility calls, in March and September, and a total number of 13 grants for stays at groups outside the CIBER-BBN were awarded.

Four grants were awarded as mobility aid for research staff at CIBER-BBN groups, with permanent calls over the year.

Year	Nº intra-CIBER-BBN awarded mobility aids	Nº external awarded mobility aids	Nº total awarded mobility aids
2011	6	10	16
2012	6	9	15
2013	1	20	21
2014	2	17	19
2015	3	18	21
2016	4	13	17

# Dissemination Programme

The 10th Annual CIBER-BBN Sessions were held in Seville on 27 to 29 November 2016, attended by around 200 researchers.

The Scientific Encounter was preceded the day before by a meeting of the director with the principal investigators of all the groups, where they shared relevant aspects about the centre's progress (scientific programme, budget aspects, welcome to new groups, evaluation of the groups, projects under way, future actions planned, etc.)

The aim of these sessions was to provide an encounter for the whole CIBER-BBN community and foster communication and cooperation between the members of the research groups, identification of the points in common and exchange of ideas.

The content of the Sessions did not involve intramural projects as in previous years, but was instead in the form of thematic sessions along with clinical professionals from the field of cancer, traumatology and neurology. There was also a special session in which certain successful cases of the NANBIOSIS structure were put forward.

The programme also included two plenary sessions: "Nanomedicine and cancer", by Professor Alberto Gabizon, from the Hebrew University of Jerusalem and "Redefining identity of disease, tissue and cells – A biomaterials paradigm", by Professor Abhay Pandit from the National University of Ireland.

There were also presentations of the last three groups that joined CIBER-BBN at the calls for Strategic Action in Health for 2015 and 2016.

Members of our External Advisory Scientific Committee and the Medical Advisory Committee took part in this event. The Management Committee had a meeting with both advisory committees at the end of the sessions.

Other events to be stressed are the ones organised with Turin University, First of all, CIBER- BBN attended a joint meeting in March in Turin. To ensure continuity of the contacts identified, in November an encounter was arranged between CIBER-BBN researchers and units of the NANBIOSIS infrastructure with researchers from Turin University. The purpose of this event was to bring researchers from both institutions together to promote scientific cooperation and joint projects.

The event was held at the residence of CSIC researchers in Barcelona. Individual presentations of research groups from both the CIBER-BBN and Turin University were given and later on there was a session of bilateral encounters, with over 75 meetings planned.

Other events attended were:

- CTLS 2016 (Core Technologies for Life Science). Heidelberg (Germany), 12–15 June 2016.
- CLINAM 2016 (European Foundation for Clinical Nanomedicine). Basel (Switzerland), 26–29 June 2016.
- Biospain 2016 (8th International Meeting on Biotechnology). Bilbao, 28–30 September 2016.
- Annual Meeting of the ETPN (European Technology Platform of Nanomedicine). Heraklion (Greece), 12–14 October 2016.





# Internationalisation Programme

Coordinator: **Cristina Rodríguez**

Last 11 May 2015 the CIBER Platform for Support for Internationalisation was set up. The **Platform for Support for Internationalisation** (PAI) came about as a joint initiative of the areas of Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Rare Diseases (CIBERER) and Respiratory Diseases (CIBERES), of the Centro de Investigación Biomédica en Red (CIBER), in order to underpin and coordinate the endeavours intended to promote the participation of its researchers in European Programmes and to create a common structure to foster internationalisation and leadership of research and innovation in these three thematic areas.

In 2016 the platform focussed its work on two main areas: fostering participation of all the CIBER groups in international projects and improving the visibility of the CIBER on an international scale.

As regards fostering the participation of CIBER groups in international projects and improving the quality of the proposals put forward, the PAI held 4 specific sessions for dissemination of the advantages of internationalisation and gave 3 specific courses on writing and managing European Projects intended for researchers and managers in the CIBER environment: “Relevant aspects in presenting and justifying European proposals in the CIBER environment” (April 2016, with 70 persons attending) and “Writing successful collaborative proposals in the H2020 setting” (Madrid edition, June 2016, with 40 attending and Barcelona Edition, September 2016, with 44 attending) which were a great success for the participants.

In order to raise the quality of the proposals and improve returns the PAI got under way a Service for editing proposals which carried out the following activities: 1) Solving doubts and positioning of proposals (contrasting the scientific idea with that of the call and issuing a grounded report with recommendations on how to adapt the idea, need for strategic partners, etc...) in which the PAI has received over 27 consultations in this respect; 2) Editing proposals (PAI has edited over 20 proposals); 3) Evaluation of results (in previous proposals or those not sent through the PAI), giving a grounded criticism of the result and proposing where there is room for improvement (12 requests in the period); 3) Seeking strategic partners (6 requests in this period, plus 6 external partners who got in touch with CIBER to propose joint cooperation).

Thanks to this work, CIBER put forward 36 new proposals in 2016, 4 new projects being granted. Expressions of interest were received for the presentation of 10 new proposals. In this field it should be stressed that CIBER has received 5 new contacts from research groups or companies in order to establish agreements for joint presentation of proposals in the H2020 environment, and 2 of these contacts have now materialised in the real presentation of two H2020 proposals.

In the field of the CIBER'S international visibility, the CIBER has done some intensive work by attending over 18 events (including informative sessions, infodays and events for seeking partners). The platform also placed special emphasis on establishing a smooth relationship with different national representatives and national points of contact, by means of specific meetings, acting as a point of contact on the institutional level. In order to improve international presence, specific meetings were held with NCPs and with the head of the H2020 programme in order to ensure easier relations. This improvement in communication has meant that the CIBER was invited to the Forum for strategic definition of the Wp2018-2020 and took an active part in defining the 2017 work programmes and IMI calls as scientific experts. It was also decided to include postulating CIBER for participation in joint measures JA-01, 02, 03, 04, 05-2016 in which the possibility of taking part in measures as associated centres was put forward. It should be mentioned that thanks to the campaign for recruiting experts promoted by the PAI, CIBER has included over 15 new profiles in the Cordis database and has promoted updating the existing ones. As a result of this work CIBERER researcher Carmen Ayuso was selected to form part of the group of experts in Ethics and Scientific Integrity, in the framework of the Science with and for Society of the 2020 Horizon (SwafS-ethics) programme, while researchers Mercedes Serrano and Isabel Varela, recently created profiles, were contacted to take part as assessors.





# 5

Platforms



# ICTS NANBIOSIS

Coordinator: **Jaume Veciana Miró**

In 2016 the internal assessment of the units went on in order to assign economic incentives in accordance with the work done the previous year, in keeping with the established assessment protocol. Yet another year the search for external financing from both public and private sources was a priority.

The platform programme was presented to international bodies and partnering events, as well as national companies, private research foundations and public research bodies. Promotion material was given out at different visits to companies, research centres and industrial associations, as well as through MATERPLAT Spanish Technology Platform, in which the NANBIOSIS Coordinator has been requested to direct the Group for Innovation in Health, or the Spanish Biotechnology Platform. Similarly, participation was promoted in international initiatives and infrastructures such as ETP Nanofutures, Eurobioimaging, ARBRE and the MOBIEU Cost Action. What is more, contacts have been got under way with EATRIS in order to establish cooperation.

A large number of national and international events were attended, including the Annual Conference on Research Platforms in Biomedicine, the Session on European Infrastructures (CTLS 2016) and partnering events such as Biospain for seeking associates, as well as having arranged a forum with groups from Turin University with over 70 B2B encounters. The First Meeting of the Scientific Advisory Committee of the NANBIOSIS was held to discuss the Strategic Infrastructure Plan, a meeting which was held coinciding with the Annual Sessions of the CIBER-BBN.

The follow-up of the cooperation work already under way with companies went on. Some examples of this are the PHYTECH (INNPACTO) project, which ended in 2016 and in which two Spanish companies and a unit from the programme are involved (Characterisation of surfaces and Calorimetry), the European BERENICE project (FP7), covering two units (for Molecular Biomaterial Processing and Nanostructuring Unit and Medicine Formulation Unit), the TERET project (RETOS- COLABORACIÓN), in which two companies are taking part (Sylentis and LeadArtis) along with the Medicine Formulation Unit, and a further two groups of the CIBER-BBN, or the DRIVE Project (H2020) in which one unit is involved. In 2016 two new projects were granted in the RETOS-COLABORACIÓN call (Development of a new bioadhesive for pterygium surgery and Development of bioprinting and biodye systems for three-dimensional regeneration of cartilage and bone) in which one unit of the NANBIOSIS is participating (Medicine formulation unit) and in which several companies are taking part, including Regemat, Bioibérica and AJL.

Thanks to the PRONANBIOSIS project, financed by the MINECO for consolidation and promotion of NANBIOSIS (in the call for Excellence networks) operating as ICTS (Unique Technical Scientific Structure) has been successfully consolidated. Several measures have been performed, such as drawing up the marketing plan (which is already being implemented) online promotion and presence on the social networks. A new person has also joined the programme to be able to carry out management tasks for the ICTS, such as for example processing 275 applications for access.

In an attempt to promote cooperation with companies, making our services more appealing, support has continued for units interested in certification to ISO 9001 standards. In 2016, the process for certifying several units was consolidated, so that units U6 (Molecular Biomaterial Processing and Nanostructuring) and U12 (Characterisation of nanostructured liquids) have obtained TECNIO Certification and U2 (Production of antibodies) is already in the process of obtaining this, while six units have ISO certification and three GLP certification.

As regards training work, we should highlight the agreement signed with the UAB to develop the practical work programme of the Advanced Nanoscience and Nanotechnology programme at certain units of NANBIOSIS, as well as obtaining financing by means of a Marie Curie measure for one unit (U10).



## Cooperation with other platforms

- Platform of the Instituto Universitario en Nanociencia de Aragón (INA).
- Centro de Cirugía de Mínima Invasión Jesús Usón.
- CICbiomaGUNE Imaging Unit.
- BIONAND (Centro Andaluz de Nanomedicine y Biotecnología).
- International Nanotechnology Laboratory (INL).

The first contacts with EATRIS have also been made to establish cooperation schemes.







# 6

Research  
Groups






LEAD RESEARCHER

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PROGRAMMES

**Bioengineering & Medical Imaging**



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**Associated members:** Gabriel Buguña, Gemma | Garzón Rey, Jorge Mario | Godignon, Philippe | Guimera Brunet, Antón | Hotter Corripio, Georgina | Palacios Raufast, Luis | Villa Sanz, Rosa

**Contributors:** Arza Valdés, Adriana | Cerón Hurtado, Nathalie Marcela

## Main lines of research

The main objective of the GBIO group is the development of technically feasible, economically viable and clinically usable micro-nano-bio systems to measure key parameters related to the state or evolution of a living organism at a given moment.

This is achieved through the development of:

- **Technology.** The key concern is the development of new technologies that can lead to the development and manufacture of microsensors not only technically and economically viable, but also adaptable to the requirements of specific applications. This means that besides the current technologies based on silicon substrates, also silicon carbide and / or polymeric substrates could be also used to fulfill specific needs because of their special properties, such as hardness, flexibility or low cost. Alternative surface treatments should be also developed in order to build new sensors, for improved function or to avoid undesired effects.
- **Devices.** The goal at this level is to develop microsensor devices, multi-micro sensors, sensing arrays or sensor platforms for measuring physical, chemical and biological parameters and components such as oxygen, impedance, pH, different type of anions and cations, temperature, or proteins, for example, using an integrated unique device. The ultimate objective is to enable easy multiple monitoring in

- applications requiring multiparametric control.
- Systems/Applications. The developed technologies and devices will constitute useful tools to be used both on the experimental bench as well as in medical and clinical applications.
- GBIO group has developed during the last few years an outstanding expertise in the design and fabrication of Micro-Nano-Bio devices based either on silicon or biocompatible polymers. Biological signals obtained with these devices are usually subjected to post-acquisition conditioning and processing with the help of totally integrated systems.

## Most relevant scientific articles

- JUNG M., BRUNE B., HOTTER G., SOLA A. Macrophage-derived Lipocalin-2 contributes to ischemic resistance mechanisms by protecting from renal injury. *Scientific Reports*. 2016;6.
- GUIMERA X., DORADO A.D., BONSFILLS A., GABRIEL G., GABRIEL D., GAMISANS X. Dynamic characterization of external and internal mass transport in heterotrophic biofilms from microsensors measurements. *Water Research*. 2016;102:551-560.
- YESTE J., ILLA X., GUTIERREZ C., SOLE M., GUIMERA A., VILLA R.. Geometric correction factor for transepithelial electrical resistance measurements in transwell and microfluidic cell cultures. *Journal of Physics D: Applied Physics*. 2016;49(37).
- MOYA A., SOWADE E., DEL CAMPO F.J., MITRA K.Y., RAMON E., VILLA R. ET AL. All-inkjet-printed dissolved oxygen sensors on flexible plastic substrates. *Organic Electronics: physics, materials, applications*. 2016;39:168-176.
- HERNANDO A., LAZARO J., GIL E., ARZA A., GARZÓN J.M., LÓPEZ-ANTÓN R. ET AL. Inclusion of Respiratory Frequency Information in Heart Rate Variability Analysis for Stress Assessment. *IEEE Journal of Biomedical and Health Informatics*. 2016;20(4):1016-1025.

## Highlights

- Participation in the Graphene Flagship, the EU's biggest research initiative, within the work package devoted to Biomedical Technologies (GrapheneCore1: Graphene-based disruptive technologies, H2020-Adhoc-2014-20)
- Approval and starting of a new European project (BrainCom: High-density cortical implants for cognitive neuroscience and rehabilitation of speech using brain-computer interfaces, FETPROACT-2016) para desarrollar una nueva generación de dispositivos prostéticos corticales que permitan la estimulación y seguimiento a gran escala de la actividad cortical para estudiar las funciones cognitivas superiores.
- 2 patents related to the methods for growing and transfer of graphene material: "Procedimiento de exfoliación y transferencia de grafeno de un sustrato de carburo de silicio dopado a otro sustrato" y "Procedimiento de obtención de Láminas de Cobre como sustrato para la producción de grafeno de alta calidad".
- Prize "Las mejores ideas de 2016 de Diario Médico" (category of Investigation&Pharmacology) to the device Liver on a Chip developed together with the group of Dr. Jordi Gracia-Sancho (IDIBAPS & CIBEREHD).





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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

- Design and synthesis of bioactive low molecular weight compounds and peptides.
- Dendrimers based on defined units of oligoethylene glycol (OEG) as multifunctional systems for the creation of new biomaterials with application to drug delivery and tissue engineering (osteogenesis).
- Drugs-polymer conjugates based on polyglutamic (PGA), OEG dendrimers and drug-polymer micelles, as nanomedicine for the advanced colorectal and triple negative breast cancer treatment. Study of the use of these platforms on monotherapy and combined therapy with or without active targeting.
- Multiple ligands as chemical tools to study various biological processes, for example: G protein-coupled receptors (GPCRs) oligomerization
- Development of protein drug delivery systems (PEGylation, peptide functionalized nanovesicles) for substitutive therapy (ie: Fabry disease and San Filippo).
- Design and synthesis of gamma peptides with capacity to cross biological barriers, such as the cytoplasmic membrane of eukaryotic cells and parasites (Leishmania) and the blood brain barrier (BBB).
- Development of target peptides for colorectal and triple negative breast cancer tissues.

- Vectorized multicomponent nanoparticles as drug delivery systems and modulators of pharmacokinetic properties.
- Multimodal imaging agents (SPECT, OI, CT and MRI). Nanoparticles for imaging diagnostic applications.
- Surface engineering for controlling cell proliferation on diverse materials.
- Development of solid phase methodology to synthesize biomolecules and other compounds.
- Bionanotechnologies as new strategy to save compounds that failed on clinical or preclinical phases.

## Most relevant scientific articles

- MENDIVE-TAPIA L., ZHAO C., AKRAM A.R., PRECIADO S., ALBERICIO F., LEE M. ET AL. Spacer-free BODIPY fluorogens in antimicrobial peptides for direct imaging of fungal infection in human tissue. *Nature Communications*. 2016;7.
- PELAY-GIMENO M., ALBERICIO F., TULLA-PUCHE J. Synthesis of complex head-to-side-chain cyclodepsipeptides. *Nature Protocols*. 2016;11(10):1924-1947.
- GIANNOTTI M.I., ABASOLO I., OLIVA M., ANDRADE F., GARCÍA-ARANDA N., MELGAREJO M. ET AL. Highly Versatile Polyelectrolyte Complexes for Improving the Enzyme Replacement Therapy of Lysosomal Storage Disorders. *ACS Applied Materials and Interfaces*. 2016;8(39):25741-25752.
- PARADIS-BAS M., TULLA-PUCHE J., ALBERICIO F. The road to the synthesis of “difficult peptides”. *Chemical Society Reviews*. 2016;45(3):631-654.
- MENDIVE-TAPIA L., BERTRÁN A., GARCÍA J., ACOSTA G., ALBERICIO F., LAVILLA R. Constrained Cyclopeptides: Biaryl Formation through Pd-Catalyzed C–H Activation in Peptides—Structural Control of the Cyclization vs. Cyclodimerization Outcome. *Chemistry - A European Journal*. 2016;22(37):13114-13119.


## Highlights

In 2016 our group has initiated a 4 years' project “Preparación facilitada de compuestos químicos relevantes en biología”, granted by MINECO (CTQ2015-6787OP). The main goal of this project is developing new synthetic methods to obtain diverse type of molecules with relevant biological activity, as antitumoral drugs, or fluorescent label molecules with application to diagnostic by imaging. Furthermore, during this year the group has continued working on the projects CHEMTOOLBOX (MINECO, SAF2014-60138-R), PENTRI (FUNDACIÓ MARATÓ TV3, TV32013-133932), TERARMET (MINECO, RTC-2014-2207-1) and the transfer technology project LIPOCEL (CIBER-BBN). The two first projects (CHEMTOOLBOX and PENTRI) are devoted to the development of drug delivery systems for advanced colorectal and triple negative breast cancer treatment, and peptide transporters. The other two, TERARMET and LIPOCEL projects are focused on the development of a protein delivery system for enzyme replacement treatment for Fabry and San Filippo diseases. During this year, the results generated for these two projects facilitated the presentation of a european project in coordination with other CIBER-BBN groups that have been granted (SMART-4-FABRY) and initiated in 2017. This project has the objective to approach the enzyme delivery system developed in collaboration with other CIBER-BBN groups to clinical phases. During this year, the group has continued working collaborative projects with private companies (Almirall, Servier, Landsteiner Genmed and Biokit).



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PROGRAMMES

**Bioengineering & Medical Imaging**



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## Main lines of research

Our major research interest is the improvement of the diagnosis, treatment and therapy response follow-up of abnormal brain masses, using noninvasive monitoring tools based in Nuclear Magnetic Resonance. With this major goal in mind, several sublines related to MR methodology are being investigated, which include:

- Treatment with conventional or novel therapeutic agents and response follow-up of preclinical brain tumour models.
- Search for molecular surrogate biomarkers of in vivo tumor therapy response, through in vitro, ex vivo and in vivo studies of cell lines, animal models and their biopsies. Correlation with molecular and cellular parameters (histopathology, genomics). Potential translation to clinical practice.
- In vivo molecular phenotyping of tumor progression and therapy response.
- Classifier development and their implementation into decision-support systems (DSS) for helping in clinical decision making in an evidence-based medicine context.
- Characterization of the type and grade of human brain tumors and other neural pathologies by imaging (MRI) and in vivo magnetic resonance spectroscopy (MRS, MRSI). Therapy response characterization in treated patients, using pattern recognition tools developed with preclinical models.



## Most relevant scientific articles

- DELGADO-GONI T., ORTEGA-MARTORELL S., CIEZKA M., OLIER I., CANDIOTA A.P., JULIA-SAPE M. ET AL. MRSI-based molecular imaging of therapy response to temozolomide in preclinical glioblastoma using source analysis. *NMR in Biomedicine*. 2016.
- CIEZKA M., ACOSTA M., HERRANZ C., CANALS J.M., PUMAROLA M., CANDIOTA A.P. ET AL. Development of a transplantable glioma tumour model from genetically engineered mice: MRI/MRS/MRSI characterisation. *Journal of Neuro-Oncology*. 2016;1-10.
- MAJOS C., COS M., CASTANER S., PONS A., GIL M., FERNÁNDEZ-COELLO A. ET AL. Preradiotherapy MR Imaging: A prospective pilot study of the usefulness of performing an MR examination shortly before radiation therapy in patients with glioblastoma. *American Journal of Neuroradiology*. 2016;37(12):2224-2230.
- CASTELLS DOMINGO X., FERRER-FONT L., DAVILA M., CANDIOTA A.P., SIMOES R.V., FERNÁNDEZ-COELLO A. ET AL. Improving Ribosomal RNA Integrity in Surgically Resected Human Brain Tumor Biopsies. *Biopreservation and Biobanking*. 2016;14(2):156-164.
- FERNÁNDEZ F., DEVIERS A., DALLY C., MOGICATO G., DELVERDIER M., CAUZINILLE L. ET AL. Presence of neural progenitors in spontaneous canine gliomas: A histopathological and immunohistochemical study of 20 cases. *Veterinary Journal*. 2016.

## Highlights

The GABRMN has established/continued scientific collaborations with research groups such as the Nanostructured Functional Materials Group (Institut Català de Nanociència i Nanotecnologia, Dr. Fernando Novio) and the Protein Phosphorylation group, from Dipartimento di scienze biomediche (Università degli Studi di Padova, Dr. Lorenzo Pinna, Dr. Maria Ruzzene), producing a joint publication and another article being prepared for submission. Moreover, the collaboration started in 2016 with Dr. Víctor Yuste from the Grup d'Investigació en Mort Cel·lular, Senescència i Supervivència (Universitat Autònoma de Barcelona), is helping to gain more insight in the study of cell death mechanisms triggered by the chemotherapeutic agents used in our brain tumor preclinical models.


Regarding research results, a new protocol of volumetric molecular imaging has been developed with excellent results in the noninvasive assessment of therapy response in our preclinical glioblastoma (GB) model. This work has been presented in national and international congresses, such as the European Society for Magnetic Resonance in Medicine and Biology annual meeting (Vienna, September 2016). On the other hand, the collaboration with the Grup de Regulació Cel·lular per Fosforilació de Proteïnes (Dr. Emili Itarte, Dr. Maria Plana) has gone more in-depth in the study of CX-4945 (CK2 inhibitor) as an alternative therapy for preclinical GB, suggesting the potential combination with temozolomide for survival improvement in tumor-bearing mice.


The TRANSACT ITN has developed its third and last year, and the same European research network has worked along the second half of 2016 in a new Marie Curie proposal, with CIBER as one of the partners. Finally, during 2016, a new predoctoral student has joined the GABRMN group, Wu Shuang from China, holding a grant from the China Scholarship Council for 4 years.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- Tissue engineering for bone and cartilage regeneration.
- Mesenchymal stem cell differentiation towards chondro-osteogenic lineages by means of 2D and 3D cultures.
- Chemical synthesis and materials processing, materials characterization and acellular essays in vitro to study the structure-properties-function relationships of the materials in biological systems.
- Development and biological functionalization of porous titanium for bone tissue engineering- Development and production of recombinant osteogenic proteins and biomimetic peptides with specific molecular domains.
- Skeletal regeneration in zebra fish.



## Most relevant scientific articles

- ORGAZ F., DZIKA A., SZYCHT O., AMAT D., BARBA F., BECERRA J. ET AL. Surface nitridation improves bone cell response to melt-derived bioactive silicate/borosilicate glass composite scaffolds. *Acta Biomaterialia*. 2016;29:424-434.
- JARA N., CIFUENTES M., MARTÍNEZ F., SALAZAR K., NUALART F. Cytoarchitecture, Proliferative Activity and Neuroblast Migration in the Subventricular Zone and Lateral Ventricle Extension of the Adult Guinea Pig Brain. *Stem Cells*. 2016.
- VISSER R., RICO-LLANOS G.A., PULKKINEN H., BECERRA J. Peptides for bone tissue engineering. *Journal of Controlled Release*. 2016;244:122-135.
- LAGUNAS A., TSINTZOU I., VIDA Y., COLLADO D., PÉREZ-INESTROSA E., PEREIRA C.R. ET AL. Tailoring RGD local surface density at the nanoscale toward adult stem cell chondrogenic commitment. *Nano Research*. 2016;1-13.
- VISSER R., BODNAROVA K., ARRABAL P.M., CIFUENTES M., BECERRA J. Combining bone morphogenetic proteins-2 and -6 has additive effects on osteoblastic differentiation in vitro and accelerates bone formation in vivo. *Journal of Biomedical Materials Research - Part A*. 2016;104(1):178-185.

## Highlights

In 2016 we have partnered with groups and companies from Rizzoli Orthopaedic Institute (Italy); Italian National Research Council – CNR (Italy); TecMinho (SME) (Portugal) and Spain to submit the proposal “Tailored photo-active Keratin nanofibres as advanced wound Dressings” to the Horizon 2020 PROPOSAL N°37, EURONANOMED II Joint Transnational Call for Proposals (2016) for “EUROPEAN INNOVATIVE RESEARCH & TECHNOLOGICAL DEVELOPMENT PROJECTS IN NANOMEDICINE. We have as well applied for funding from Call: H2020-MSCA-IF-2016, presenting the proposal “Osteoinductive functionalization of biomaterials with biomimetic peptides containing specific binding domains or with nanotechnological graphene coating for bone tissue engineering, SILKOGRAF”.

We have obtained funding from the Instituto de Salud Carlos III through the RETICS call, being accepted our membership into de Network of Cell Therapy (TerCel) for the next 5-year period 2017-20.

We have also obtained funding from the Andalusian Regional Government “Desarrollo de un Preparado de Ingeniería Tisular para el tratamiento de Osteonecrosis Maxilar Aséptica” (PI-0339-2014), IP: Rick Visser.

The article *Act Biomaterialia* 29:424-34 quickly getting much attention from the media, and being Dr.

Leonor Santos-Ruiz (CIBER-BBN researcher) interviewed in several radio and TV programmes.


In collaboration with Cell Therapy Network (TerCel), our group has joined a team that leads two Clinical Assays:


- “Treatment Of Maxillary Bone Cysts With Autologous Bone Mesenchymal Stem Cells (MSV-H) (BIOMAX)” (NCT01389661).
- “Intravenous Infusion of Fucosylated Phase I Clinical Trial to Evaluate The Intravenous Infusion Of Autologous Fucosylated Bone Marrow Mesenchymal Cells Therapy In Patients With Established Osteoporosis” (NCT02566655).



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- **Biomaterials for the repair of abdominal wall defects.** This research has the purpose of repairing damaged and/or missing tissues mainly located in the abdominal wall. Several types of biomaterials for clinical use have been used in this line as supports, new designs and modifications thereof being developed. Different collagen bioprotheses as well as composites meshes and prosthetic materials with polymeric coatings that can reduce inflammation, accelerate healing process or prevent infection are currently being assayed. Tissue adhesives have recently been introduced in this line of research as a strategy for fixing prosthetic materials for hernia repair.
- **Repair of skin defects.** One of the alternatives for the repair of skin defects, especially in patients with compromised healing (diabetics, torpid vascular ulcers and pressure ulcers) can be improved through tissue engineering strategies. Essentially work is being conducted with two experimental models: muscle-derived stem cells for repairing excisional skin defects with encouraging results, and the design of polymers for the controlled release of healing modulating drugs.
- **Repair and vascular pathology.** Research has been conducted within this line in healing/ restenosis, with special interest in the modulation thereof. The problem of arterial substitution by means of biomaterials for clinical use and cryopreserved vessels has also been approached. Finally, tissue engineering techniques are used for the purpose of improving the viability of prosthetic materials through

the creation of a cell coating and the incorporation of bioactive substances. Currently being working on venous insufficiency in pregnancy and in the search for predictive markers.

- **Osteogenic regeneration.** This research line was introduced in our department as a result of collaboration with the group COFIBIC. Regeneration of critical bone defects using tissue engineering techniques, by implanting osteogenic constructs, and aspects of biocompatibility bone substitutes in different experimental models, are currently in progress.

## Most relevant scientific articles

- PASCUAL G, SOTOMAYOR S, RODRÍGUEZ M, PÉREZ-KÖHLER B, KÜHNHARDT A, FERNÁNDEZ-GUTIÉRREZ M ET AL. Cytotoxicity of Cyanoacrylate-Based Tissue Adhesives and Short-Term Preclinical In Vivo Biocompatibility in Abdominal Hernia Repair. PLoS one. 2016;11(6):e0157920.
- CALVO B., PASCUAL G., PENNA E., PÉREZ-KHOLER B., RODRÍGUEZ M., BELLÓN J.M.. Biomechanical and morphological study of a new elastic mesh (Ciberlastic) to repair abdominal wall defects. Journal of the Mechanical Behavior of Biomedical Materials. 2016;59:366-378.
- FERNÁNDEZ-GUTIÉRREZ M., RODRÍGUEZ-MANCHENO M., PÉREZ-KOHLER B., PASCUAL G., BELLÓN J.M., ROMÁN J.S.. Structural Analysis and Application of n-Alkyl Cyanoacrylate Surgical Adhesives to the Fixation of Meshes for Hernia Repair. Macromolecular Bioscience. 2016;16(12):1803-1814.
- SOTOMAYOR S., PASCUAL G., BLANC-GUILLEMAUD V., MESA-CILLER C., GARCÍA-HONDUVILLA N., CIFUENTES A. ET AL. Effects of a novel NADPH oxidase inhibitor (S42909) on wound healing in an experimental ischemic excisional skin model. Experimental Dermatology. 2016.
- VILA M., GARCÍA A., GIROTTI A., ALONSO M., RODRÍGUEZ-CABELLO J.C., GONZÁLEZ-VÁZQUEZ A. ET AL. 3D silicon doped hydroxyapatite scaffolds decorated with Elastin-like Recombinamers for bone regenerative medicine. Acta Biomaterialia. 2016;45:349-356.

## Highlights

In connection with our research line in **biomaterials for the repair of abdominal wall defects**, the second year of the national project “R&D Excellence Projects” SAF2014-55022-P, “Bioassay of a new cyanoacrylate for internal use (n-octyl/CIAH) of implanted prosthetic materials for the repair of hernia defects” CIANOMESH”, has been successfully carried out. In addition, two transfer contracts (Art. 83) have been signed with the company Medtronic in the field of prosthetic infection. The productivity of the line has been significant with eight published articles (four Q1). A number of invited papers and presentations have been presented at the 10th World Biomaterials Congress in Montreal, 51st Congress of the ESSR held in Prague and 38th International Congress of the EHS in Rotterdam.

Regarding our line of research in the **repair of skin defects**, in 2016 an article in Experimental Dermatology (Q1) has been published, derived from the results obtained from an Art. 83 signed with SERVIER. An important contract has been signed in the area of pharmacological healing, with the company Genzyme Corporation. A communication was presented at the 32nd ECTRIMS Congress.

Within the line of **repair and vascular pathology**, the last year of the National Research Project “Venous insufficiency in pregnancy: search for predictive markers” has been successfully completed, funded by the Instituto de Salud Carlos III (PI13 / 01513). Several papers have been presented at the XXXII LIAC Meeting on Vascular Research, held in Italy, 9th European Elastin Meeting, Germany and 2016 American Society for Matrix Biology (ASMB), held in the USA.

Regarding the line of **osteogenic regeneration**, the activity of the group has been focused on the SCAFFBONE intramural project. An article in Acta Biomaterialia (Q1) has been published and several papers have been presented at the III Iberoamerican Congress of Histology, held in Mexico and ASMB.





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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- **TISSUE ENGINEERING:** Study of interactions between cells and biomaterials implanted in live animals for tissue regeneration. We use an analysis platform based in bioluminescence and fluorescence procedures, that allows rapid and comparative analysis of biomaterials to optimize individualized applications.
- **TUMOUR CELL THERAPY:** Development of optimized cell therapies against brain tumors and other types of incurable cancers. The therapy strategy is based on the use of stem cells with tumour homing capacity, that are genetically modified to express a cytotoxic gene (e.g., thymidine kinase) that can transform a harmless pro-drug into a cytotoxic agent, inducing localized cell death in the tumour proximity (bystander effect).
- **INTERACTION BETWEEN TUMOUR AND THERAPEUTIC CELLS:** The objective is to understand the interactions between therapeutic and tumour cells, that lead to the elevated tumour killing effect in our model of bystander therapy. Bioluminescence and fluorescence imaging procedures are used to monitor the fate of therapeutic cells and tumours.
- **MONITORING CONVENTIONAL TUMOUR THERAPY.** The non invasive imaging platform permits the measurement of tumour response to therapeutic strategies during time, in the same experimental animal, improving data consistency and reproducibility, as well as, savings in animal resources.

## Most relevant scientific articles

- VILA O.F., GARRIDO C., CANO I., GUERRA-REBOLLO M., NAVARRO M., MECA-CORTES O. ET AL. Real-time bioluminescence imaging of cell distribution, growth, and differentiation in a three-dimensional scaffold under interstitial perfusion for tissue engineering. *Tissue Engineering - Part C: Methods*. 2016;22(9):864-872.
- SÁNCHEZ-PURRA M., RAMOS V., PETRENKO V.A., TORCHILIN V.P., BORROS S. Double-targeted polymersomes and liposomes for multiple barrier crossing. *International Journal of Pharmaceutics*. 2016;511(2):946-956.
- JAYARAM D.T., RAMOS-ROMERO S., SHANKAR B.H., GARRIDO C., RUBIO N., SÁNCHEZ-CID L. ET AL. In Vitro and in Vivo Demonstration of Photodynamic Activity and Cytoplasm Imaging through TPE Nanoparticles. *ACS Chemical Biology*. 2016;11(1):104-112.
- DUCHI S., RAMOS-ROMERO S., DOZZA B., GUERRA-REBOLLO M., CATTINI L., BALLESTRI M. ET AL. Development of near-infrared photoactivable phthalocyanine-loaded nanoparticles to kill tumor cells: An improved tool for photodynamic therapy of solid cancers. *Nanomedicine: Nanotechnology, Biology, and Medicine*. 2016;12(7):1885-1897.
- OH S., BORROS S. Mucoadhesion vs mucus permeability of thiolated chitosan polymers and their resulting nanoparticles using a quartz crystal microbalance with dissipation (QCM-D). *Colloids and Surfaces B: Biointerfaces*. 2016;147:434-441.

## Highlights

The Cell Therapy group has continued working in the area of cell therapy against tumors. Random introduction of DNA sequences in the human genome is inherently dangerous due to the possibility of mutating antioncogenes. To avoid this, we have used the CRISPR/Cas9 to generate therapeutic mesenchymal stem cells (MSCsTer) bearing the thymidine kinase gene in a specific location of the genome. Moreover, we have demonstrated that such cells have antiangioma therapeutic capacity, equivalent to the virally modified ones.

Since discovering that MSCsTer used against gliomas are not killed in vivo by the Ganciclovir treatment, we were forced to assume that their therapeutic effect was mediated by an exosome or exosome-like based mechanism. Therefore, during the past year we have initiated a project to facilitate large scale purification of extracellular vesicles for therapy.

A consequence of anti-replication therapy against tumors is the appearance of a pool of therapy resistant glioma stem cells, that we can detect and quantify by bioluminescence imaging, capable of recapitulating tumors upon release from therapy. We believe that these cells are the last resource of therapy resistance and, in consequence, have aimed the project on their eradication.


The team has been funded by: a MINECO project, a Retos Collaboration project with Instituto Químico de Sarria (Barcelona) and SAGETIS, the Cell Therapy Network (TERCEL) and by a CIBER "Transference" project. The group has collaborated with CIBER groups for Biomaterials for Regenerative Therapy (IBEC); Bioengineering and Tissue Regeneration (UMA-Bionand) and Nanostructured Surfaces and Nanoparticle (NFP-INA), as well as with the Cardiac Insuficiency and Regeneration Group Hospital Germans Trias i Pujol.





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 **Group Website**

PROGRAMMES

**Biomaterials & Advanced Therapies**



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**Contributors:** Corell Almuzara, Alfredo | Galindo de la Rosa, Sara | López Paniagua, Marina | Reinoso Tapia, Roberto | Soriano Romani, Laura

## Main lines of research

### VERTICAL RESEARCH LINES:

- Advances therapies. Target diseases: Corneal blindness caused by limbal stem cell deficiency. Field of research: Cell therapy, Tissue engineering, Clinical Trials
- Inflammation. Target diseases: Dry Eye Syndrome, Allergy, Other immune-based diseases. Field of research: In vitro models, Biomarkers and new therapies, Environmental stress, Contact lenses.
- Nanomedicine. Target diseases: Dry Eye Syndrome, Allergy, Other immune-based diseases. Field of research: Drug delivery systems, Gene therapy, Gene silencing.

### HORIZONTAL RESEARCH LINES:

- Physiology and Immunology. Field of research: Characterization of eye associated lymphoid tissue in health and disease.
- Clinical trials. Target disease: Ocular surface inflammation, Limbal stem cell deficiency, Intraocular inflammation (Uveítis), Contact lens-associated pathologies. Field of research: Cell therapy, Drug therapy, Contact lenses.

## Most relevant scientific articles

- PINTO-FRAGA J., LÓPEZ-MIGUEL A., GONZÁLEZ-GARCÍA M.J., FERNÁNDEZ I., LÓPEZ-DE-LA-ROSA A., ENRÍQUEZ-DE-SALAMANCA A. ET AL. Topical Fluorometholone Protects the Ocular Surface of Dry Eye Patients from Desiccating Stress: A Randomized Controlled Clinical Trial. *Ophthalmology*. 2016;123(1):141-153.
- COCHO L., FERNÁNDEZ I., CALONGE M., MARTÍNEZ V., GONZÁLEZ-GARCÍA M.J., CABALLERO D. ET AL. Biomarkers in ocular chronic graft versus host disease: Tear cytokine- and chemokine-based predictive model. *Investigative Ophthalmology and Visual Science*. 2016;57(2):746-758.
- SOBAS E.M., REINOSO R., CUADRADO-ASENSIO R., FERNÁNDEZ I., MALDONADO M.J., PASTOR J.C. Reliability of potential pain biomarkers in the saliva of healthy subjects: Inter-individual differences and intersession variability. *PLoS ONE*. 2016;11(12).
- LÓPEZ-PANIAGUA M., NIETO-MIGUEL T., DE LA MATA A., GALINDO S., HERRERAS J.M., CORRALES R.M. ET AL. Successful Consecutive Expansion of Limbal Explants Using a Biosafe Culture Medium under Feeder Layer-Free Conditions. *Current Eye Research*. 2016;:1-11.
- LÓPEZ-PANIAGUA M., NIETO-MIGUEL T., DE LA MATA A., DZIASKO M., GALINDO S., REY E. ET AL. Comparison of functional limbal epithelial stem cell isolation methods. *Experimental Eye Research*. 2016;146:83-94.

## Highlights

IOBA-UVa group is working in TWO intramural projects:


- **BioScaff-EYE: “Bio-engineered Stem Cell Niches in Ocular Surface Reconstruction for Corneal Blindness”**, coordinated by IOBA-UVa was transferred to Ferrer (Ferrer International SA) in 2014. Originally three groups are working: IOBA-UVa-Valladolid, clinical-basic research group (PI: M. Calonge, IBEC-Barcelona (PI: E. Engel), and NanoBioCel-Vitoria (PI: JL. Pedraz), both basic research groups, along with the research department of Ferrer Advanced Biotherapeutics. During 2016, a European patent application was filed claiming the polymeric membranes and their potential application in the field of ocular surface stem cell deficiency and its repair. Additionally, the necessary industrial escalation was accomplished by IBEC and FAB, transferring the procedures to a GMP-operating company, where they are optimizing the production along with IOBA-UVa input, meaning lots of in-vitro and in-vivo experimental procedures back and forth. The cellular component has also started its GMP-producing phase in a company specialized in this kind of development.
- **EYEPOC-II: “Point Of Care Biosensor Devices To Detect Biomarkers As Evaluation End-Points For Therapeutic Clinical Trials In Ocular Surface Inflammation”**, granted in 2014, renewed in 2016. It is coordinated by IOBA-UVa, the clinical-basic research group (PI: A. Enríquez-de-Salamanca), NB4D-CISC (PI: R. Galve), CIN2-CISC (PI: L. Lechuga) and GQNA-CISC (PI: R. Eritja). During 2016 we worked on WP1, Analysis of microRNAs expression in Dry Eye Disease (DED) patients’ conjunctival epithelial cells and/or tears. Patients and controls were recruited and clinically under controlled environmental conditions (constant temperature (22oC) and relative humidity (40%), in our environmental chamber, IOBA-CERLab). (tasks 1.1-1.2). Samples (tears and conjunctival impression cytologies (CIC)) were collected for microRNA evaluation (task 1.3). Task 1.4 (Micro RNA analysis) was initiated, including CIC miRNA isolation/quantification. Our previous results in pooled samples showed encouraging alterations in the levels of some molecules. We are already collecting samples in patients and healthy subjects to evaluate the levels of 84 inflammation-related microRNAs by RT-PCR in individual samples.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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**Contributors:** Gugutkov, Decnho

## Main lines of research

- Development of new functional biomaterials for tissue engineering, based on calcium phosphate, glasses, polymers and composites.
- Cell bioengineering: interactions between cells and biomaterials for manufacturing biocompatible materials for tissue regeneration and repair.

## Most relevant scientific articles

- OLIVEIRA H., CATROS S., BOIZIAU C., SIADOUS R., MARTÍ-MUNOZ J., BAREILLE R. ET AL. The proangiogenic potential of a novel calcium releasing biomaterial: Impact on cell recruitment. *Acta Biomaterialia*. 2016;29:435-445.
- GUGUTKOV D., GUSTAVSSON J., CANTINI M., SALMERÓN-SÁNCHEZ M., ALTANKOV G.. Electrospun fibrinogen-PLA nanofibres for vascular tissue engineering. *Journal of Tissue Engineering and Regenerative Medicine*. 2016.
- VILA M., GARCÍA A., GIROTTI A., ALONSO M., RODRÍGUEZ-CABELLO J.C., GONZÁLEZ-VÁZQUEZ A. ET AL. 3D silicon doped hydroxyapatite scaffolds decorated with Elastin-like Recombinamers for bone regenerative medicine. *Acta Biomaterialia*. 2016;45:349-356.
- VILA O.F., GARRIDO C., CANO I., GUERRA-REBOLLO M., NAVARRO M., MECA-CORTES O. ET AL. Real-time bioluminescence imaging of cell distribution, growth, and differentiation in a three-dimensional scaffold under interstitial perfusion for tissue engineering. *Tissue Engineering - Part C: Methods*. 2016;22(9):864-872.
- FORGET J., AWAJA F., GUGUTKOV D., GUSTAVSSON J., GALLEGO FERRER G., COELHO-SAMPAIO T. ET AL. Differentiation of Human Mesenchymal Stem Cells Toward Quality Cartilage Using Fibrinogen-Based Nanofibers. *Macromolecular Bioscience*. 2016;:1348-1359.

## Highlights

Among our lines of research, we have worked on microparticles to produce new bioinks to print organs such as bone and produce microtissues as systems to model pathologies like cancer. This project has been funded by MINECO.

A project for transference related to a new dressing to treat chronic and diabetic ulcers (Dermoglass) have been funded for the first edition of CAIXAIMPULSE, a new program supported by Obra Social La Caixa to bring science to the market. Next year we will be able to test our product in large animals and a patent is being prepared to protect the invention. Moreover, this project obtained an award from the EITHealth to help for the IP protection and the scalability studies and commercialization of the product.

Within an intramural project, in collaboration with the group of Prof. Rodriguez-Cabello from the University of Valladolid, the group developed microstructured biomimetic hydrogels using new crosslink methods that induce bone formation in in vivo models. These biomaterials have also been combined with 3D printed hydroxyapatite scaffolds to enhance bone formation in collaboration with Prof. Vallet and Prof. Bujan.

We have also collaborated with a group of traumatologists in Vall d'Hebron Hospital to produce microstructured materials to heal bone fractures by the enhancement of angiogenesis and osteogenesis. Three new intramural projects have started related to bone and cardiac regeneration and cancer therapies.





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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Alagia, Adele

## Main lines of research

- Development of new molecules which bind to DNA. Study of the interaction of drugs with DNA.
- Synthesis of oligonucleotides with non-natural nucleosides.
- Synthesis of modified RNA for the inhibition of gene expression by the RNA interference mechanism.
- Development of novel formulations for gene therapy and gene silencing.
- Synthesis and structural studies of quadruplex-forming oligonucleotides.
- Triple helix-forming oligonucleotides. Application of triplex affinity capture for the analysis of nucleic acid sequences.
- Two-dimensional DNA crystals. Origami DNA.
- Synthesis of oligonucleotide-peptide conjugates.
- Use of oligonucleotides in biosensors. Surface functionalization with nucleic acid derivatives.
- Study of DNA repair processes with the aim of developing inhibitors that can be used to avoid resistance to chemotherapy.



## Most relevant scientific articles

- OJEDA E., PURAS G., AGIRRE M., ZARATE J., GRIJALVO S., ERITJA R. ET AL. The influence of the polar head-group of synthetic cationic lipids on the transfection efficiency mediated by niosomes in rat retina and brain. *Biomaterials*. 2016;77:267-279.
- ALAGIA A., ERITJA R. siRNA and RNAi optimization. *Wiley Interdisciplinary Reviews: RNA*. 2016.
- VENGUT-CLIMENT E., GÓMEZ-PINTO I., LUCAS R., PENALVER P., AVINÓ A., FONSECA GUERRA C. ET AL. Glucose-Nucleobase Pseudo Base Pairs: Biomolecular Interactions within DNA. *Angewandte Chemie - International Edition*. 2016.
- HERNÁNDEZ-AINSA S., RICCI M., HILTON L., AVINÓ A., ERITJA R., KEYSER U.F. Controlling the reversible assembly of liposomes through a multistimuli responsive anchored DNA. *Nano Letters*. 2016;16(7):4462-4466.
- GRIJALVO S., MAYR J., ERITJA R., DÍAZ D. D. Biodegradable liposome-encapsulated hydrogels for biomedical applications: A marriage of convenience. *Biomaterials Science*. 2016;4(4):555-574.


## Highlights


A number of formulations for the delivery of nucleic acids that have been effective for gene therapy have been successfully developed as a result of an intramural project with the NANOBIOCEL and NN-UMH groups of CIBER-BBN. New formulations have been optimized for the transfection of siRNA molecules in order to facilitate the treatment of degenerative diseases of the retina. To achieve this objective funding was provided through a collaborative project with the companies Sylentis, Leitat and Leadartis. In collaboration with a group from the University of Cambridge lipid-oligonucleotides containing a photosensitive group was developed. The introduction of these compounds into liposomes has allowed the association and dissociation of liposomes by light. It also highlights the success achieved in the design of structures that stabilize non-canonical forms of DNA such as triplex, i-motif and non-natural mating with carbohydrates and its application in the detection of miRNA. The influence of chemical modifications at the ends of the siRNAs on the potency and selectivity of these siRNAs has been studied in detail, obtaining derivatives with greater potency and greater selectivity in the specific downregulation of the gene expression. Finally, DNA nanostructures of increasing complexity have been prepared in order to facilitate the cellular entry of therapeutic nucleic acids. Early results indicate that the prepared structures facilitate the cellular entry of DNA-based drugs. In order to achieve this objective, there has been an extraordinary funding through an Explora project.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- Pathophysiology of sleep apnea and acute lung injury in patients and animal models.
- Tissue engineering and regenerative medicine in respiratory diseases.
- Nanotechnologies and lab-on-a-chip for the study and characterization of the mechanical behavior of cells and tissue systems.
- Instrumentation for diagnostic, therapeutic and monitoring of sleep apnea and acute lung injury.

## Most relevant scientific articles

- SUNYER R., CONTE V., ESCRIBANO J., ELOSEGUI-ARTOLA A., LABERNADIE A., VALON L. ET AL. Collective cell durotaxis emerges from long-range intercellular force transmission. *Science*. 2016;353(6304):1157-1161.
- KHALYFA A., ALMENDROS I., GILELES-HILLET A., AKBARPOUR M., TRZEPIZUR W., MOKHLESI B. ET AL. Circulating exosomes potentiate tumor malignant properties in a mouse model of chronic sleep fragmentation. *Oncotarget*. 2016;7(34):54676-54690.
- URIARTE J.J., MEIRELLES T., DEL BLANCO D.G., NONAKA P.N., CAMPILLO N., SARRI E. ET AL. Early impairment of lung mechanics in a murine model of marfan syndrome. *PLoS ONE*. 2016;11(3).
- ISETTA V., MONTSERRAT J.M., SANTANO R., WIMMS A.J., RAMANAN D., WOEHRLE H. ET AL. Novel approach to simulate sleep apnea patients for evaluating positive pressure therapy devices. *PLoS ONE*. 2016;11(3).
- CAMPILLO N., JORBA I., SCHAEDEL L., CASALS B., GOZAL D., FARRE R. ET AL. A novel chip for cyclic stretch and intermittent hypoxia cell exposures mimicking obstructive sleep apnea. *Frontiers in Physiology*. 2016;7(JUL).

## Highlights

The group has focused its work on two of the programs of CIBERES, addressed to study obstructive sleep apnea (OSA) and acute lung injury (ALI). Part of the group research has been carried out in the framework of contracts with companies and of two funded joint-projects with CIBER-BBN groups. A first main outcome in the field of OSA has been the development and characterization of a novel chip system capable of realistically simulating the main OSA stimuli at cell level. The chip allows cell application of controlled fast patterns of intermittent hypoxia and cyclic stretch at breathing and heart frequencies. A prove of concept application study on bone marrow-derived stem cells was carried out. In another study, we found that circulating exosomes modulate cancer progression (proliferation, migration and extravasation) in a mouse model of sleep fragmentation mimicking OSA, potentially explaining the adverse cancer outcomes observed in OSA. Concerning OSA treatment, we developed a novel bench test setting to test automatic CPAP devices. The model allows simulating a patient's night including different breathing features in each sleep phase. In the ALI program, the group has focused on the studying the crosstalk between cells and extracellular matrix (ECM). On the one hand, we used a mouse Marfan model (mutation in ECM fibrillin) to document that alterations in the ECM may induce distinct the micro- and macro-mechanical mechanical changes in the lung. In addition, we have provided novel evidence of different mechanisms driving isolated and collective cells migration in the presence of non-homogeneous ECM stiffness (durotaxis). We found that collective durotaxis is far more efficient than single-cell durotaxis, appearing as a potential robust mechanism to direct cell migration in lung epithelial/endothelial repair in ALI.




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PROGRAMMES

**Bioengineering & Medical Imaging**



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**Contributors:** Pérez Vidal, Carlos

## Main lines of research

- Gene therapy:
  1. Reprogramming cells in vivo and in vitro for the regeneration of the retina.
  2. Development of new nanoparticles to perform as vehicles for nucleic acids (DNA, RNA)
- Development of a cortical visual neuroprosthesis for the blind
- Studies of visual function in animal models
- Development of biomedical technologies:
  1. Development of robots to assist in surgery and surgery simulations.
  2. Development of devices for neurorehabilitation and robot assisted rehabilitation.
  3. Development of non-invasive brain-computer interfaces (BCI) based on electroencephalography (EEG) electrooculography (EOG) for disabled people.
  4. Development of technology for the detection of breast cancer.
  5. Development of new generations of multifunctional intraocular lenses.
  6. Development of software for neural signal analysis.
- Biocompatibility studies (in vitro and in vivo).
- Neuroimaging (fMRI, DTI, etc).



## Most relevant scientific articles

- IZQUIERDO-SERRA M., BAUTISTA-BARRUFET A., TRAPERO A., GARRIDO-CHARLES A., DÍAZ-TAHOSES A., CAMARERO N. ET AL. Optical control of endogenous receptors and cellular excitability using targeted covalent photoswitches. *Nature Communications*. 2016;7.
- MONES J., LEIVA M., PENA T., MARTÍNEZ G., BIARNES M., GARCÍA M. ET AL. A swine model of selective geographic atrophy of outer retinal layers mimicking atrophic AMD: A phase I escalating dose of subretinal sodium iodate. *Investigative Ophthalmology and Visual Science*. 2016;57(10):3974-3983.
- AYUSO J.M., VIRUMBRALES-MUNOZ M., LACUEVA A., LANUZA P.M., CHECA-CHAVARRÍA E., BOTELLA P. ET AL. Development and characterization of a microfluidic model of the tumour microenvironment. *Scientific Reports*. 2016;6.
- MARTÍNEZ-ÁLVAREZ A., CRESPO-CANO R., DÍAZ-TAHOSES A., CUENCA-ASENSI S., VICENTE J.M.F., FERNÁNDEZ E. Automatic Tuning of a Retina Model for a Cortical Visual Neuroprosthesis Using a Multi-Objective Optimization Genetic Algorithm. *International Journal of Neural Systems*. 2016.
- NORMANN R.A., FERNÁNDEZ E. Clinical applications of penetrating neural interfaces and Utah Electrode Array technologies. *Journal of Neural Engineering*. 2016;13(6).

## Highlights


The group coordinates the European Project AIDE focused on the development of multimodal technologies adaptable to the individual needs of people with different types of disabilities. In addition, the group coordinates various research projects related to retinal degenerative diseases and is facing the challenge of creating an intracortical visual neuroprosthesis designed to interface with the occipital cortex as a means through which a limited but useful visual sense could be restored to profoundly blind patients (ClinicalTrials.gov identifier: NCT02983370).



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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Lozano de la Cruz, Tania

## Main lines of research

- New dendrimer synthesis and functionalization strategies.
- Biomedical applications of dendrimers as nucleic acid carriers (antisense oligonucleotides, interference RNA, etc.) for cancer and HIV gene therapy.
- Biomedical applications of dendrimers as drug carriers (for anti-inflammatory agents, antiviral, antitumor agents, etc).
- Development of dendrimers as antiviral agents (especially as HIV inhibitors) and antibacterial agents.
- Development of dendrimers for neurodegenerative diseases.
- Development of dendrimers in vaccines.
- Development of metal complexes for their antiviral, antibacterial and/or anti-cancer use.

## Most relevant scientific articles

- PENA-GONZÁLEZ C.E., GARCÍA-BRONCANO P., OTTAVIANI M.F., CANGIOTTI M., FATTORI A., HIERRO-OLIVA M. ET AL. Dendronized Anionic Gold Nanoparticles: Synthesis, Characterization, and Antiviral Activity. *Chemistry - A European Journal*. 2016;22(9):2987-2999.
- CENA-DÍEZ R., VACAS-CÓRDOBA E., GARCÍA-BRONCANO P., DE LA MATA F.J., GÓMEZ R., MALY M. ET AL. Prevention of vaginal and rectal herpes simplex virus type 2 transmission in mice: Mechanism of antiviral action. *International Journal of Nanomedicine*. 2016;11:2147-2162.
- BRAVO-OSUNA I., VICARIO-DE-LA-TORRE M., ANDRÉS-GUERRERO V., SÁNCHEZ-NIEVES J., GUZMÁN-NAVARRO M., DE LA MATA F.J. ET AL. Novel water-soluble mucoadhesive carbosilane dendrimers for ocular administration. *Molecular Pharmaceutics*. 2016;13(9):2966-2976.
- SEPÚLVEDA-CRESPO D., VACAS-CÓRDOBA E., MÁRQUEZ-MIRANDA V., ARAYA-DURÁN I., GÓMEZ R., MATA F.J.D.L. ET AL. Effect of Several HIV Antigens Simultaneously Loaded with G2-NN16 Carbosilane Dendrimer in the Cell Uptake and Functionality of Human Dendritic Cells. *Bioconjugate Chemistry*. 2016;27(12):2844-2849.
- PERISE-BARRIOS A.J., FUENTES-PANIAGUA E., SÁNCHEZ-NIEVES J., SERRAMIA M.J., ALONSO E., REGUERA R.M. ET AL. Improved Efficiency of Ibuprofen by Cationic Carbosilane Dendritic Conjugates. *Molecular Pharmaceutics*. 2016;13(10):3427-3438.

## Highlights


The activity of the group during 2016 has been centered in the development of new dendritic nanosystems in two directions: (i) design of improved non-viral vectors for gene therapy in HIV and cancer and (ii) design of HIV antiviral, antibacterial, anticancer and antineurodegenerative agents, funded by european (IRSES) and national (CTQ2014-54004-P, MINECO and PIE14/00061, INTERCIBER) projects. The research carried out, focused in the search of a new therapeutic approach based on the use of anionic dendrimer, gold and PLGA nanoparticles towards not only the HIV treatment but also other viruses like Herpes or Hepatitis C. Also, we were working in the use of cationic dendritic systems against bacteria and parasites in the search of structure/activity relationships. In the other hand, new cationic dendritic systems have been evaluated in ocular administration, as well as metallodendrimers based on ruthenium as new anticancer agents. Finally, cationic carbosilane dendrimers with and without the binding of chemical chaperones have been prepared for future applications in neurodegenerative diseases.

Results of the research has led to 17 publications. The group has continued intensifying its activities related to technology transfer applying for a national Spanish patent based on the preparation of carbosilane dendrons functionalized with fatty acid at the focal point for the formation of micelles and their uses. In addition, a PCT extension of a national patent on the use of metallic nanoparticles stabilized with carbosilane dendrons for biomedical applications was carried out. In this sense, in December of 2016, we obtained the first prize in the 1º call for the best national patent of the University of Alcalá.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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**Contributors:** Araque Monrós, Carmen

## Main lines of research

The research group of the Centre for Biomaterials and Tissue Engineering at Universitat Politècnica de València specializes in developing supporting biomaterials for cell transplantation in regenerative medicine and tissue engineering therapies.

Among the biomaterials developed by the group are macroporous scaffolds with different pore structures produced either from medical grade biodegradable polymers or with new synthetic polymers or chemically modified naturally occurring polysaccharides or proteins. Examples of products used in various biomedical applications are:

- Hydrogels based on crosslinked gelatin and hyaluronic acid in the presence of cells without compromising their viability
- Biostable or biodegradable synthetic “scaffolds” with modified collagen, fibrin, hyaluronic acid or chitosan surface coatings
- Channeled hyaluronic acid supports with the ability to stimulate axonal growth
- Biodegradable or biostable synthetic microspheres with bioactive coatings
- Biodegradable nanofiber mats
- Controlled delivery systems for the release of drugs or bioactive molecules based on the above materials

These materials are being used in the regeneration of different tissues and in therapies for regenerative medicine:

- Regeneration of articular cartilage
- Bone substitutes
- Regeneration of cornea and keratoprosthesis
- Neural regeneration
- Blood Cancers
- Cardiovascular Regeneration
- Muscle regeneration



## Most relevant scientific articles

- SHANTHINI G.M., SAKTHIVEL N., MENON R., NABHIRAJ P.Y., GÓMEZ-TEJEDOR J.A., MESEGUER-DUENAS J.M. ET AL. Surface stiffening and enhanced photoluminescence of ion implanted cellulose – polyvinyl alcohol – silica composite. *Carbohydrate Polymers*. 2016;153:619-630.
- POVEDA-REYES S., MOULISOVA V., SANMARTÍN-MASIA E., QUINTANILLA-SIERRA L., SALMERÓN-SÁNCHEZ M., FERRER G.G.. Gelatin-Hyaluronic Acid Hydrogels with Tuned Stiffness to Counterbalance Cellular Forces and Promote Cell Differentiation. *Macromolecular Bioscience*. 2016.
- RICO P., MNATSAKANYAN H., DALBY M.J., SALMERÓN-SÁNCHEZ M. Material-Driven Fibronectin Assembly Promotes Maintenance of Mesenchymal Stem Cell Phenotypes. *Advanced Functional Materials*. 2016;26(36):6563-6573.
- MARQUES S.M., RICO P., CARVALHO I., GÓMEZ RIBELLÉS J.L., FIALHO L., LANCEROS-MÉNDEZ S. ET AL. MC3T3-E1 Cell Response to Ti1-xAgx and Ag-TiNx Electrodes Deposited on Piezoelectric Poly(vinylidene fluoride) Substrates for Sensor Applications. *ACS Applied Materials and Interfaces*. 2016;8(6):4199-4207.
- ORTUNO-LIZARAN I., VILARINO-FELTRER G., MARTÍNEZ-RAMOS C., PRADAS M.M., VALLES-LLUCH A. Influence of synthesis parameters on hyaluronic acid hydrogels intended as nerve conduits. *Biofabrication*. 2016;8(4).

## Highlights

The components of the group are principal researchers of the following ongoing projects:

- Projects funded by the Spanish Ministry of Economy and Competitiveness, MINECO:
  - Biohybrids for the promotion of axonal outgrowth and the regeneration in the central and peripheral nervous systems MAT2015- 66666-C3-1-R;
  - Research Network for the Development of Biofunctionalized Titanium Implants. MAT2014-52905-REDIT
  - Local mechanical stimulation of mesenchymal stem cells to enhance osteogenic and chondrogenic differentiation in regenerative medicine. MAT2013-46467-C4-1-R.
  - Modular neurocables: multiplying neural connections «EXPLORA» Project DPI2015-72863-EXP
  - Muscle regeneration after injury. Engineered biodegradable ion-loaded scaffolds to promote muscle regeneration. MAT2015-69315-C3-1-R,
  - Multifunctional polymeric supports for indirect cellular co-culture and chemical stimulation aimed at mimicking in vitro renal tissue - DPI2015-65401-C3-2-R.
- Program of the Generalitat Valenciana for funding projects of research groups of excellence. Prometeo 2016. Bone marrow analogue to personalize the treatment of blood cancer patients. PROMETEO/2016/063.
- Projects conducted in collaboration with medical groups of the Hospital Universitari i Politècnic/ Instituto de Investigación Sanitaria La Fe New endoscopy system Endoworm 3.0. (ENDOWORM 3.0.) Biomimetic 3D environments for the culture of myeloma cells (BIO3D-MIELOMA).
- European projects: Network for Development of Soft Nanofibrous Construct for Cellular Therapy of Degenerative Skeletal Disorders (FIBROGELNET) FP7-PEOPLE-2012-IAPP (PIAP-GA-2012-324386).
- CIBER-BBN Technology Transfer Program Project Proposals: Tissue Engineering for Bone Augmentation for Dental Implant Fixation, in collaboration with ZVIT Medica SL. and LABRET-UMA CIBER-BBN group
- Awards: *Diario Médico*. Awards for Best Ideas in the Health Sector 2016 Implant to regenerate articular cartilage.
- Awards: The project Autologous microsphere scaffolds for the regeneration of articular cartilage by tissue engineering was selected for the Idea2global FIPSE- MIT Program.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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**Contributors:** Delgado Rastrollo, María | Vadillo Rodríguez, Virginia

## Main lines of research

- Evaluation, characterization and prevention of adhesion of microorganisms to surfaces and biofilm formation. Consideration of external conditions acting on the adhesion, mainly, composition and dynamic characteristics of media in the process.
- Chemical, physicochemical and topographic characterization of surfaces.

## Most relevant scientific articles

- CRESPO L., HIERRO-OLIVA M., BARRIUSO S., VADILLO-RODRÍGUEZ V., MONTEALEGRE M.A., SALDANA L. ET AL. On the interactions of human bone cells with Ti6Al4V thermally oxidized by means of laser shock processing. *Biomedical Materials (Bristol)*. 2016;11(1).
- CIFUENTES S.C., BENSAMAR F., GALLARDO-MORENO A.M., OSSWALD T.A., GONZÁLEZ-CARRASCO J.L., BENAVENTE R. ET AL. Incorporation of Mg particles into PDLLA regulates mesenchymal stem cell and macrophage responses. *Journal of Biomedical Materials Research - Part A*. 2016.
- GÓMEZ-FLORIT M., PACHA-OLIVENZA M.A., FERNÁNDEZ-CALDERON M.C., CÓRDOBA A., GONZÁLEZ-MARTÍN M.L., MONJO M. ET AL. Quercitrin-nanocoated titanium surfaces favour gingival cells against oral bacteria. *Scientific Reports*. 2016;6.
- MONJE A., GONZÁLEZ-GARCÍA R., FERNÁNDEZ-CALDERÓN M.C., HIERRO-OLIVA M., GONZÁLEZ-MARTÍN M.L., DEL AMO F.S.-L. ET AL. Surface topographical changes of a failing acid-etched long-term in function retrieved dental implant. *Journal of Oral Implantology*. 2016;42(1):12-16.
- PENA-GONZÁLEZ C.E., GARCÍA-BRONCANO P., OTTAVIANI M.F., CANGIOTTI M., FATTORI A., HIERRO-OLIVA M. ET AL. Dendronized Anionic Gold Nanoparticles: Synthesis, Characterization, and Antiviral Activity. *Chemistry - A European Journal*. 2016;22(9):2987-2999.

## Highlights


The projects and results that we have obtained along 2016 are related to the analysis of the characteristics of the surfaces, especially those more directly related to the microbiological colonization. At present, it is getting materials that improve the capabilities of implants and prostheses, by better cellular responses to them, but, in return, tend to favour the development of infections, if they get contaminated with bacteria. The materials on which we are working, in collaboration with the group FIOBI-la Paz, are being designed to seek the maximum synergy between both effects, improvement in cellular response and prevention of bacterial colonization in case of contamination. We are performing different non-trivial analyses on the response material-microorganisms, under different conditions, simulating the actual situations of possible contaminations. We also progress in the control of the optimal characteristics of the degradation of our materials and in the characterization of alternative materials to the conventional ones, for the reduction of infections. The research is carried out thanks to the funding obtained in national calls, both projects and networks, European, and by collaboration with companies of the sector. We also participated in several intramural projects and also, independently, collaborated with other CIBER groups in the characterization of different materials.



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PROGRAMMES

**Bioengineering & Medical Imaging**



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**Contributors:** Estrada Petrocelli, Luis Carlos | Romero Lafuente, Sergio | Serna Higueta, Leidy Yanet | Solá Soler, Jordi

## Main lines of research

- DNA sequence signal processing.
- Analysis of muscle signals to assess musculoskeletal and rehabilitation process pathologies.
- Non-invasive monitoring of breathing muscle activity.
- Systems for the diagnosis of patients with obstructive sleep apnea syndrome (OSAS).
- Obtaining new cardiac risk scores and aid for the early detection of myocardial ischemia by means of electrocardiographic signal analysis.
- Study of the breathing pattern to assess extubation of patients with heart failure.
- Study of the non-linear activity of the Autonomic Nervous System (ANS) and the cardiorespiratory interrelation.
- New EEG signal analysis techniques for the evaluation of drugs.
- Signal and image integration in the virtual Physiological human environment.



## Most relevant scientific articles

- DOMINGO-ALMENARA X., BREZMES J., VINAIXA M., SAMINO S., RAMÍREZ N., RAMON-KRAUEL M. ET AL. ERah: A Computational Tool Integrating Spectral Deconvolution and Alignment with Quantification and Identification of Metabolites in GC/MS-Based Metabolomics. *Analytical Chemistry*. 2016;88(19):9821-9829.
- MIGLIORELLI C., ALONSO J.F., ROMERO S., MANANAS M.A., NOWAK R., RUSSI A. Influence of metallic artifact filtering on MEG signals for source localization during interictal epileptiform activity. *Journal of Neural Engineering*. 2016;13(2).
- VARGA A.W., WOHLLEBER M.E., GIMÉNEZ S., ROMERO S., ALONSO J.F., DUCCA E.L. ET AL. Reduced slow-wave sleep is associated with high cerebrospinal fluid  $\alpha\beta 42$  levels in cognitively normal elderly. *Sleep*. 2016;39(11):2041-2048.
- LOZANO M., FIZ J.A., JANÉ R. Automatic Differentiation of Normal and Continuous Adventitious Respiratory Sounds Using Ensemble Empirical Mode Decomposition and Instantaneous Frequency. *IEEE Journal of Biomedical and Health Informatics*. 2016;20(2):486-497.
- ESTRADA L., TORRES A., SARLABOUS L., JANÉ R. Improvement in Neural Respiratory Drive Estimation from Diaphragm Electromyographic Signals Using Fixed Sample Entropy. *IEEE Journal of Biomedical and Health Informatics*. 2016;20(2):476-485.

## Highlights

The group has developed basic and translational research in the framework of the projects:

- “Multimodal physiological biomarkers for non-invasive monitoring and home healthcare of COPD patients with comorbidities” (DPI2015-68820-R), 2016-18. PI: Raimon Jané.
- “Cost effective self-management of urinary incontinence addressed to women across Europe” (643535 - WOMEN-UP, H2020), 2015-18. PI: Miguel Ángel Mañanas.
- “Serious games on heart failure patients. Estimation of their benefits on the Spanish health system” (TEC2013-44666-R), 2014-15. PI: Pere Caminal, Alexandre Perera.
- “Design of methods for assessing processes of neurological and neuromuscular decline associated with aging” (NEUROAGING, DPI2014-59049-R), 2015-17. PI: Miguel Ángel Mañanas.
- “Biomedical Signal Processing and Interpretation (BIOSPIN)” (2014 SGR 1569), 2014-16. PI: Raimon Jané.
- “Bioinformatics and Biomedical Signals Laboratory (B2SLab)” (2014 SGR 1063), 2014-16. PI: Alexandre Perera.

Furthermore, the group has participated in two intramural projects of the CIBER-BBN (2016-2017):

- M-OLDOSA: “Multimodal analysis and m-Health tools for diagnostic and monitoring improving of Obstructive Lung Disease and Obstructive Sleep Apnea patients”. Coordinator: Raimon Jané Campos.
- MultiTools2Heart: “Multiscale computational tools to improve diagnosis, risk assessment and treatment in prevalent heart diseases”. Coordinator: Juan Pablo Martínez Cortés.


In addition, the following five doctoral theses have been presented:

- “Computational Representation and Discovery of Transcription Factor Binding Sites”. 01/02/2016. Universitat Politècnica de Catalunya (UPC). Autor: Joan Maynou. Director: Alexandre Perera.
- “Multichannel analysis of normal and continuous adventitious respiratory sounds for the assessment of pulmonary function in respiratory diseases”. 15/07/2016. UPC. Autor: Manuel Lozano. Director: Raimon Jané.
- “Analysis of the Interlimb similarity of motor patterns for improving stroke assessment and neurorehabilitation”. 27/10/2016. UPC. Autor: Oiane Urrea. Director/a: Alicia Casals, Raimon Jané.
- “Evaluación no invasiva del impulso neural respiratorio y su relación con la respuesta mecánica mediante el análisis de señales electromiográficas de músculos respiratorios”. 07/11/2016. UPC. Autor: Luis Estrada. Director: Abel Torres.
- “Detección de Isquemia de Miocardio y Estudio de la Respuesta Autónoma Asociada mediante Procesamiento de la Señal de EGG”. 29/11/2016. UPC. Autor: Rudys Magrans. Director: Pedro Gomis.



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PROGRAMMES

**Bioengineering & Medical Imaging**



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**Contributors:** Alcaine Otín, Alejandro | Borges de Almeida, Rute Alexandra | Carro Fernández, Jesús | Lazaro Plaza, Jesús | Llamedo, Mariano | Orini, Michele | Sánchez Tapia, Carlos

## Main lines of research

- Non-invasive markers based on ECG pathology characterization and arrhythmia risk identification. The main target is to search for non-invasive indices that predict malignant arrhythmic risk and, at the same time, improve the personalized treatment decision, like the implantation of ICD.
- Intra-cavitary electrogram signal processing (EGM) to improve surgery planning and therapy delivery. The main target is the ablation procedures guiding. (from AF, focal VT, or slow conduction channel at ventricles) based on information derived from EGM recorded during intervention, so to obtain successful procedures with minimal collateral damage at cardiac tissue.
- Modeling and Simulation of Cardiac Electrophysiology. The electrophysiological bases of atrial and ventricular arrhythmia are still largely unknown. A strategy is proposed to better dig into the knowledge of these bases by multi-scale computational modeling, so allowing improvements in the design of drugs targeting specific ion channel, and better characterizations of the information underlying the ECG and EGM signals through more robust markers.
- Evaluation and non-invasive quantification of the autonomic nervous system (ANS). The ANS has a very important regulatory role in situations such as physiologic (exercise, stress, emotions ...) as well as

pathologic (cardiovascular and mental disorders, obstructive sleep apnea, etc.). The variability present on signal as heart rate (HRV), blood pressure (BPV) or photoplethysmography (PPG) is influenced by the ANS activity, reason why their specific quantification and their interaction among the different signals, allows a non-invasive evaluation of the ANS status.

- Processing and characterization of biomedical signals in respiratory pathologies. The ambulatory diagnosis of patients suffering from sleep diseases is a very relevant health challenge. Solving this challenge from easy to record biomedical signals (ECG, PPG) will represent a huge advance. We target the characterization of these signal changes following respiratory patterns changes, as deep of respiration, frequency, the obstructive or central apnea occurrence and their relation to cardiovascular disorders.

## Most relevant scientific articles

- LAGUNA P., MARTÍNEZ CORTÉS J.P., PUEYO E. Techniques for Ventricular Repolarization Instability Assessment from the ECG. *Proceedings of the IEEE*. 2016;104(2):392-415.
- BAUMERT M., PORTA A., VOS M.A., MALIK M., COUDERC J.-P., LAGUNA P. ET AL. QT interval variability in body surface ECG: Measurement, physiological basis, and clinical value: Position statement and consensus guidance endorsed by the European Heart Rhythm Association jointly with the ESC Working Group on Cardiac Cellular Electrophysiology. *Europace*. 2016;18(6):925-944.
- PUEYO E., ORINI M., RODRÍGUEZ J.F., TAGGART P. Interactive effect of beta-adrenergic stimulation and mechanical stretch on low-frequency oscillations of ventricular action potential duration in humans. *Journal of Molecular and Cellular Cardiology*. 2016;97:93-105.
- HERNANDO A., LÁZARO J., GIL E., ARZA A., GARZÓN J.M., LÓPEZ-ANTÓN R. ET AL. Inclusion of Respiratory Frequency Information in Heart Rate Variability Analysis for Stress Assessment. *IEEE Journal of Biomedical and Health Informatics*. 2016;20(4):1016-1025.
- BOLEA J., PUEYO E., ORINI M., BAILÓN R. Influence of heart rate in non-linear HRV indices as a sampling rate effect evaluated on supine and standing. *Frontiers in Physiology*. 2016;7(NOV).

## Highlights

- Awarded Funding for a project from the Spanish National Research Agency, led by Profs. Juan Pablo Martinez y Esther Pueyo: “DPI2016-75458-R: Multi-scale physiology-driven computational tools to assist in the assessment and management of cardiac dysfunctions”.
- Prof. Pablo Laguna was invited keynote speaker at the “2016 IEEE Statistical Signal Processing Workshop” Symposium, where he presented a KetyNote Talk entitle “Review” on signal processing techniques for ablation guiding in atrial fibrillation entitled “Physiologically driven, model-based, multi-modal biomedical signal processing approaches”.
- The group had hosted four researchers from other research labs (2 Predoc, and 2 Postdoc). They have done short research stays, in periods going from 2 weeks to 3 months. These researchers come from: 1 Portugal, 1 Argentina, 1 Italy and 1 Spain.
- It has been incorporate into the group a senior researcher, Laura Ordovás, by the competitive international program call ARAID, supported by Gobierno de Aragón.
- During this year the group IP, Prof. Pablo Laguna, has hold the Presidency of the “Board of Director Computing in Cardiology”
- As research production, the group has published a total of 15 papers and 16 conference proceedings (in one case obtaining the young investigator award and in other being finalist), and has defended two doctoral Ph. D. thesis.





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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

Led by Full Professor Laura M. Lechuga, the NanoBiosensors and Bioanalytical Applications Group, focuses its activities inside the Nanomedicine area and is involved in the development of novel nanobiosensors devices based on plasmonics, nanoplasmonics, silicon photonics and optomechanics principles, including surface biofunctionalization, microfluidics and complete lab-on-a-chip integration for point-of-care devices.

The nanobiosensors are applied in clinical diagnostics, environmental control, and genomics and proteomics research. The activities range from the basic research to the technological implementation of complete sensing platforms, following the way to the industrial transfer of our research into products.



## Most relevant scientific articles

- HUERTAS C.S., CARRASCOSA L.G., BONNAL S., VALCARCEL J., LECHUGA L.M. Quantitative evaluation of alternatively spliced mRNA isoforms by label-free real-time plasmonic sensing. *Biosensors and Bioelectronics*. 2016;78:118-125.
- SOLER M., ESTÉVEZ M.-C., MORENO M.D.L., CEBOLLA A., LECHUGA L.M. Label-free SPR detection of gluten peptides in urine for non-invasive celiac disease follow-up. *Biosensors and Bioelectronics*. 2016;79:158-164.
- MALDONADO J., GONZÁLEZ-GUERRERO A.B., DOMÍNGUEZ C., LECHUGA L.M. Label-free bimodal waveguide immunosensor for rapid diagnosis of bacterial infections in cirrhotic patients. *Biosensors and Bioelectronics*. 2016;85:310-316.
- SOLER M., ESTÉVEZ M.-C., VILLAR-VÁZQUEZ R., CASAL J.I., LECHUGA L.M. Label-free nanoplasmonic sensing of tumor-associate autoantibodies for early diagnosis of colorectal cancer. *Analytica Chimica Acta*. 2016;930:31-38.
- GONZÁLEZ-GUERRERO A.B., MALDONADO J., DANTE S., GRAJALES D., LECHUGA L.M. Direct and label-free detection of the human growth hormone in urine by an ultrasensitive bimodal waveguide biosensor. *Journal of Biophotonics*. 2016.

## Highlights

During 2016 we have progressed towards the consecution of integrated and multiplexed devices with interferometric nanophotonic biosensors and (nano)plasmonic biosensors. We have demonstrated their feasibility in several application fields, such as in the research line focused on the cellular pathways studies, which has been consolidated. In this regard, quantitative evaluation of alternatively spliced mRNA isoforms with label-free real-time sensing has been achieved. miRNA detection in biological media at exceptionally low limits of detection (aM range) has also been successfully demonstrated. These results have been summarized in three high impact factor publications. We keep focused also on other applications with clinical interest: detection of cancer biomarkers (i.e. autoantibodies, within project RETOS Colaboración COLONTEST); the specific detection of infectious diseases such as tuberculosis (EU-Project POCKET and additional collaborations); the detection of sepsis (EU-Project RAIS). In the environmental field, we have progressed in the detection of marine pollutants (EU-Project BRAAVOO).

New projects have been granted during 2016: two CIBER-BBN intramural projects (PcP-SENS and EYE-POC), dedicated to POC (Point-of-care) device development for the specific detection of *Pneumocystis jirovecii* Pneumonia and the Dry-eye disease, respectively. PcP-SENS has been awarded as Project of Excellence (PcP-SENS). Two new projects also granted focus on the development of integrated plasmonic prototypes: URINETEST (RETOS-Colaboración, RTC-2016-5452-1) for the monitoring of gluten-free diet by detecting gluten toxic peptides in urine, and PreDICT (RETOS Investigación, TEC2016-78515-R), towards de design and fabrication of an advanced multiplexed device for disease detection, progression and therapy follow-up in lung cancer. In the integrated nanophotonic biosensors research line we have been granted with the NANOFOTOSENS project (Fundación Domingo Martínez) for the development of a novel ultrasensitive photonic nanosensor integrating a new class of porous materials (MOF, metal organic frameworks) as specific receptors for the fast and specific detection of minute concentration of gas pollutants for environmental quality control.



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PROGRAMMES

**Bioengineering & Medical Imaging**



## GROUP MEMBERS

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## Main lines of research

### THYROID CANCER

- Markers of prognostic prediction.
  - Implication of 21 genes in CDT. Development of data base, and a private collection of serum and tissue bank of epithelial thyroid cancer (more of 200 cases). We found the relationship between the expression of ABCG2/BRCP transporter gene and the aggressiveness of the TPC-1 human cell-line of thyroid cancer. We have identified differential hyper- and under-expression of genes in PTC and FTC. 120 proteins have been identified by proteomic analysis.
- In vitro and in vivo evaluation of an original thyroid chemotherapy.
  - PGLA nanoparticles, loaded with an inhibitor of tyrosinase, recognize the neoplastic cells by a monoclonal antibody against EGFR.

### DIABETES MELLITUS, METABOLIC SYNDROME, OBESITY, CARDIOMETABOLIC RISK

- Autoimmune Diabetes Mellitus.
  - EU Research Consortium that has characterized the genetics, the immunology, the metabolic and the clinical phenotype of LADA in 11 European countries
- Telemedicine and Intelligent Systems for the Therapeutic Optimization of Diabetes Mellitus.
  - PREDIRCAM Project. Original technological platform of CIBER-BBN, previously validated; at present, a multicentric clinical trial is being developed in 3 Spanish University Hospitals. (Coordination, EDUAB-HSP)
  - CONCEPTT: Continuous Glucose Monitoring (CGM) in Women with Type 1 Diabetes in Pregnancy Trial. First worldwide clinical trial to demonstrate the benefits of CGMS in diabetic pregnancy. EDUAB-HSP is a Member of the Steering Committee too (countries involved: Canada, Israel, Italy, Spain USA).

- DALI Project: Lifestyle intervention in the prevention of Gestational Diabetes (GDM). It is a EU Research Project (7th Framework).
- Telemedicine and Intelligent Systems for Therapeutic Optimization of Diabetes Mellitus. Investigation of combined open and closed loop systems to achieved normoglycemia in type 1 diabetes.
- DM-2, Obesity, Metabolic Syndrome, Hyperlipidemia, Cardiovascular Risk.
  - We investigate the role of vitamin D in the prevention of DM and the MS (one PhD Thesis already ended in 2013).
- Endocrinology of Reproduction (Diabetes and Thyroid).
  - Monogenic diabetes and pregnancy. Investigation of the prevalence of MODY-2 and 3, as well as fetomaternal morbidities.
  - Gestation and Diabetes. Research activities involving macrosomia, influences of race, and adaptative changes of therapeutic insulin regimens.

## Most relevant scientific articles

- HARREITER J., SIMMONS D., DESOYE G., CORCOY R., ADELANTADO J.M., DEVLIEGER R. ET AL. IADPSG and WHO 2013 gestational diabetes mellitus criteria identify obese women with marked insulin resistance in early pregnancy. *Diabetes Care*. 2016;39(7):e90-e92.
- FEIG D.S., ASZTALOS E., CORCOY R., DE LEIVA A., DONOVAN L., HOD M. ET AL. CONCEPTT: Continuous Glucose Monitoring in Women with Type 1 Diabetes in Pregnancy Trial: A multi-center, multi-national, randomized controlled trial - Study protocol. *BMC Pregnancy and Childbirth*. 2016;16(1).
- BENHALIMA K., MATHIEU C., DAMM P., VAN ASSCHE A., DEVLIEGER R., DESOYE G. ET AL. Erratum to: A proposal for the use of uniform diagnostic criteria for gestational diabetes in Europe: an opinion paper by the European Board & College of Obstetrics and Gynaecology (EBCOG) (*Diabetologia*, 10.1007/s00125-015-3615-7). *Diabetologia*. 2016;59(8):1791.
- CAIMARI F., VALASSI E., GARBAYO P., STEFFENSEN C., SANTOS A., CORCOY R. ET AL. Cushing's syndrome and pregnancy outcomes: a systematic review of published cases. *Endocrine*. 2016;;1-9.
- GARCÍA-PATTERSON A., MINAMBRES I., ADELANTADO J.M., GICH I., PUIG T., DE LEIVA A. ET AL. Sex ratio at birth is associated with type 1 diabetes characteristics. *Acta Diabetologica*. 2016;;1-11.

## Highlights


- **Main results of research activities:** Pregnant women with a BMI > 29 underwent a 75 g-OGTT in early pregnancy. GDM depicted greater insulin resistance, BMI, waist circumference, blood pressure, triglycerides, free fatty acids, 3-beta-hydroxybutyrate, and heart rate at screening. Prepregnancy BMI was a significant predictor of early GDM. (EU Project DALI. *Diabetes Care* 2016;39:e90-e92).  
We investigated the association between maternal diabetes and sex ratio at birth (SRB) in women with DM-1. SRB was significantly associated with 3 diabetes characteristics: diabetes duration, first-trimester HbA1c, and insulin dose. (*Acta Diabetologica* (DOI 10.1007/s00592-016-09-0). This study (CONCEPTT Study Protocol, sponsored by JDRFI) investigates whether the use of real-time continuous glucose monitoring (RT-CGM) will improve glycemic control in women with type 1 diabetes who are pregnant (214) or planning pregnancy (110). (ClinicalTrials.gov identifier: NCT01788527). The primary outcome is the change in HbA1c. Secondary outcomes include maternal hypoglycemia, CGM time-in, above and below target, glucose variability, maternal and neonatal outcomes. (*BMC Pregnancy and Childbirth* 2016: 167-175).
- **Doctoral Thesis: Silent Atherosclerosis in type 1 diabetes.** This research demonstrated the importance of glycemic control in patients with DM-1 prospectively followed from the onset during more than 20 years. This proposal was quite confirmed within the early phase of the disease (metabolic imprinting). 33% of patients developed subclinical atherosclerosis and qualitative alterations of HDL related to phospholipase A2. An excess of epicardial fat identified patients with severe cardiometabolic risk. (PhD Candidate, Cristina Colom. Thesis Directors, A. de Leiva and A. Chico, UAB-2016-cum laude).
- **Textbook of Diabetes and Pregnancy.** M. Hod, L. Jovanovic, GD Di Renzo, A. de Leiva and O. Langer have coedited a textbook written by a cadre of international experts. A comprehensive review, with new chapters devoted to obesity, bariatric surgery and epidemiology. A key reference for maternal-fetal medicine specialists and diabetologists. (CRC Press-2016).






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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

- Preparation of metallic nanoparticles with controlled size, shape and chemical composition, for the design of biosensors for plasmonic detection and surface enhanced Raman scattering (SERS): towards biomarkers detection and development of new contrast agents for SERS imaging.
- Design and synthesis of plasmonic platforms functionalized with biomolecules, drugs, hydrogel polymer type temperature and pH sensitive, capable of delivering drugs by application of external stimuli such as light: optical hyperthermia.
- Development of decorated nanoparticles with immunogenic and antigenic molecules and study of their adjuvant properties: vaccines desing.
- Contrast agents for multimodal imaging PA, MRI, CT and PET: nanoparticles for applications in preclinical diagnostic molecular imaging.
- Development of nanostructured surfaces to control cell adhesion and cellular communication in various materials.
- Synthesis of complex oligosaccharides and its application in microarray technology: Microarrays of synthetic N-glycans / Oligosaccharide chemistry in solid phase / Microarray preparation and reading



## Most relevant scientific articles

- BODELÓN G., MONTES-GARCÍA V., LÓPEZ-PUENTE V., HILL E.H., HAMON C., SANZ-ORTIZ M.N. ET AL. Detection and imaging of quorum sensing in *Pseudomonas aeruginosa* biofilm communities by surface-enhanced resonance Raman scattering. *Nature Materials*. 2016;15(11):1203-1211.
- GINER-CASARES J.J., HENRIKSEN-LACEY M., GARCÍA I., LIZ-MARZÁN L.M. Plasmonic Surfaces for Cell Growth and Retrieval Triggered by Near-Infrared Light. *Angewandte Chemie - International Edition*. 2016.
- FERNÁNDEZ C., GONZÁLEZ-RUBIO G., LANGER J., TARDAJOS G., LIZ-MARZÁN L.M., GIRALDO R. ET AL. Nucleation of Amyloid Oligomers by RepA-WH1-Prionoid-Functionalized Gold Nanorods. *Angewandte Chemie - International Edition*. 2016;55(37):11237-11241.
- BRZEZICKA K., VOGEL U., SERNA S., JOHANNSSSEN T., LEPENIES B., REICHARDT N.-C. Influence of Core  $\beta$ -1,2-Xylosylation on Glycoprotein Recognition by Murine C-type Lectin Receptors and Its Impact on Dendritic Cell Targeting. *ACS Chemical Biology*. 2016;11(8):2347-2356.
- ESPINOSA A., SILVA A.K.A., SÁNCHEZ-IGLESIAS A., GRZELCZAK M., PECHOUX C., DESBOEUF K. ET AL. Cancer Cell Internalization of Gold Nanostars Impacts Their Photothermal Efficiency In Vitro and In Vivo: Toward a Plasmonic Thermal Fingerprint in Tumoral Environment. *Advanced Healthcare Materials*. 2016.

## Highlights

During 2016, activities within the intramural projects of the nanomedicine area were continued, coordinating the excellence project, NANOTLVAC and participating in the following projects coordinated by different CIBER-BBN groups: GOLIATH, NANOPROBE, DYNAMIC-VASC- 2, and GLYCOTHYROIDCANCER.


- Among the most notable achievements of the group were the establishment of the company Asparia Glycomics, specialized in the production and commercialization of reagents, reference standards, kits and software for the analysis of glycans in clinical diagnosis and for the control of the quality of biopharmaceuticals. The business initiative markets the leading technology developed by Niels Reichardt's laboratory to quantify glycans more accurately and faster than existing solutions on the market.
- Within a line of translational medicine, the group of Prof. Liz-Marzán collaborates with the Biodonostia and Biocruces Institutes of Sanitary Research (both accredited by the ISCIII) in the detection of Tumor markers. This project focuses on the development of a lateral flow device for the specific detection of nucleic acids in the blood of cancer patients.
- It is also worth noting the collaboration between the group of Dr. Niels Reichardt and the group of Dr. Emilio Pérez-Trallero (Area of infectious diseases) in Biodonostia in the development of a faster method of identification of antibiotic resistance of bacterial pathogens based in mass spectrometry.
- In addition, two patent applications have been accepted: "Method for the characterization of intermolecular interactions" and "Methods for making microarrays and their uses"
- We have participated in different projects at the European, national and regional level highlighting two projects funded by the Health Department of the Basque Government within the Ris3 research and innovation strategy in bioscience-health 2020. In addition, we have received and trained more than 33 Students from different countries, obtaining 5 of them the doctoral degree.




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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Navas Jiménez, Luis Carlos

## Main lines of research

- Development of animal models of disseminated human solid tumors and hematological neoplasias for the molecular study of metastatic stem cells and metastasis development.
- Preclinical development of nanoconjugates for targeted delivery and receptor-mediated antimetastatic therapy in solid tumors and inhibitory of dissemination in haematological neoplasias.
- Identification of molecular markers for the prediction of response to therapy and personalized therapy in oncology.

## Most relevant scientific articles

- TERRA X., GÓMEZ D., GARCÍA-LORENZO J., FLORES J.C., FIGUEROLA E., MORA J. ET AL. External validation of sTWEAK as a prognostic noninvasive biomarker for head and neck squamous cell carcinoma. *Head and Neck*. 2016.
- PAVÓN M.A., ARROYO-SOLERA I., CÉSPEDES M.V., CASANOVA I., LEÓN X., MANGUES R. uPA/uPAR and SERPINE1 in head and neck cancer: Role in tumor resistance, metastasis, prognosis and therapy. *Oncotarget*. 2016;7(35):57351-57366.
- VÁZQUEZ E., MANGUES R., VILLAVERDE A. Functional recruitment for drug delivery through protein-based nanotechnologies. *Nanomedicine*. 2016;11(11):1333-1336.
- CÉSPEDES M.V., FERNÁNDEZ Y., UNZUETA U., MENDOZA R., SERAS-FRANZOSO J., SÁNCHEZ-CHARDI A. ET AL. Bacterial mimetics of endocrine secretory granules as immobilized in vivo depots for functional protein drugs. *Scientific Reports*. 2016;6.
- CÉSPEDES M.V., GUILLÉN M.J., LÓPEZ-CASAS P.P., SARNO F., GALLARDO A., ÁLAMO P. ET AL. Lurbinectedin induces depletion of tumor-associated macrophages, an essential component of its in vivo synergism with gemcitabine, in pancreatic adenocarcinoma mouse models. *DMM Disease Models and Mechanisms*. 2016;9(12):1461-1471.

## Highlights

During this year, we have enhanced the focus of the group towards developing and evaluating the nanoconjugate proposed in the CIBER-BBN intramural project, Nanomets, for which we have count with active funding from a FIS Project and an Integrated Project of Excellence of the ISCIII, a Marató TV3 Project and two Transference Projects, one from AGAUR and another that covers the support of the the Advisory Board of the EC-funded Consortium ENATRANS. We have also continued contract work with two Spanish Pharmaceutical Companies, one of them receiving funding from a Retos MINECO project. One Miguel Servet, and two Sara Borrell Researchers, and Clinical Specialists, in Surgery or Medical Oncology, that are doing their PhD, are currently working in the laboratory. Two new PhD students were incorporated to the group after getting contracts for resaerch training from ISCIII and AGAUR. Two doctoral dissertations directed by group members have been defended. The PI of the group was invited speaker in three International Conferences on Molecular Imaging, Personalized Cancer Medicine or Targeted Drug Delivery. He was also appointed to the French Institut National du Cancer Translational Research Scientific Committee. Together with Villaverde's group, our group has demonstrated specific-uptake of the Nanomets protein nanocarrier and the drug-nanoparticle conjugate to metastasis stem cells, opening a new approach to achieve selective antimetastatic effect. We are now setting the knowledge base that will allow the constuction of protein-based nanomedicines that incorporate the requiered functional domains to achieved targeted drug delivery to specific cell types. Our group has also achieved selective killing of tumor associated macrophages of the stroma using a marketed drug and demonstrated its sinergistic antitumor effect when combined with a genotoxic drug that directly kill cancer cells. We established new collaborations with Celine Gongora of the Montpellier Insttute National de la Sante (France).



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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

The Nanobiotechnology for Diagnostics (Nb4D) research group has been a recognized and awarded research group of the Catalanian Government since 2005. The general objective of its research is the investigation of new approaches and strategies to improve the efficiency of current diagnostic methods. To achieve this goal its research addresses three fundamental specific objectives:

1. The development and characterization of bioreceptors with tailored properties.
2. The preparation of biohybrid functional materials through the incorporation of specific bioreceptors onto micro/ nanostructured materials and devices
3. The investigation of new nanobiotechnological approaches for the development of a new generation of tools and devices that will increase the effectiveness of diagnosis in the clinical, food safety and environmental fields.

The scientific activity of Nb4D began in 1996 and has been focused on the development of antibodies and the establishment of immunochemical methods. The group has accumulated a large collection of immunoreagents against various types of analytes.

In the course of the Nb4D group, several stages can be defined, all of them characterised by a continuous increase in the number of researchers and funding, which is achieved through participation in Spanish and European competitive calls and contracts with companies, and output, in terms of publications and patents. The scientific activity of the group is reflected in the number of publications (more than 180 scientific publications in high impact international journals), participation in international conferences, the number of



patents and scientific training activities performed through the supervision of doctoral theses (more than 20 theses read) and divulgation of courses to PhD students and specialised technical personnel.

Since 2009 the group is responsible for the CAbS (Custom Antibody Service) a technological facility created by the group through CSIC and CIBER-BBN and whose aim is to provide services and scientific advice to public and private research centres and companies, in relation to the production of specific antibodies and bioconjugates and the establishment of immunochemical methods.

Regarding the clinical sector, Nb4D is interested in and develops projects in the following areas:

1. Cardiovascular Diseases 2. Infectious Diseases 3. Neurologic and Neurodegenerative Diseases 4. Therapeutic Drug Monitoring 5. Adverse Drug Reactions

## Most relevant scientific articles

- PASTELLS C., PASCUAL N., SÁNCHEZ-BAEZA F., MARCO M.-P. Immunochemical Determination of Pyocyanin and 1-Hydroxyphenazine as Potential Biomarkers of Pseudomonas aeruginosa Infections. *Analytical Chemistry*. 2016;88(3):1631-1638.
- PASTELLS C., MARCO M.-P., MERINO D., LOZA-ÁLVAREZ P., PASQUARDINI L., LUNELLI L. ET AL. Two photon versus one photon fluorescence excitation in whispering gallery mode microresonators. *Journal of Luminescence*. 2016;170:860-865.
- SALVADOR J.-P., MARCO M.-P. Amperometric Biosensor for Continuous Monitoring Irgarol 1051 in Sea Water. *Electroanalysis*. 2016;28(8):1833-1838.
- HASSANI N.E.A.E., BARAKET A., NETO E.T.T., LEE M., SALVADOR J.-P., MARCO M.-P. ET AL. Novel strategy for sulfapyridine detection using a fully integrated electrochemical Bio-MEMS: Application to honey analysis. *Biosensors and Bioelectronics*. 2016.
- RONCADOR G., ENGEL P., MAESTRE L., ANDERSON A.P., CORDELL J.L., CRAGG M.S. ET AL. The European antibody network's practical guide to finding and validating suitable antibodies for research. *mAbs*. 2016;8(1):27-36.

## Highlights

Nb4D continues to work on the development of diagnostic devices to be used in the clinical diagnosis field as well as the food safety and environmental monitoring areas.

The group was awarded a grant from ACCIÓ (Agency for Business Competitiveness) of the Generalitat of Catalonia to provide support to groups who are seeking to be accredited with the TECNIO seal. The aim is to help define and boost our action plans for technology transfer (marketing) while simultaneously preparing the group to achieve higher levels of quality control and subsequently the quality assurance seal from Tecnio.

The project "A new approach for the diagnosis of Pseudomonas aeruginosa infections" has been selected by the CaixaImpulse programme which provides finance to develop the scientific project and work on the valorisation plan while also providing mentors to monitor and support the future project or spin-off.

The group will be host to three Early Stage Researchers as part of the Marie Skłodowska Curie Actions whose aim is to enable research focussed organisations to host talented foreign researchers and to create strategic partnerships with leading institutions worldwide. The group is hosting one ESR as part of the ND4ID "New Diagnostics for Infectious Diseases" project. The group will also host 2 ESRs for the FoodSmartphone "Smartphone analysers for on-site testing of food quality and safety".

The group continues to collaborate with the Pharmasans Labs Inc. (USA) company to develop immunoreagents against biomarkers of neurodegenerative diseases and has begun to develop immunoreagents against pterins, known cofactors used in the biosynthesis of neurotransmitters.

The group has been working on various projects related to clinical diagnosis including the ImmunoQS project whose objective is to investigate immunochemical strategies for diagnosis and therapy based on Quorum sensing. The group is also investigating the possible molecular links between diabetes and neurodegenerative diseases.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

**SOFT TISSUES:** This line is focused in the experimental study of the mechanical and microstructural behaviour of materials mainly on biomaterials and biological tissue. The analysis of the composition, morphology, microstructure and macroscopic behaviour allow to develop advance constitutive law able to reproduce the main physical features of the materials. The principal experimental tests are uniaxial, biaxial, compressive, shear stress, indentation, inflation, tomography, histology, in order to capture phenomena such as elastic, viscoelastic, fatigue or softening behaviours. Histological and microstructural tests permit to extract important information to model and simulate the response of the tissue at microstructural or cellular level. Interactions of the tissue with biomaterials or medical devices have been also studied.

Concerning the cardiovascular research line, our group has a wide experience in the development of constitutive laws and also experimental characterization of blood vessels. Currently our research lines are focused on simulating multiphysics and multiscale phenomena. We have developed advanced constitutive laws to reproduce inelastic effects that incorporate microstructural information, which finally will determine the macroscopic response of the tissue.

**MCROFLUIDICS:** Modeling and simulation of the functional behaviour of tissues and organs with application in the evaluation of pathologies and surgery, pre-operative planning and virtual surgery. The main fields of application are related to the musculoskeletal system, the cardiovascular system and other tissues such as trachea, eye or breast. / Mechanobiology with emphasis on bone remodelling, bone healing and bone morphogenesis, implant osteointegration and wound healing, taking into consideration the effect of the

mechanical environment in cell response. / Tissue engineering, analysing the design of ceramic, polymeric and biological scaffolds and meshes in tissue regeneration, including the interaction scaffold-tissue. / Cell biophysics, studying cell transduction and signalling mechanisms, derived from the mechanical environment (deformation, stiffness of the substrate...) and of the intra-extramembrane electric potential. / Design of bioreactors for biomimetic stimulation of cell cultures with special focus on the application of controlled strains and flow. / Development of microactuators, microfluidic networks for the study of cell biology under in vitro biomimetic environments. / Design, fabrication and development of novel in vitro diagnostic systems based on microfluidics. / Micro-technology for life science applications.

## Most relevant scientific articles

- SÁEZ P., GARCÍA A., PENA E., GASSER T.C., MARTÍNEZ M.A. Microstructural quantification of collagen fiber orientations and its integration in constitutive modeling of the porcine carotid artery. *Acta Biomaterialia*. 2016.
- DE MIGUEL D., GALLEGU-LLEYDA A., AYUSO J.M., PEJENAUTE-OCHOA D., JARAUTA V., MARZO I. ET AL. High-order TRAIL oligomer formation in TRAIL-coated lipid nanoparticles enhances DR5 cross-linking and increases antitumour effect against colon cancer. *Cancer Letters*. 2016;383(2):250-260.
- AYUSO J.M., VIRUMBRALES-MUNOZ M., LACUEVA A., LANUZA P.M., CHECA-CHAVARRÍA E., BOTELLA P. ET AL. Development and characterization of a microfluidic model of the tumour microenvironment. *Scientific Reports*. 2016;6.
- OLIVAN S., CALVO A.C., RANDO A., HERRANDO-GRABULOSA M., MANZANO R., ZARAGOZA P. ET AL. Neuroprotective effect of non-viral gene therapy treatment based on tetanus toxin C-fragment in a severe mouse model of spinal muscular atrophy. *Frontiers in Molecular Neuroscience*. 2016;9(AUG).
- MANZANO S., ARMENGOL M., PRICE A.J., HULLEY P.A., GILL H.S., DOBLARÉ M. ET AL. Inhomogeneous response of articular cartilage: A three-dimensional multiphasic heterogeneous study. *PLoS ONE*. 2016;11(6).

## Highlights

During 2016, the group maintained the research lines established in previous years but a strong effort has been carried out to focus its activity more to the public sector. Several research projects have been granted during 2016 to carry out research for life science applications. Thanks to that effort, the group obtained public funding around EUR 350.000. Some of the projects are:

- **European Projects:** An integrated pilot line for micro-fabricated medical devices. InForMed. ECSEL Joint Undertaking. ECSEL-2014-2.
- **National Projects:** Diseño y mejora de dispositivos intravasculares recubiertos de fármaco mediante una herramienta computacional. Aplicación al diseño de stents y balones en lesiones estenóticas. / Respuesta del tejido corneal al tratamiento del cross-linking. Aplicación al tratamiento del queratocono. / Desarrollo de un sistema basado en microtecnología que integra co-cultivos celulares organizados, andamiaje específico y microsensores: Hacia un modelo in-vitro de riñón. / Desarrollo de un sistema portátil y de bajo coste para la detección de contaminantes en alimentos basados en microfluídica. / Industrialización de un dispositivo microfluídico para la determinación in situ y cuantitativa del consumo de drogas de abuso en saliva. Brioapps ALPHASIP; D.G.A / SMART\_FOOT: Sistema de apoyo a la planificación preoperatoria de cirugías de pie y al diseño inteligente de prótesis plantares personalizadas. / Estimulación mecánica local de células mesenquimales de cara a su diferenciación osteogénica y condrogénica en medicina regenerativa. / Incidencia de los fenómenos de transporte en la hidrólisis enzimática y aplicación de mecánica de fluidos computacional en problemas de escalado (MIXING).
- Other Projects: CA701- Heterogeneous INCEPTION. Catrene Organization. – PneumoSIP- Acoust effective Solution for the Rapid Diagnostic of Pneumonia. PHC-12-2014. Clinical Research for the validation of biomarkers and/or diagnostic medical devices - Therapy Optimization in Glioblastoma: An Integrative Human Data-Based Approach Using Mathematical Models. James S. McDonnell Foundation, Collaborative activity award.
- Patents: SU-8 micro coriolis mass flow sensor. P100233NL00 / Dispositivo para la medida no destructiva de propiedades físicas asociados al estado de conservación de objetos. U201630453 / Sensor, dispositivo y procedimiento para la determinación de la concentración de solutos en disoluciones. PCT/ES2016/070764.





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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

- **Development of nanometric devices with ‘molecular gates’ for controlled release**  
Our objective is to develop nano-systems containing “molecular gates” for releasing a certain payload at will. For that purpose, nanometric mesoporous solids are used as support. Such gated mesoporous silica nanoparticles are able to retain a cargo inside the pore system and deliver it upon the application of a target chemical (redox molecules, selected anions, pH changes, etc.), physical (such as temperature, magnetic fields or light) or biochemical (such as enzymes, antigens, DNA) stimuli.
- **Molecular probes**  
We have experience in developing molecular chemical probes in which the recognition process is coupled to signaling. This applies to the design of probes for the in vitro or in vivo chromo-fluorogenic detection of molecules of interest.
- **Transverse capacities**  
Organic and inorganic synthesis  
Preparation/functionalization of mesoporous materials  
Preparation/functionalization of inorganic nanoparticles (gold, silver, oxides, silica, etc.)



## Most relevant scientific articles

- AZNAR E., OROVAL M., PASCUAL L., MURGUÍA J.R., MARTÍNEZ-MANEZ R., SANCENÓN F. Gated Materials for On-Command Release of Guest Molecules. *Chemical Reviews*. 2016;116(2):561-718.
- Díez P., SÁNCHEZ A., DE LA TORRE C., GAMELLA M., MARTÍNEZ-RUIZ P., AZNAR E. ET AL. Neoglycoenzyme-Gated Mesoporous Silica Nanoparticles: Toward the Design of Nanodevices for Pulsatile Programmed Sequential Delivery. *ACS Applied Materials and Interfaces*. 2016;8(12):7657-7665.
- OROVAL M., CORONADO-PUCHAU M., LANGER J., SANZ-ORTIZ M.N., RIBES A., AZNAR E. ET AL. Surface Enhanced Raman Scattering and Gated Materials for Sensing Applications: The Ultrasensitive Detection of Mycoplasma and Cocaine. *Chemistry - A European Journal*. 2016.
- RIBES A., XIFRE-PÉREZ E., AZNAR E., SANCENÓN F., PARDO T., MARSAL L.F. ET AL. Molecular gated nanoporous anodic alumina for the detection of cocaine. *Scientific Reports*. 2016;6.
- POLO L., GÓMEZ-CEREZO N., AZNAR E., VIVANCOS J.-L., SANCENÓN F., ARCOS D. ET AL. Molecular gates in mesoporous bioactive glasses for the treatment of bone tumors and infection. *Acta Biomaterialia*. 2016.

## Highlights

During 2016, we began the intramural projects NANOPROBE, NANOTARGET, GBM ON CHIP, the new editions of the projects NANOHYPERTERMIA and SPRING and the collaborative project “Search for biomarkers for the early detection of Alzheimer’s disease in the Vallecas project cohort”. In addition, we have continued with the development of MICHORMON-PRO and AUDIOMC transfer projects and the SEPAR-CIBERES-CIBERBBN TARMAC project. In the framework of all these projects, we have developed different systems applied to both therapy and disease diagnosis. In addition, we have started our new project of the National plan on intelligent nanomaterials, probes and devices for the integrated development of new tools applied to the biomedical field, a new RETOS project and two joint projects between researchers of the Polytechnic University of Valencia and IIS La Fe for the establishment of a smart drug discovery platform and for the development of a new kit for the detection of candida.

Like other years, we have continued with an intense scientific activity publishing 31 articles in international journals with high impact factor. Among them, we can highlight the works dealing with ultrasensitive detection using gated nanoparticles and SERS, in collaboration with the group of Luís M. Liz-Marzán or the development of a system for the treatment of infections and bone tumors using bioactive mesoporous glasses combined with molecular gates, in collaboration with the group of María Vallet.

At international level, we have continued with the development of the NANOTUN3D project. In addition, we have hosted five students and researchers from India, Czech Republic, France and Italy. In addition, three of our predoctoral students have been in Ireland for short stays.

Finally, in 2016 our group has also had an intense formative activity. We participated in the CIBER-BBN training program where one of our students got a research initiation grant and later a pre-doctoral fellowship from the Universitat Politècnica de València. In addition, six of our students have defended their doctoral thesis during this year.



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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

- HIV/AIDS, paediatric, immunology, age, inflammation, viral latency, microbicides against HIV; HCV, HSV, HIV vaccine, carbosilane dendrimers, nanomedicine, gene therapy, transfection, dendritic cells, immunogens, new therapies, animal models, HIV cohort, HIV biobank, biobanks.

## Most relevant scientific articles

- SEPÚLVEDA-CRESPO D., VACAS-CÓRDOBA E., MÁRQUEZ-MIRANDA V., ARAYA-DURAN I., GÓMEZ R., MATA F.J.D.L. ET AL. Effect of Several HIV Antigens Simultaneously Loaded with G2-NN16 Carbosilane Dendrimer in the Cell Uptake and Functionality of Human Dendritic Cells. *Bioconjugate Chemistry*. 2016;27(12):2844-2849.
- PERISE-BARRIOS A.J., FUENTES-PANIAGUA E., SÁNCHEZ-NIEVES J., SERRAMÍA M.J., ALONSO E., REGUERA R.M. ET AL. Improved Efficiency of Ibuprofen by Cationic Carbosilane Dendritic Conjugates. *Molecular Pharmaceutics*. 2016;13(10):3427-3438.
- CENA-DÍEZ R., VACAS-CÓRDOBA E., GARCÍA-BRONCANO P., DE LA MATA F.J., GÓMEZ R., MALY M. ET AL. Prevention of vaginal and rectal herpes simplex virus type 2 transmission in mice: Mechanism of antiviral action. *International Journal of Nanomedicine*. 2016;11:2147-2162.
- SEPÚLVEDA-CRESPO D., CENA-DÍEZ R., JIMÉNEZ J.L., ÁNGELES MUNOZ-FERNÁNDEZ M.. Mechanistic Studies of Viral Entry: An Overview of Dendrimer-Based Microbicides as Entry Inhibitors Against Both HIV and HSV-2 Overlapped Infections. *Medicinal Research Reviews*. 2016.
- CENA-DÍEZ R., GARCÍA-BRONCANO P., DE LA MATA F.J., GÓMEZ R., MUNOZ-FERNÁNDEZ M.A. Efficacy of HIV antiviral polyanionic carbosilane dendrimer G2-S16 in the presence of semen. *International Journal of Nanomedicine*. 2016;11:2443-2450.

## Highlights

Along the year 2016 we have been recognized for our innovative concepts involving the use of dendrimers as versatile nano-vectors for the treatment of HIV-1 and HSV-2 in National and International Congress. We work on two concepts: nanotechnology and dendrimers with various characteristics for use in gene therapy, drug carriers and in infectious diseases. We would like to highlight the use as i) therapeutics nanovaccines against the HIV-1 infection. The greatest challenge in designed anti-miRNA therapy for HIV-1 is delivering the miRNAs to relevant cells in vitro and in vivo. One potential delivery approach that may be amenable to large-scale production is the use of dendrimers that efficiently deliver miRNAs, particularly if they can be modified with targeting ligands promoting preferential uptake into the relevant cells and in h-BLT mouse model as a consequence comprising the HIV-1 reservoir; ii) to prevent sexually transmitted viruses. The technology developed this year has shown a great efficacy of dendrimers as prophylaxis as microbicides against HIV-1, and HIV-1/HSV-2 co-infection. Our dendrimer, G2-S16 is a promising candidate for future microbicide first-in-human clinical trial in the field for prevention of vaginal HIV-1-infection in women. We have elaborated a preclinical Phase I, First-in-Human, randomized, double-blind, placebo-controlled study to assess the Safety, Tolerability and Acceptability of the 3% G2-S16 gel as vaginal microbicide in healthy sexually active women. Information from this study help us decide whether this gel is safe to move onto the next phase. Design: Phase I, randomized, double blind, placebo-controlled, parallel-group study; primary objective: To assess the safety of 7 consecutive daily vaginal applications of 3% G2-S16 gel in healthy, sexually active, HIV-uninfected women; Outcome Measures: Safety, Tolerability and Acceptability. Aspilation has considered that this phase I clinical study is appropriate to evaluate the safety and tolerability of G2-S16 as a FIH trial.



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🌐 **Group Website**

PROGRAMMES

**Bioengineering & Medical Imaging**



### GROUP MEMBERS

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**Contributors:** Gallego, Judit | Herance Camacho, Raúl | Martí Fuster, Berta | Pino Sorroche, Francisco | Roé Vellvé, Núria

## Main lines of research

- Monte Carlo Simulation: development and optimization of simulators.
- Tomographic reconstruction in emission tomography.
- Quantification of neurotransmission SPECT studies in neurodegenerative diseases.
- Quantification of PET studies with radiotracers binding beta-amyloid protein in Alzheimer disease.
- Multimodal image analysis in refractory epilepsy.
- Statistical analysis of emission tomography images.
- Statistical analysis of functional and structural MRI.
- Parametric images obtained from the diffusion tensor.
- Development of high-field MRI acquisition protocols (7T) for animals.



## Most relevant scientific articles

- GISPERT J.D., SUÁREZ-CALVET M., MONTE G.C., TUCHOLKA A., FALCÓN C., ROJAS S. ET AL. Cerebrospinal fluid sTREM2 levels are associated with gray matter volume increases and reduced diffusivity in early Alzheimer's disease. *Alzheimer's and Dementia*. 2016;12(12):1259-1272.
- SUÁREZ-CALVET M., KLEINBERGER G., ARAQUE CABALLERO M.A., BRENDEL M., ROMINGER A., ALCOLEA D. ET AL. sTREM2 cerebrospinal fluid levels are a potential biomarker for microglia activity in early-stage Alzheimer's disease and associate with neuronal injury markers. *EMBO Molecular Medicine*. 2016.
- DEMIRTAS M., TORNADOR C., FALCÓN C., LÓPEZ-SOLA M., HERNÁNDEZ-RIBAS R., PUJOL J. ET AL. Dynamic functional connectivity reveals altered variability in functional connectivity among patients with major depressive disorder. *Human Brain Mapping*. 2016.
- GISPERT J.D., MONTE G.C., FALCÓN C., TUCHOLKA A., ROJAS S., SÁNCHEZ-VALLE R. ET AL. CSF YKL-40 and pTau181 are related to different cerebral morphometric patterns in early AD. *Neurobiology of Aging*. 2016;38:47-55.
- MAYORAL M., MARTÍ-FUSTER B., CARRENO M., CARRASCO J.L., BARGALLO N., DONAIRE A. ET AL. Seizure-onset zone localization by statistical parametric mapping in visually normal 18F-FDG PET studies. *Epilepsia*. 2016;57(8):1236-1244.

## Highlights

### DOCTORAL THESIS:

- Gemma Monté Rubio. Universitat de Barcelona. "Computational analysis of schizophrenia: Implementation of a multivariate model of anatomical differences".
- Judith Gallego Blanco. Universitat Politècnica de Catalunya. "Quantification of dopaminergic neurotransmission SPECT studies with 123I-labelled radioligands".
- Javier Jiménez González. Universitat Politècnica de Catalunya. "Improvements in the registration of multimodal medical imaging: application to intensity inhomogeneity and partial volume corrections".

### NEW PROJECTS:

- European Project. H2020-IMI2-JTI-2015-05. Topic 4 - AMYPAD (Amyloid Imaging to prevent Alzheimer's Disease), (<http://amypad.org/>). Rol JD Gispert WP-leader.
- Cohort Projects CIBER. "Búsqueda de biomarcadores para la detección temprana de la enfermedad de Alzheimer en la cohorte del proyecto Vallecas".

### INTERNATIONAL COLLABORATIONS :

- JD Gispert member of the Imaging Scientific Advisory Group of the project IMI-EPAD (European prevention of Alzheimer's Dementia; <http://ep-ad.org/>)
- Dr Aldo Badano from Center for Devices and Radiological Health de la U.S. Food and Drug Administration. The activity is focused on the Monte Carlo simulation of RX detectors for medical imaging.
- Dr. Luca Cozzi from Humanitas Cancer Center, Milano, Italia. Dr. Cozzi is a scientific advisor to Varian and acts as a liaison between one of our groups and the company.
- Prof. Vasily Shvedunov from Lomonosov Moscow State University. We collaborate in the development of a microtron prototype with application in intraoperative radiotherapy. The beam modifiers are designed using the PENELOPE/penEasy code.
- Dr. Alberto Bravin from European Synchrotron Radiation Facility (ESRF, Grenoble, France). PENELOPE/penEasy is being evaluated for dosimetric studies of a new radiotherapy technique using synchrotron radiation in the framework of the EU action FP7 COST TD1205 (<https://www.syra3.eu>).



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PROGRAMMES  
**Nanomedicine**



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## Main lines of research

- **Microencapsulation of alive cells:** Design and optimization of polymeric systems for immobilization of cells with therapeutic activity. This system provides protection to cells against the host's immune response due to its technological design, and at the same time, it turns into a controlled release pharmaceutical system.
- **Micro and nano-particles as vaccine administration systems of peptides and proteins:** Promising results obtained by our research group support the use of these drug (antigen) carrier systems to develop vaccines, as demonstrated by the results after their administration by different routes in laboratory animals (mice and monkeys), inducing a sustained and strong immune response.
- **Non-viral vectors for gene therapy purposes:** Design and optimization of non-viral vectors based on lipidic and polymeric nanoparticles to transfect eukaryotic cells with therapeutic genes.
- **Development of modified release formulations:** Development and optimization of drug delivery systems based on new polymers to obtain a sustained release profile of drugs.
- **Pharmacokinetic and biopharmaceutical evaluation of modified drug delivery and therapeutic**

### systems obtained with bio technologic products.

- **Nanocarriers for pulmonary administration:** the aim of this work line is the design, optimization and characterization of vehicles in the nanometric range that are intended to be administered pulmonary. These systems present many advantages, such as mucoadhesion, biodegradability, no first pass effect hence the possibility to reduce the dose, good tolerability, deep lung deposition of the drug and sustained release of the API thus longer dosing interval. These systems are applied for the nanoformulation of DNA, peptide, antineoplastics and antibiotics.

## Most relevant scientific articles

- OJEDA E., PURAS G., AGIRRE M., ZARATE J., GRIJALVO S., ERITJA R. ET AL. The influence of the polar head-group of synthetic cationic lipids on the transfection efficiency mediated by niosomes in rat retina and brain. *Biomaterials*. 2016;77:267-279.
- HERNANDO S., GARTZIANDIA O., HERRÁN E., PEDRAZ J.L., IGARTUA M., HERNÁNDEZ R.M.. Advances in nanomedicine for the treatment of Alzheimer's and Parkinson's diseases. *Nanomedicine*. 2016;11(10):1267-1285.
- OJEDA E., PURAS G., AGIRRE M., ZARATE J., GRIJALVO S., ERITJA R. ET AL. The role of helper lipids in the intracellular disposition and transfection efficiency of niosome formulations for gene delivery to retinal pigment epithelial cells. *International Journal of Pharmaceutics*. 2016;503(1-2):115-126.
- GARTZIANDIA O., EGUSQUIAGUIRRE S.P., BIANCO J., PEDRAZ J.L., IGARTUA M., HERNÁNDEZ R.M. ET AL. Nanoparticle transport across in vitro olfactory cell monolayers. *International Journal of Pharmaceutics*. 2016;499(1-2):81-89.
- GARCÍA-ORUE I., GAINZA G., GUTIÉRREZ F.B., AGUIRRE J.J., EVORA C., PEDRAZ J.L. ET AL. Novel nanofibrous dressings containing rhEGF and Aloe vera for wound healing applications. *International Journal of Pharmaceutics*. 2016.

## Highlights

- Boosting the line of pulmonary formulations through Feder Funds from the NANBIOSIS Platform with the purchase of a cascade impactor system.
- Eleven publications of indexed magazines.
- Four thesis defended in the Drug Delivery, Tissue Engineering and Gene Therapy.
- A total of five national projects, of which two are Retos-Colaboración.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



## GROUP MEMBERS

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## Main lines of research

USER CENTERED DESIGN AND BIOMEDICAL APPLICATIONS (R+D+i).

The main Healthcare Technology areas in which the IBV is active are:

Orthopaedic Implants Surgery: hip, knee and spine implants, osteosynthesis and personalized implants. / Dental implants and prosthesis. / Surgical instruments. / Applications for ophthalmology. / Personalization of medical devices to meet the anatomical and physiological needs of the patient. / Veterinary implants.

FUNCTIONAL ASSESSMENT OF HUMAN MOVEMENTS.

Human gait studies / Musculo-skeletal diseases on workplace / Orthopaedic and surgical treatments evaluation / Technical aids for disabled people evaluation.

TECHNOLOGY CONSULTANCY.

The IBV puts its know-how at the service of companies within the sector, to help improve their products.

Assistance is available for:

- The biomechanical definition, selection, design and evaluation of new biomaterials (ceramics, metals and polymers) used for regenerating bone and cartilage tissues.
- The selection of biomaterials to be used in medical devices.
- All stages of product development and design:



- Detecting the needs of the patient and surgeon. / Defining the design specifications. / Selecting the manufacturing techniques and materials. / Developing the conceptual designs and details of the product. / Collaboration in defining the processes required for manufacturing an CE market approved medical device. / Consultation regarding the definition of any tests required to obtain CE marking for the product. / Collaboration with companies in preparing the documents required to obtain CE marking of medical devices certification: defining essential requirements; carrying out risk analyses, and clinical justification of the design.

- Locomotor system pathologies study and evaluation.
- Orthopaedic and surgical repair systems study and evaluation from a functional point of view.

BIOMECHANICAL EVALUATION OF MEDICAL DEVICES.

TRAINING.

TIC APPLICATIONS.

## Most relevant scientific articles

- DÍAZ-RODRÍGUEZ M., VALERA A., PAGE A., BESA A., MATA V. Dynamic Parameter Identification of Subject-Specific Body Segment Parameters Using Robotics Formalism: Case Study Head Complex. *Journal of Biomechanical Engineering*. 2016;138(5).
- MARSTON H.R., KROLL M., FINK D., DE ROSARIO H., GSCHWIND Y.J. Technology use, adoption and behavior in older adults: Results from the iStoppFalls project. *Educational Gerontology*. 2016;42(6):371-387.
- LÓPEZ-VICENTE A., ARTACHO-PÉREZ C., JARQUE-BOU N., RAYA R., LLORIA M., BELDA-LOIS J.-M. ET AL. Adaptive inputs in an interface for people with Dyskinetic Cerebral Palsy: Learning and usability. *Technology and Disability*. 2016;28(3):79-89.


## Highlights


- GTS-IBV is in charge of design and manufacturing of internal and external structures of a PET equipment to early detection of Alzheimer disease. This project (CAREMiBRAIN) is led by Oncovision, Spanish small enterprise, and it has been funded by the European Commission (H2020-SMEINST-2-2015-PHC-12-2015-P).
- Helios de Rosario is the IP of the European funded project my-AHA (H2020-PHC-2015) that has the main aim to reduce frailty risk by improving physical activity and cognitive function, psychological state, social resources, nutrition, sleep and overall well-being. It will empower older citizens to better manage their own health, resulting in healthcare cost savings. my-AHA will use state-of-the-art analytical concepts to provide new ways of health monitoring and disease prevention through individualized profiling and personalized recommendations, feedback and support.
- Participation in EIT-HEALTH, KIC (Knowledge and Innovation Communities) in health.
- Development of a personalised device to block the left atrial appendage for reducing the risk of cerebral stroke by thromboembolism (funded by CDTI).
- CUSTOM-ON-BODY: Definition of a design methodology to personalised products adapted to the morphological variability of the population. These products should be manufactured by flexible production technologies.
- EUROHANDFEET: Study of the anthropometric characteristics of the child population to improve safety, ergonomics and psychomotricity of products for children.
- Participation in the 2nd Bohnes Colloquium with the objective to improve the knowledge of human locomotor system's structure and functioning, and to implement effective digital tools and technologies, to be used in arts, skills, and professions.



LEAD RESEARCHER

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PROGRAMMES

## Bioengineering & Medical Imaging



### GROUP MEMBERS

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## Main lines of research

- Oscillatory activity of the brain: Towards the understanding of the normal cognition and brain disorders; cerebral basis of cognitive function in healthy people and in patients with neurological and psychiatric diseases.
- Advanced biomedical imaging technologies: Neuroimaging biomarkers in aging and dementia; simultaneous EEG-fMRI Recording; functional and structural connectivity.
- Diabetes technologies to apply the available technologies to optimize follow-up and metabolic control of people suffering from diabetes.
- Neurorehabilitation Engineering: to help restore, minimize and/or compensate the alterations, those typically appear on a person after suffering a Traumatic Brain Injury (TBI) or a stroke; Neurorehabilitation processes modeling: dysfunctional and hybrid bionics models; Smart monitoring of cognitive and physical rehabilitation.
- Development of sensors and medical devices based on nanoparticles: hyperthermia induction in living tissues (optical and radiofrequency); biosensors based on nanoparticles for early diagnosis of bacterial diseases.
- Development of biofunctionalized nanomaterials for biomedical applications: Design and manufacture of biocompatible and stable nanostructures for RMI contrast agents for in vivo early diagnosis of Alzheimer disease; Labeling of human neural precursor cells for in vivo cell tracking in cell replacement therapies against neurodegenerative diseases.
- Computational systems biology & study of structure and function in cultured neuronal networks.

- Exploring the physiopathological mechanisms of connexinopathies: Role of Connexin-36 in Epilepsy; Therapeutic approaches for stroke in preclinical models.
- Interaction of brain functions with very low frequency and intensity pulsed electromagnetic fields; Pain Brain DTI-MRI Function in Transgenic mice; Pulsed Magnetic Field Stimulation to enhance Neurite Growth.
- Bioinspired fibres for biomedical applications applied to biostructural prosthesis.
- Microanatomical and neurochemical alterations of the cerebral cortex in Alzheimer's.
- Biomedical Informatics: natural language processing, indexing and knowledge discovery; MEG data analysis. Big data analytics to predict biomarkers for early stages of Alzheimer and Parkinson.
- Technology to empower healthy habits to manage habit changing.

## Most relevant scientific articles

- FERNÁNDEZ-GARCÍA L., MARI-BUYE N., BARIOS J.A., MADURGA R., ELICES M., PÉREZ-RIGUEIRO J. ET AL. Safety and tolerability of silk fibroin hydrogels implanted into the mouse brain. *Acta Biomaterialia*. 2016;45:262-275.
- CABALLERO-RUIZ E., GARCÍA-SÁEZ G., RIGLA M., VILLAPLANA M., PONS B., HERNANDO M.E. Automatic classification of glycaemia measurements to enhance data interpretation in an expert system for gestational diabetes. *Expert Systems with Applications*. 2016;63:386-396.
- MARTÍNEZ-MORENO J.M., SÁNCHEZ-GONZÁLEZ P., LUNA M., ROIG T., TORMOS J.M., GÓMEZ E.J. Modelling ecological cognitive rehabilitation therapies for building virtual environments in brain injury. *Methods of Information in Medicine*. 2016;55(1):50-59.
- GARCÍA-GARCÍA F., BENITO P.J., HERNANDO M.E. Automatic identification of physical activity intensity and modality from the fusion of accelerometry and heart rate data. *Methods of Information in Medicine*. 2016;55(6):533-544.
- AHUMADA L.A.C., GONZÁLEZ M.X.R., SANDOVAL O.L.H., OLMEDO J.J. S. Evaluation of hyaluronic acid dilutions at different concentrations using a quartz crystal resonator (QCR) for the potential diagnosis of arthritic diseases. *Sensors (Switzerland)*. 2016;16(11).

## Highlights

- Highlights: Core partner of the EIT-Health program; Collaboration in HBP (Human Brain Project); Early biomarker MEG-based for cognitive decline in the early stages of dementia, multicenter study (MAGIC)
- Patents: 4 in 2016
- Start-ups: Nauta Tecnomedical Research.s.l. and Brain Investigation.s.l.
- Research outcomes: Cognitive functions and neurophysiological phenomena in normal subjects and in patients with different neurological or psychiatric disorders. Design of medical devices: development of new sensors and nanoparticles-based instruments. Optics, Photonics and Biophotonics (UPM): develop label-free optical in-vitro diagnostic systems. Technologies for Healthy Ageing: comprehensive frailty and functional decline assessment, and cognitive decline biomarkers to phenotype the effects of ageing on brain functional networks. Understanding the structural and functional organization of biological systems using nonlinear dynamics and network science. Cell therapy based on biomaterials, pharmacologic approaches to treat stroke and Alzheimer's diseases. Therapeutic applications and clinical trials of low intensity and frequency electromagnetic fields, applied to fibromyalgia, chronic fatigue, muscle injury. New biomaterials, mainly based on silk fibroin or collagen, for applications in tissue engineering. Data Mining and Simulation of medical information to extract knowledge. Diabetes Technologies development: artificial pancreas, telemedicine platforms, and algorithms for physical activity in diabetes. Surgical Simulation: Planning and Image Guided Surgery, Technology for minimally invasive surgery. Neurorehabilitation services and modeling, modeling and intelligent adaptation of upper-limb neurorehabilitation therapies, knowledge management and data mining applied to neurorehabilitation, analysis and classification of structural alterations resulting from an acquired brain injury based on medical imaging.
- Education: Flagship (E-Labs) BIOTEL Lab - Biomedical technology Entrepreneurship and Innovation Lab. Digital learning: MOOCs for careers to manage the functional loss. MOOC to promote/ health literacy and lifestyle changes in elderly citizens/patients.
- International Conferences organisation: FRAILTY. A societal challenge in need of integrated solutions, 27-28 Oct 2016. Madrid. II Symposium on Magnetoencephalography: From Research to Clinical applications. Madrid.



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PROGRAMMES

**Biomaterials & Advanced Therapies**

GROUP MEMBERS

**Staff members:** Ferrer Lorente, Raquel

**Associated members:** Bedford Gaus, Sylvia | Pulecio Rojas, Julián Andrés

## Main lines of research

- Acquisition and maintenance of pluripotency.
- Mechanisms controlling cartilage, osteogenic and cardiac cells, retinal pigmented epithelial cells and haematopoietic cells.
- Mechanisms controlling heart muscle cell differentiation.
- Mechanisms controlling organ regeneration in vertebrates.



## Most relevant scientific articles

- PRIETO J., LEÓN M., PONSODA X., SENDRA R., BORT R., FERRER-LORENTE R. ET AL. Early ERK1/2 activation promotes DRP1-dependent mitochondrial fission necessary for cell reprogramming. *Nature Communications*. 2016;7.
- TEKELI I., AUJARD I., TREPAT X., JULLIEN L., RAYA A., ZALVIDEA D. Long-term in vivo single-cell lineage tracing of deep structures using three-photon activation. *Light: Science and Applications*. 2016;5(6).
- CAPELLERA-GARCÍA S., PULECIO J., DHULIPALA K., SIVA K., RAYON-ESTRADA V., SINGBRANT S. ET AL. Defining the Minimal Factors Required for Erythropoiesis through Direct Lineage Conversion. *Cell Reports*. 2016;15(11):2550-2562.
- VASSENA R., HEINDRYCKX B., PECO R., PENNINGG G., RAYA A., SERMON K. ET AL. Genome engineering through CRISPR/Cas9 technology in the human germline and pluripotent stem cells. *Human Reproduction Update*. 2016;22(4):411-419.
- PULECIO J., ALEJO-VALLE O., CAPELLERA-GARCÍA S., VITALONI M., RIO P., MEJÍA-RAMÍREZ E. ET AL. Direct Conversion of Fibroblasts to Megakaryocyte Progenitors. *Cell Reports*. 2016;17(3):671-683.

## Highlights

During 2016, the group Centre of Regenerative Medicine in Barcelona has focused its research activities on the development of biomedical applications of cell reprogramming. These activities have pursued the design of strategies of regenerative medicine in the context of cardiac disease, with the ultimate goal of generating tissue engineering constructs useful for treating end-stage heart failure.

The collaborative and ambitious Integrated Project of Excellence (PIE1400061) coordinated by our group, which comprises a consortium of 12 research groups members of 4 different CIBER, has allowed to develop the model of neuronal dysfunction in Lafora disease based on patient-specific induced pluripotent stem cells and to progress in the search for molecular links between diabetes and neurodegenerative disorders.

During this year, among the most relevant milestones of our group, it is worth to highlight our study regarding the possibility to convert skin cells into megakaryocytes able to produce platelets. An achievement with a great impact on the media.

The intense activity in the group work areas is reflected in numerous publications in indexed high impact journals, 3 PhD theses defended and new funds obtained from the competitive calls:

- 20153430. Investigating genetic and mechanistic interactors in Familial Cardiomyopathy through advanced disease (FUNDACIÓ LA MARATÓ DE TV3).
- COMRD15-1-0013. Teràpies Avançades a Catalunya. ADVANCECAT. Comunitat NEXTHEALTH, BIOCAT (BIOCAT, FEDER, GENCAT).
- RD12/0019/0019. RETICS- Red de Terapia Celular (ISCI, FEDER).
- SAF2015-71863-REDT. Estudio de las interacciones genéticas y mecanísticas en la miocardiopatía familiar mediante modelaje avanzado de la enfermedad (MINECO).
- SAF2015-69706-R. Diseño de estrategias para controlar la proliferación, diferenciación y maduración de cardiomiocitos humano (MINECO, FEDER).

In addition, in 2016 our group has started 2 intramural projects, in one of them as coordinator.



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PROGRAMMES  
**Nanomedicine**



#### GROUP MEMBERS

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**Contributors:** Alemany, Anna | Camuñas Soler, Joan | Mañosas Castejón, María | Ribezzi Crivellari, Marco

## Main lines of research

The research group led by Dr. Ritort investigates the energetic of biological processes at the molecular level in the broadest sense, from the fundamental understanding of irreversible phenomena at the microscopic scale to the most advanced applications that can characterize and measure molecular interactions with a resolution of tenths of kilocalories per mole (kcal/mol). All this is done through a multidisciplinary approach combining single molecule experiments and biochemical measures of phenomenological theories used in the field of biophysics, as well as fundamental principles of statistical physics applied to physicochemical systems out of equilibrium.

Characterized the broad perspective our research gives a wide range of applications ranging from the study of the binding of a peptide to protein, aggregation kinetics of complexes formed by drugs that bind to nucleic acids and the study of interactions antigen-antibody.

Our group is internationally recognized for having made fundamental advances in the understanding and characterization of the energetic of folding and assembly of nucleic acids, characterization of molecular motors that regulate DNA replication and fundamental theories describing the behavior of disordered systems out of equilibrium. Over the coming years, we will continue working on these lines of research that have proved so profitable. However, the overture to begin a new line related to the fundamental problem

of molecular evolution in order to better understand the physical principles that describe the increasing complexity and diversification of mutant molecular populations. The objectives set by the group are listed below:

- Determination of the thermodynamics of nucleic acids to high resolution.
- Dynamic force spectroscopy and molecular imprinting methods.
- Thermodynamics of small systems and systems out of equilibrium.
- Molecular Motors.
- Experiments of molecular evolution and recognition with single molecule techniques.

## Most relevant scientific articles

- DIETERICH E., CAMUNAS-SOLER J., RIBEZZI-CRIVELLARI M., SEIFERT U., RITORT F. Control of force through feedback in small driven systems. *Physical Review E - Statistical, Nonlinear, and Soft Matter Physics*. 2016;94(1).
- CAMUNAS-SOLER J., RIBEZZI-CRIVELLARI M., RITORT F. Elastic Properties of Nucleic Acids by Single-Molecule Force Spectroscopy. *Annual Review of Biophysics*. 2016;45:65-84.
- HODEIB S., RAJ S., MANOSAS M., ZHANG W., BAGCHI D., DUCOS B. ET AL. Single molecule studies of helicases with magnetic tweezers. *Methods*. 2016;105:3-15.

## Highlights

We have started a new European project (H2020-FETOPEN-2014-2015-RIA): Protein sequencing using optical single molecule real-time detection (PROSEQO).

We have obtained a project in the 2016 call for R & D Projects of the State Program for the Promotion of Scientific and Technical Research of Excellencies of MINECO. The project is called Investigations of Intermolecular Interactions in Nucleic Acids, Proteins and Drugs by Single Molecule Assays (FIS2016-80458-P).

We have opened a new technology transfer line where we construct optical tweezer instrumentation for research groups from public and private institutions that are interested in opening lines of molecular or cellular characterization with single cell or molecule manipulation techniques. In September 2016, we signed a contract with the University of Padova (Italy) for the construction of one of these instruments. We have made a qualitative leap in the expansion of our experimental capabilities at the single cell level. On the one hand, we can measure the rheological properties of the cell membrane (passive microrheology). The results obtained were the starting point for a collaboration with the group Nanobioengineering (intramural project SPLEEN-RA). On the other hand, we can measure the deformation of red blood cells at real time by applying controlled forces, which opens the door to study, not only the rheological properties of the membrane, but also the interaction of the cytoskeleton with the membrane. In addition, in 2016 we took the first steps to use our optical tweezers device in cells attached to a substrate in order to mimic the in vivo situation of such cells.

We have applied the single molecule footprinting technique developed in 2015 for the study of interaction of small molecules with DNA (Netropsin and dendrimers). The results obtained allowed us to start a collaboration with the group Dendrimer Group for Biomedical Applications (intramural project SINDERNA).



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PROGRAMMES

**Bioengineering & Medical Imaging**



### GROUP MEMBERS

**Staff members:** Naranjo Hernández, David

**Associated members:** Gómez Cía, Tomás | Reina Tosina, Luis Javier | Román Martínez, Isabel | Salgueira Lazo, Mercedes

**Contributors:** Barbarov Rostan, Gerardo Andrés | Callejón Leblic, María Amparo | Calvillo Arbizu, Jorge

## Main lines of research

- **Multiscale computational modeling for multimodal diagnosis:** methods and technologies for the detection of biological and pathological events and to provide a quantitative understanding of the relationships between elements of complex biological systems through the integration of personalized knowledge in multiple scales: from genomic and proteomic level to whole body level.
- **Integration Architectures for health and social services:** integration architectures for heterogeneous and distributed health services that allow the access, knowledge generation and management of personalized medical care delivery. Integration architectures for the provision of standard-based health and social services. Intermediation software technologies (middleware) to support service architectures for generating new medical/clinical knowledge in real-time.
- **Smart devices for ambient assisted living:** development of methods and techniques for designing and validating assisted living environments through distributed intelligent devices. Application to the elderly and chronic pathologies. Development of methodologies and techniques for the design and validation of wearable systems based on the concepts of design-for-all and design space for citizens with special needs.



- **Methods and techniques of electromagnetism applied to medical nanotechnology:** modeling and characterization of the interactions of electromagnetic fields with biological tissues at different levels, and their applications; design of intelligent devices for therapy/diagnosis at micro-/nano level, and communications.

## Most relevant scientific articles

- TALAMINOS A., LÓPEZ-CERERO L., CALVILLO J., PASCUAL A., ROA L.M., RODRÍGUEZ-BANO J. Modelling the epidemiology of Escherichia coli ST131 and the impact of interventions on the community and healthcare centres. *Epidemiology and Infection*. 2016;1-9.
- TALAMINOS-BARROSO A., ESTUDILLO-VALDERRAMA M.A., ROA L.M., REINA-TOSINA J., ORTEGA-RUIZ F.. A Machine-to-Machine protocol benchmark for eHealth applications - Use case: Respiratory rehabilitation. *Computer Methods and Programs in Biomedicine*. 2016;129:1-11.

## Highlights

### INDUSTRIAL TRANSFER

international extension patent “Intelligent bioimpedance sensor for biomedical applications”. National patent application: “Intelligent platform for the monitorization of body composition and assessment of the nutritional and hydration state of the user”. Press notes concerning patent P200201710 (fall detection) have been covered by 30+ newspapers and a tv report by Telemadrid. Contact with diverse social/health institutions (Sanitas Mayores, Atenzia). A collaboration agreement has been signed with Fundación ATAM for the validation of the prototype in groups of persons with different impairments. Participation in the international advisory board of project EPSILON (ATAM).

### CLINICAL TRANSFER

research and development of a prototype of smart shirt applied to the rehabilitation in COPD, in collaboration with the Unit of Respiratory Diseases (HUVR), within grant PI15/00306. Expression of interest of Prof. Félix del Campo (Hospital Río Hortega) to adapt the smart shirt to the monitorization of sleep apnea. Grant application to the Research Program at US for its implementation (approved), together with other grants for patent development. Ongoing validation for E-Nefro platform (grant DTS15/00195) in five hospitals. Given the number of patients under the program, it was necessary to extend the number of research nephrologists. Start of collaboration with Dr. Pablo Mir (IBIS) for the application of IBC techniques to neuromodulation (NeuroIBC intramural project). Ongoing collaboration with Drs. Álvaro Pascual and Jesús Rodríguez-Baño (HUVM), leading to a paper published in an international journal and another in review process.

### DIFFUSION

Invited keynote lecture, Foro de los Consejos Sociales de las Universidades de Andalucía” (UCO). Other invited lectures: “Feminismo, masculinidades e ingeniería” (UCO), “Ingeniería y Accesibilidad” (Real Academia de Ingeniería).

### EDUCATION

PhD Thesis Dissertation of Dr. Amparo Callejón (with honors). Supervision of 4 end-of-degree thesis and 5 BSc thesis.

### AWARDS

Prof. Laura M. Roa has been recipient of the “Premio Fama de la US a la trayectoria investigadora en el área de Ingeniería y Arquitectura”.



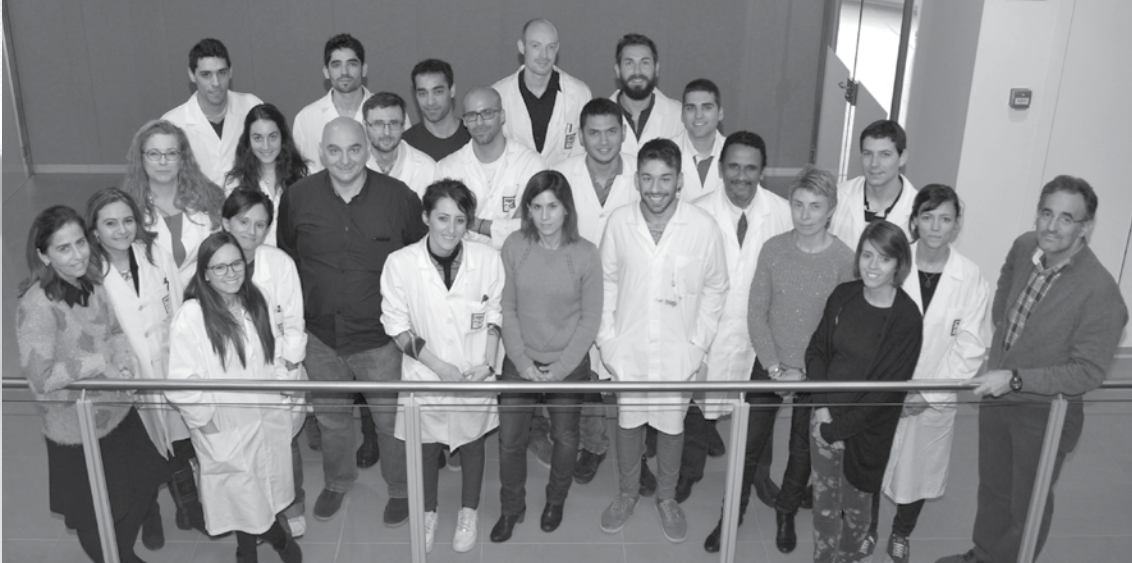
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PROGRAMMES

**Biomaterials & Advanced Therapies**



## GROUP MEMBERS

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**Contributors:** Fernández Colino, Alicia | García Lera, Rocío | Misbah Elzehiri, Mohamed Hamed | Pinedo Martín, Guillermo | Piña Lancho, María Jesús

## Main lines of research

- New “smart” materials.
- Hydrogels for tissue bioengineering.
- Injectable self-gelling and bioactive systems for biomedical applications.
- Bioactive and micro-patterned surfaces.
- Thermosensitive and bioactive surfaces for cell harvesting devices.
- Nanofibers for tissue engineering application.
- Nanocarriers for “targeted drug delivery”.
- Nanoparticles for the development of inhalable vaccines.

## Most relevant scientific articles

- RODRÍGUEZ-CABELLO J.C., ARIAS F.J., RODRIGO M.A., GIROTTI A. Elastin-like polypeptides in drug delivery. *Advanced Drug Delivery Reviews*. 2016.
- VILA M., GARCÍA A., GIROTTI A., ALONSO M., RODRÍGUEZ-CABELLO J.C., GONZÁLEZ-VÁZQUEZ A. ET AL. 3D silicon doped hydroxyapatite scaffolds decorated with Elastin-like Recombinamers for bone regenerative medicine. *Acta Biomaterialia*. 2016;45:349-356.
- PINA M.J., GIROTTI A., SANTOS M., RODRÍGUEZ-CABELLO J.C., ARIAS F.J. Biocompatible ELR-Based Polyplexes Coated with MUC1 Specific Aptamers and Targeted for Breast Cancer Gene Therapy. *Molecular Pharmaceutics*. 2016;13(3):795-808.
- PUTZU M., CAUSA F., NELE V., DE TORRE I.G., RODRÍGUEZ-CABELLO J.C., NETTI P.A. Elastin-like-recombinamers multilayered nanofibrous scaffolds for cardiovascular applications. *Biofabrication*. 2016;8(4).
- SINGH S., DEMCO D.E., RAHIMI K., FECHETE R., RODRÍGUEZ-CABELLO J.C., MOLLER M. Coacervation of Elastin-Like Recombinamer Microgels. *Macromolecular Rapid Communications*. 2016.

## Highlights

In 2016 BIOFORGE's funding came from 13 research projects and 2 networks with different funding sources. As for the Projects, BIOFORGE participated in 5 European projects funded by the European Commission (FP7-Health-2011, FP7-ITN-2012, H2020-ITN-2014 and H2020-NMP-2014) and ERA-NET (ERA-IB); 5 national projects funded by the Spanish Ministry of Economy and Competitiveness belonging to the Programme Societal Challenges; and 3 regional projects funded by the Ministry of Education of the Regional Government of Castilla y León. As far as the Networks is concerned, BIOFORGE took part in 2 Biomaterial Networks funded by the Carlos III Health Institute (CIBER-BBN and Regenerative Medicine and Cell Therapy Network of Castilla y León).

In this period, 10 articles were published in international journals, 9 of them in indexed high impact journals. Furthermore, the European Patent A temperature-sensitive bioactive biopolymer and associated cell-harvesting method (12796308.0) was requested in June 2016 and it was validated in Spain in December 2016.

The group members attended many scientific meetings giving around 18 oral presentations and 3 invited plenary talks.

Three PhD thesis with European mention were presented by the researchers Alicia Fernández Colino, Mohamed Hamed Misbah and María Jesús Piña Lancho. The three of them received the highest qualification.

The training activities of the group included invited conferences and contributing to four master programs of the University of Valladolid. Moreover, BIOFORGE organized the Workshop "Biomimetic Hydrogels", in the framework of the Marie Curie Network BIOGEL (H2020-ITN-2014), to which 16 students from 13 European institutions attended.





LEAD RESEARCHER

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PROGRAMMES

**Biomaterials & Advanced Therapies**

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## Main lines of research

- Development of cell therapy and tissue engineering strategies for cartilage repair.
- Ex vivo models of cartilage defect for the evaluation of cartilage regeneration.
- Proteomic, genomic and histomorphologic studies of the chondrogenic differentiation of mesenchymal stem cells derived from different sources.
- Characterization of proteins and peptides as biomarkers of the cartilaginous tissue that could ultimately be used in the monitoring of cell therapy strategies for articular cartilage defects.



## Most relevant scientific articles

- FERNÁNDEZ-PERNAS P., FAFIAN-LABORA J., LESENDE-RODRÍGUEZ I., MATEOS J., DE LA FUENTE A., FUENTES I. ET AL. 3, 3', 5-triiodo-L-thyronine Increases In Vitro Chondrogenesis of Mesenchymal Stem Cells from Human Umbilical Cord Stroma Through SRC2. *Journal of Cellular Biochemistry*. 2016.
- ROCHA B., CALAMIA V., BLANCO F.J., RUIZ-ROMERO C. Identification of factors produced and secreted by mesenchymal stromal cells with the SILAC method. *Methods in Molecular Biology*. 2016;1416:551-565.
- ROCHA B., CILLERO-PASTOR B., BLANCO F.J., RUIZ-ROMERO C.. MALDI mass spectrometry imaging in rheumatic diseases. *Biochimica et Biophysica Acta - Proteins and Proteomics*. 2016.
- LAGUNAS A., TSINTZOU I., VIDA Y., COLLADO D., PÉREZ-INESTROSA E., PEREIRA C.R. ET AL. Tailoring RGD local surface density at the nanoscale toward adult stem cell chondrogenic commitment. *Nano Research*. 2016;1-13.
- BURGUERA E.F., MEIJIDE-FAILDE R., BLANCO F.J. Hydrogen sulfide and inflammatory joint diseases. *Current Drug Targets*. 2016;17(16).

## Highlights

In 2016, GBTTC-CHUAC has initiated the project “Applied public-private research enabling osteoarthritis clinical headway” (APPROACH) financed by IMI, until 2020. The APPROACH consortium brings together a highly qualified and multidisciplinary group of stakeholders that will set up – for the first time – a broad database of different OA patients as well as a longitudinal cohort based on innovative stratification methods that identifies different osteoarthritis phenotypes. This will allow for the development of guidelines for differentially diagnosing the right patient for the right treatment.

Regarding Training, Dra. Clara Sanjurjo Rodríguez, has obtained her PhD with Sum Cum Laude distinction for her dissertation “Bone and Cartilage Tissue Engineering using MSC and biomaterials”. In 2016, Cristina Pereira Rodríguez, has been incorporated to the group with an i-PFIS contract and will continue with the research line “Study of chondrogenesis in RGD-dendrimer nanopatterned PLLA substrates” within the intramural project of excellence CHONDRONANONET.

As a result of the activity of the group in the role of hydrogen sulfide in osteoarthritis, Elena F. Burguera, Ángela Vela Anero, Rosa Meijide and Francisco J. Blanco have been distinguished with the following awards:

- Special Jury Prize, 2016 Innovative Spa Research Awards (European Spas Association, ESPA). Vichy, France.
- VIII International Award Marcial Campos for Thermal Research with the work “Anti-inflammatory, anti-oxidant and anti-catabolic properties of hydrogen sulfide in osteoarthritis”, Spain.

Finally, the activity of the group in the promotion of scientific culture and the visibility of women in science has received funding from FECYT for the project “Women Scientists in Biomedicine: a track and field career”. In addition, the project “Biomedicine with and for Society” has been distinguished as a “Inspiring Practice in the Promotion of Scientific Culture” 2015 by FECYT.



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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Funes Luque, Miriam | Izquierdo García, David | Pardo, Wilmer Alfonso

## Main lines of research

The scientific activity of NANOMED-IBEC group is focused in the application of nanotechnology and Bioengineering to the development of new diagnostic tools (point-of-care devices for diagnosis or for food safety applications) and to the development of organ-on-chip for in vitro studies.

To do that, the group is subdivided in three main research lines:

- **Biosensors and Lab-on-a-chip for clinical diagnosis and food safety applications:**
  - Development of DNA sensors for the detection of cancer biomarkers.
  - Development of antibody-based sensors for the detection of pathogen microorganisms.
  - Development of olfactory sensors based on G-protein coupled receptors for the detection of volatiles.
  - Development of ion-selective electrodes (ISE) for nutrient analysis.
  - Development of sensors based on conducting polymers.
  - Development of microfluidic platforms for simple handling and detection.
  - Development of microfluidic platforms for bacteria counting and sorting.
- **Materials for the study of cellular response:**
  - Design, production and characterization of micro/nanoenvironments made of different biocompatible materials for the study of cell proliferation, migration and differentiation. In particular, study of the

effects of extracellular matrix. Which include:

- Effects of nanoscale ligand distribution on cell adhesion and differentiation.
- Biophysics of migration and differentiation onto biological matrices.
- Study of interactions between magnetic nanoparticles and cells.

- **Microfluidic systems and organ-on-chip devices.**

- Development of a microfluidic system for blood/plasma filtering.
- Development of a spleen model on a chip (splenon-on-a-chip).
- Development of a microfluidic system for neurobiological studies.

## Most relevant scientific articles

- PARRA-CABRERA C., SAMITIER J., HOMS-CORBERA A. Multiple biomarkers biosensor with just-in-time functionalization: Application to prostate cancer detection. *Biosensors and Bioelectronics*. 2016;77:1192-1200.
- LAGUNAS A., TSINTZOU I., VIDA Y., COLLADO D., PÉREZ-INESTROSA E., PEREIRA C.R. ET AL. Tailoring RGD local surface density at the nanoscale toward adult stem cell chondrogenic commitment. *Nano Research*. 2016;1-13.
- EGUIZABAL C., HERRERA L., DE ONATE L., MONTSERRAT N., HAJKOVA P., IZPISUA BELMONTE J.C. Characterization of the Epigenetic Changes During Human Gonadal Primordial Germ Cells Reprogramming. *Stem Cells*. 2016.
- URRIOS A., PARRA-CABRERA C., BHATTACHARJEE N., GONZÁLEZ-SUAREZ A.M., RIGAT-BRUGAROLAS L.G., NALLAPATTI U. ET AL. 3D-printing of transparent bio-microfluidic devices in PEG-DA. *Lab on a Chip - Miniaturisation for Chemistry and Biology*. 2016;16(12):2287-2294.
- CABALLERO D., KATURI J., SAMITIER J., SÁNCHEZ S. Motion in microfluidic ratchets. *Lab on a Chip - Miniaturisation for Chemistry and Biology*. 2016;16(23):4477-4481.

## Highlights

- Project for real time hypoxia detection system in fetus, in collaboration with Hospital Sant Joan de Deu-Hospital Clinic.
- Collaboration with the company Genómica (mixed unit) to develop a point-of-care diagnostic system to detect papilloma virus.
- Euronanomed Project “Nanovax”





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PROGRAMMES

**Biomaterials & Advanced Therapies**



## GROUP MEMBERS

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**Contributors:** Palao Suay, Raquel | Parra Ruiz, Francisco Jesús

## Main lines of research

- **Preparation of selfcuring polymeric systems for surgery.** The line is centered in the development of selfcuring polymer systems of low toxicity, high biocompatibility for application for the biomechanical stabilization of prosthesis and as controlled delivery systems of bioactive compounds (antibiotics, bactericide, anti-inflammatory agents, antithromobgenic).
- **Polymer Drugs and targeting systems.** Preparation of bioactive polymer systems with targeting properties for the application and release of wellknown bioactive compounds with anti-inflammatory action, antithrombogenic, antiproliferative, antioxidant. This is one of the main lines of the group, with cooperation with companies of the biomedical and pharmaceutical fields. Bioactive polymer systems have been designed for bioactive coatings of drug eluted stents DES for coronary treatment, bioactive abdominal meshes with antibiotic action at local level (targeting), intraocular lenses with controlled proliferative action and antiangiogenic actions, polymer drugs with low toxic action for cancer therapy.
- **Biodegradable polymer systems for surgery and pharmacy.** Design and development of resorbable polymer systems as porous scaffolds of great interest in processes of tissue regeneration (Tissue



Engineering). The polymer systems offer wide spectra of formulations with hydrophobic or hydrophilic character, which allows the preparation of 3D scaffolds to be applied in regeneration of bone tissue, epidermal or connective tissues, with specific properties. Several patents have been registered and are on transfer processes to several companies of the biomedical device sector.

- **Application of supercritical technologies for the preparation of porous systems.** Based on the application of carbonic anhydride in supercritical conditions for the preparation of clean bioactive polymer systems and composites for different applications. The technology allows the development of systems for Tissue Engineering and drug delivery systems. Also, the preparation of systems with bioactive compounds sensitive to the pH or temperature are considered in this section.

## Most relevant scientific articles

- PALAO-SUAY R., AGUILAR M.R., PARRA-RUIZ F.J., MAJI S., HOOGENBOOM R., ROHNER N.A. ET AL.  $\alpha$ -TOS-based RAFT block copolymers and their NPs for the treatment of cancer. *Polymer Chemistry*. 2016;7(4):838-850.
- PALAO-SUAY R., GÓMEZ-MASCARAQUE L.G., AGUILAR M.R., VÁZQUEZ-LASA B., ROMÁN J.S. Self-assembling polymer systems for advanced treatment of cancer and inflammation. *Progress in Polymer Science*. 2016;53:207-248.
- MARTÍN-SALDANA S., PALAO-SUAY R., TRINIDAD A., AGUILAR M.R., RAMÍREZ-CAMACHO R., SAN ROMÁN J. Otoprotective properties of 6 $\alpha$ -methylprednisolone-loaded nanoparticles against cisplatin: In vitro and in vivo correlation. *Nanomedicine: Nanotechnology, Biology, and Medicine*. 2016;12(4):965-976.
- MARTÍN-DEL-CAMPO M., ROSALES-IBÁÑEZ R., ALVARADO K., SAMPEDRO J.G., GARCÍA-SEPÚLVEDA C.A., DEB S. ET AL. Strontium folate loaded biohybrid scaffolds seeded with dental pulp stem cells induce: In vivo bone regeneration in critical sized defects. *Biomaterials Science*. 2016;4(11):1596-1604.
- FERNÁNDEZ-GUTIÉRREZ M., RODRÍGUEZ-MANCHENO M., PÉREZ-KOHLER B., PASCUAL G., BELLÓN J.M., ROMÁN J.S. Structural Analysis and Application of n-Alkyl Cyanoacrylate Surgical Adhesives to the Fixation of Meshes for Hernia Repair. *Macromolecular Bioscience*. 2016;16(12):1803-1814.


## Highlights

Respect to the development of systems and products, it is worth noting that the team has designed and fabricated biodegradable membranes to stimulate cartilage repair, project that has been developed in collaboration with the company BIOIBERICA and at moment, the company has to make the decision to present an international patent. Bioactive nanoparticles of low toxicity based on mitocans (agents with activity on mitochondria) have been developed with good results for cancer treatment. This system, fabricated by molecular design in physiological conditions, has been loaded with corticoids (methyl-prednisolone, dexamethasone) and applied to inhibit cis-platin effects associated to chemotherapy which produced deafness in the patient. The application of a nanoparticles suspension in the inner ear of animals gave excellent results to inhibit cis-platin locally. This system has attracted the attention of a pharmaceutical company that is interested in its application and commercialization. These projects allowed presenting 3 doctoral theses with maximum qualification in Spanish universities, and with contributions not only relevant in the academic field, but also with important implications of transfer as novel products and processes to the productive sector. One thesis was presented under confidentiality and the company concerned is adapting its production in Germany. Likewise, the nanoparticle system loaded with dexamethasone, developed in collaboration with the ORL team of Hospital Puerta de Hierro de Madrid, will be transferred shortly to the company Beacon Biomedicine by means of a transfer cooperation agreement with CIBER-BBN.



LEAD RESEARCHER

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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Carmona Rioja, Daniel | Encabo Berzosa, María del Mar | Giménez Mazas, Marta | Gómez Jiménez, Virginia | Gómez Navascués, Leyre | Hueso Martos, José Luis | Navascués García, Nuria | Pellejero Alcázar, Ismael | Urbiztondo Castro, Miguel Ángel | Usón Muñoz, Laura

## Main lines of research

- **Catalysis and catalytic reactors:** Synthesis of catalytic nanoparticle clusters (metallic, bimetallic, core/shell and metal oxides) as well as methods for their deposition on different substrates (carbon nanostructures, mesoporous silica, zeolites). The direct heating of the active centers by unconventional techniques (microwave heating by laser irradiation or by magnetic hyperthermia) is especially interesting for our group. This specific topic has received one of the prestigious ERC Advanced Grants.
- **Molecular recognition - sensors:** Design of nanostructured materials with specific interactions with specific molecules and micro-gas sensors for high sensitivity and selectivity.
- **Nanomedicine:** Research on the biomedical applications of nanomaterials in cancer therapies (optical hyperthermia), gene therapy (nanoparticles as transfection vectors) and bactericidal applications (reservoirs for antimicrobial agents). Applications are tested in collaboration with other groups in this field: Dr N. Villaboa (HULP, Madrid - gene therapy and cell scaffolds), Dr Carles Arus (UAB - Medical Imaging), Dr MA de Gregorio (UZ - combination therapies in oncology), Dr L. Luján (UZ - bactericidal applications in trauma). In this area, an ERC Advanced Grant has been recently awarded.
- **Nanocomposites:** Development of polymer based composites with different types of nanomaterials with mechanical reinforcement applications, bactericidal plastics, magnetic and barrier films.

- **Nanosafety:** Analysis of the impact of nanomaterials in workplaces through the development of novel sampling and identification techniques at different scale. Labeling methods are under research to identify the emission of nanoparticles in various common handling operations with nanomaterials, as well as nanosafety procedures. An European project of the EU FP7 (Nanovalid) is ongoing in this field.

In addition to these five specific research topics, the group continues working on the chemical synthesis of nanomaterials. The research combines the developments that have led to the preparation of bimetallic nanoparticles by novel routes on a wet basis, with new synthesis methods, including microreactors, laser pyrolysis and electrospinning. Both laser pyrolysis and microreactors as belonging to the group of enabling technologies, which allow new goals in reproducibility and scale-up production of nanomaterials. As for the electrospinning, this is a new infrastructure that allows the preparation of nanowires, formed by different materials.

## Most relevant scientific articles

- GRACIA J., ESCUIN M., MALLADA R., NAVASCUÉS N., SANTAMARÍA J. Nano-heaters: New insights on the outstanding deposition of dielectric energy on perovskite nanoparticles. *Nano Energy*. 2016;20:20-28.
- LUQUE-MICHEL E., LARREA A., LAHUERTA C., SEBASTIÁN V., IMBULUZQUETA E., ARRUEBO M. ET AL. A simple approach to obtain hybrid Au-loaded polymeric nanoparticles with a tunable metal load. *Nanoscale*. 2016;8(12):6495-6506.
- RAMÍREZ A., HUESO J.L., SUÁREZ H., MALLADA R., IBARRA A., IRUSTA S. ET AL. A Nanoarchitecture Based on Silver and Copper Oxide with an Exceptional Response in the Chlorine-Promoted Epoxidation of Ethylene. *Angewandte Chemie - International Edition*. 2016;55(37):11158-11161.
- XIE L., SHEN Y., FRANKE D., SEBASTIÁN V., BAWENDI M.G., JENSEN K.F. Characterization of Indium Phosphide Quantum Dot Growth Intermediates Using MALDI-TOF Mass Spectrometry. *Journal of the American Chemical Society*. 2016;138(41):13469-13472.
- SEBASTIÁN V., SMITH C.D., JENSEN K.F. Shape-controlled continuous synthesis of metal nanostructures. *Nanoscale*. 2016;8(14):7534-7543.

## Highlights

### RESEARCH PROJECTS:

- European Training Network for Continuous Sonication and Microwave Reactors. UE (European Training Networks). 01/10/2016-30/10/2018.
- REVALPET / Reciclaje y revalorización de botellas de leche en materiales innovadores. UE 01/10/2016-30/09/2019.
- CTQ2016-77147-R. Nuevas estrategias para la conversión de CO2 utilizando catalizadores bajo radiación electromagnética. MINECO. 30/12/2016 – 29/12/2019.
- CTQ2016-79419-R: Tecnologías avanzadas de adsorción, detección sers y catálisis para guerra química. MINECO. 30/12/2016-29/12/2019.

### RESEARH TRANSFER:

- Nuevas soluciones nanotecnológicas para proporcionar nuevas funcionalidades al agua de contacto en el proceso siderúrgico de laminación en caliente “nanowater” contrato privado con arcelormittal innovación, investigación e inversión, s.l. 01/03/2016-31/12/2016.
- Nanomateriales. Estudio de la exposición laboral por inhalación en las distintas etapas del ciclo de vida del nanomaterial. Instituto nacional de seguridad e higiene en el trabajo. 20/05/2016-02/202/2017 Pilar Lobera.
- Master services agreement. Zs Pharma inc. 25/07/2016-21/12/2016.

### PATENTS:

- Artal Lahoz, M.C, Lafuente Adiego, M, Martinez Solanas, E; Pellejero Alcázar, I; Pina Iritia, M.P.; Sanz Naval, J. “Household appliance component for a household appliance” BSH Electrodomésticos España. S.A. P201530848. Country: Spain. 16/06/2015.





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PROGRAMMES

**Bioengineering & Medical Imaging**



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**Contributors:** Castro González, Carlos | Esteban Sanz-Dranguet, Óscar | Fernández de Manuel, Laura | Jiménez Carretero, Daniel | Luengo Oroz, Miguel Ángel | Pastor Escudero, David | Wollny, Gert

## Main lines of research

- Multimodal diagnosis.
- Cardiovascular imaging.
- High resolution preclinical imaging.
- Microscopy image analysis for modeling embryo development.
- Software utilities for image-guided medical diagnosis and treatment.
- On-line mobile games for analyzing medical images through crowdsourcing.



## Most relevant scientific articles

- ESTEBAN O., ZOSSO D., DADUCCI A., BACH-CUADRA M., LEDESMA-CARBAYO M.J., THIRAN J.-P. ET AL. Surface-driven registration method for the structure-informed segmentation of diffusion MR images. *NeuroImage*. 2016;139:450-461.
- ESTEBAN O., CARUYER E., DADUCCI A., BACH-CUADRA M., LEDESMA-CARBAYO M.J., SANTOS A. Diffantom: Whole-brain diffusion MRI phantoms derived from real datasets of the human connectome project. *Frontiers in Neuroinformatics*. 2016;10(FEB).
- JIMÉNEZ-CARRETERO D., ESTEPAR R.S.J., CACIO M.D., LEDESMA-CARBAYO M.J. Automatic synthesis of anthropomorphic pulmonary ct phantoms. *PLoS ONE*. 2016;11(1).
- ROSSINI L., MARTÍNEZ-LEGAZPI P., VU V., FERNÁNDEZ-FRIERA L., PÉREZ DEL VILLAR C., RODRÍGUEZ-LÓPEZ S. ET AL. A clinical method for mapping and quantifying blood stasis in the left ventricle. *Journal of Biomechanics*. 2016.
- ZORRAQUINO C., BUGALHO R., ROLO M., SILVA J.C., VECKLANS V., SILVA R. ET AL. Asymmetric Data Acquisition System for an Endoscopic PET-US Detector. *IEEE Transactions on Nuclear Science*. 2016;63(1):213-221.

## Highlights

As part of the research line to develop new tools for the analysis of pulmonary images to extract relevant biomarkers for the clinical study of cardiopulmonary diseases, our group has collaborated with the Brigham and Women's Hospital (Boston MA, USA) in a project financed by the National Institutes of Health, Bethesda MD, USA (Award No. 4R01HL116473-04) through a research contract. In this work a new method for the separation of pulmonary arterial and venous trees in CT lung images has been proposed and translated to the clinical study of the impact of vascular remodeling in smokers.

The project TEAM-Leuko that aims to develop a fast and cheap non-invasive neutrophil test for lymphoma patients has started pilot clinical trials in Hospital La Paz (Madrid) and Massachusetts General Hospital (Boston MA, USA) with the financial support of Massachusetts Institute of Technology Deshpande Center for Technological Innovation (Cambridge MA, USA).

The mobile application Olymtrip has been recognized as one of the "Best Ideas in 2016" awarded by *Diario Médico*. It was developed in collaboration with Hospital Clínic (Barcelona) and ISGlobal to early detect infections and to collect data on the health status of the Spanish athletes during the Rio 2016 Olympic Games.

miCROWDscopy, a project to develop crowd-computing systems to allow citizens to collaborate through on-line video games on global health challenges like the diagnosis of malaria and tuberculosis, has received the European Foundations Award for Responsible Research & Innovation.



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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Cortijos Aragonés, Albert | López Martínez, Montserrat | Oliva Herrera, Mireia | Pozuelo Ruiz, Marta

## Main lines of research

- **Electrochemical STS of biomimetic membranes with redox systems.** Measuring the energy levels of a protein under a variety of experimental conditions (in the presence of illumination or certain cofactors and partner proteins) will provide new insights into the detailed electron transfer mechanisms.
- **Mechanical stability at the molecular level.** Nanomechanics of lipid bilayers and other biosystems. Understanding the effect of mechanical stress on biological membranes is of fundamental importance since cells are known to naturally perform their function under the effect of a complex combination of forces.
- **Development and application of light-activated nanoswitches to control the activity of protein complexes and cells.** We will develop new optical switches (like the light-gated glutamate receptor LiGluR) in order to study the processes involved in neurosecretion, exocytosis and endocytosis.
- **Vectorization of therapeutically active molecules.** We prepare and characterize therapeutic agent (drugs, peptides, proteins, genetic material...) release systems based on supramolecular conjugates which allow reaching the point of action in a directed and effective manner.

## Most relevant scientific articles

- ARAGONÉS A.C., HAWORTH N.L., DARWISH N., CIAMPI S., BLOOMFIELD N.J., WALLACE G.G. ET AL. Electrostatic catalysis of a Diels-Alder reaction. *Nature*. 2016;531(7592):88-91.
- ARAGONÉS A.C., ARAVENA D., CERDA J.I., ACIS-CASTILLO Z., LI H., REAL J.A. ET AL. Large Conductance Switching in a Single-Molecule Device through Room Temperature Spin-Dependent Transport. *Nano Letters*. 2016;16(1):218-226.
- ROVIRA X., TRAPERO A., PITTOLO S., ZUSSY C., FAUCHERRE A., JOPLING C. ET AL. OptoGluNAM4.1, a Photoswitchable Allosteric Antagonist for Real-Time Control of mGlu4 Receptor Activity. *Cell Chemical Biology*. 2016;23(8):929-934.
- GIANNOTTI M.I., ABASOLO I., OLIVA M., ANDRADE F., GARCÍA-ARANDA N., MELGAREJO M. ET AL. Highly Versatile Polyelectrolyte Complexes for Improving the Enzyme Replacement Therapy of Lysosomal Storage Disorders. *ACS Applied Materials and Interfaces*. 2016;8(39):25741-25752.
- IZQUIERDO-SERRA M., BAUTISTA-BARRUFET A., TRAPERO A., GARRIDO-CHARLES A., DÍAZ-TAHOES A., CAMARERO N. ET AL. Optical control of endogenous receptors and cellular excitability using targeted covalent photoswitches. *Nature Communications*. 2016;7.

## Highlights

In 2016, we have reported for the first time the electrostatic catalysis of a Diels–Alder reaction (<http://dx.doi.org/10.1038/nature16989>) and the large conductance switching of a single-molecule device (<http://dx.doi.org/10.1021/acs.nanolett.5b03571>).

In addition, we have extended the study of multiphoton excitation of azobenzene dyes that we pioneered two years ago (<http://dx.doi.org/10.1021/acs.joc.5b01402>). We have also discovered new light-regulated pharmacological ligands for important targets in pain (<http://dx.doi.org/10.1016/j.chembiol.2016.06.013>) and a breakthrough method to conjugate light-regulated ligands to their endogenous receptors, that we have applied as a strategy for vision restoration (<http://dx.doi.org/10.1038/ncomms12221>).

We have obtained competitive funding from two European projects, one as coordinators (ERA-Net Synthetic Biology) and the other as partners of the European FET Flagship Human Brain Project. We have also obtained 2 grants from MINECO and several competitive fellowships for the lab members.

We have also published, in collaboration with other CIBER-BBN groups, results that demonstrate that polyelectrolyte complexes are highly versatile and feasible drug delivery system for improving the enzyme replacement therapy in lysosomal storage disorders (<http://dx.doi.org/10.1021/acsami.6b08356>).

In the framework of the “nanomechanics of Biosystems” line, we have developed, within a network of excellent international collaborators, the combination of AFM and X-Ray techniques (including in situ AFM using a home-built sample holder for X-Ray experiments) to study lipid membranes in physiological environment (<http://doi.org/10.1107/S1600577515016318>), that will allow to investigate receptor independent interaction of small molecules with model membranes.

We are furthermore establishing a new, distinctive research direction on nanomechanical properties of redox proteins (<http://dx.doi.org/10.1021/acs.jpcc.5b06382>) and their relevance to leukemia (E-Leukemia and E-leukemia+ CIBER-BBN intramural projects and NanoET-Leukemia).



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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Andretta, Elena | Bazzocco, Sarah | García Aranda, Natalia | García Latorre, Laura

## Main lines of research

Our group develops research projects mainly focused on oncology and rare diseases.

These projects are conducted around three preferred work areas:

- **Area 1:** biomarkers and therapeutic targets from suitable experimental models, as molecular biomarkers, diagnostic providers in biosensors (nanodiagnosis) or for biofunctionalizing new nanomedicines and therapeutic targets for designing new more effective treatments or alternative therapeutic strategies (new nanomedicines).
- **Area 2:** experimental chemistry and applied nanotechnology, especially enhancing the study of polymeric nanomedicines, through simpler chemical synthesis designs and potential scalability, as well as new experimental genomic therapies (iRNA, artificial non-viral vectors, etc.) and the study of biomedical applications based on nanotechnology (biosensors) and new biomaterials.
- **Area 3:** Validation of targets and functional studies. This is essential for obtaining concept tests and preclinical studies of new biomarkers and targets, as well as of new nanomedicines including: biodistribution, toxicity, therapeutic activity, specificity, functional molecular studies, etc., in different in vitro and in vivo experimental models.



- **Technological Platform on Nanomedicine.**

The in vivo experimentation unit allows data to be obtained on the systemic behaviour of biomarkers (biodistribution, pharmacokinetics, pharmacodynamics, toxicity and therapeutic activity) using imaging techniques, combining invasive and non-invasive procedures.

This unit also enables nanomedicine-based therapies to be tested on conventional cell lines and primary cultures (loss and gain of function experiments and gene expression analysis, as well as studying control of expression at various levels: transcriptional [gene transfection, inducible systems], posttranscriptional [RNAi] and at the protein level [antagonists and antibody neutralization]).

## Most relevant scientific articles

- GIANNOTTI M.I., ABASOLO I., OLIVA M., ANDRADE F., GARCÍA-ARANDA N., MELGAREJO M. ET AL. Highly Versatile Polyelectrolyte Complexes for Improving the Enzyme Replacement Therapy of Lysosomal Storage Disorders. *ACS Applied Materials and Interfaces*. 2016;8(39):25741-25752.
- CABRERA I., ABASOLO I., CORCHERO J.L., ELIZONDO E., GIL P.R., MORENO E. ET AL.  $\alpha$ -Galactosidase-A Loaded-Nanoliposomes with Enhanced Enzymatic Activity and Intracellular Penetration. *Advanced Healthcare Materials*. 2016;5(7):829-840.
- GENER P., DE SOUSA RAFAEL D.F., FERNÁNDEZ Y., ORTEGA J.S., ARANGO D., ABASOLO I. ET AL. Cancer stem cells and personalized cancer nanomedicine. *Nanomedicine*. 2016;11(3):307-320.
- ANDRADE F., FONTE P., COSTA A., REIS C.C., NUNES R., ALMEIDA A. ET AL. Pharmacological and toxicological assessment of innovative self-Assembled polymeric micelles as powders for insulin pulmonary delivery. *Nanomedicine*. 2016;11(17):2305-2317.
- URIA N., ABRAMOVA N., BRATOV A., MUNOZ-PASCUAL F.-X., BALDRICH E. Miniaturized metal oxide pH sensors for bacteria detection. *Talanta*. 2016;147:364-369.

## Highlights

We have developed new biosensors able to detect bacteria for biomedical applications from biological fluids by using miniaturized metal oxide base pH sensors. Further, we have also developed a new biological based system that allows in vitro/in vivo tracking of cancer stem cells. This system is based on bioluminescent specific genetic vectors and is being used to develop new targeted drug delivery systems (DDS) as anticancer agents. A new DDS has been tested to improve sensitivity of cancer stem cells to chemotherapy with success. Finally, we together with other CIBER's groups have also advance a specific DDS for enzyme replacement therapy for Fabry disease in cooperation with industrial partners. A GMP production pilot line is ongoing.



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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Homs, María

## Main lines of research

- Study of surfactant self-assembly processes in multicomponent systems and structural characterization of the self-assemblies.
- Study of nano-emulsion formation by condensation (low-energy) emulsification methods.
- Design and fabrication of advanced nanomaterials (nanoparticles, solid foams) using surfactant self-assemblies and colloidal dispersions as structure directing agents (templates).
- Development of multifunctional nanocarriers as delivery systems by nano-emulsion and microemulsion templating.
- Study of drug release from nanostructured carriers.
- Development of organic and inorganic materials with dual meso/macroporous structure for biomedical applications.
- Development of stimulus-responsive biocompatible hydrogels.
- Surface modification of polymeric materials, textile fibers and nanostructured materials.

## Most relevant scientific articles

- MAGANA J.R., HOMS M., SOLANS C., OBIOLS-RABASA M., SALONEN L.M., RODRÍGUEZ-ABREU C. Self-Assembly and Formation of Chromonic Liquid Crystals from the Dyes Quinaldine Red Acetate and Pyronin y. *Journal of Physical Chemistry B*. 2016;120(1):250-258.
- FORNAGUERA C., CALDERO G., SOLANS C. Electrolytes as a tuning parameter to control nano-emulsion and nanoparticle size. *RSC Advances*. 2016;6(63):58203-58211.
- MAGANA J.R., KOLEN'KO Y.V., DEEPAK F.L., SOLANS C., SHRESTHA R.G., HILL J.P. ET AL. From Chromonic Self-Assembly to Hollow Carbon Nanofibers: Efficient Materials in Supercapacitor and Vapor-Sensing Applications. *ACS Applied Materials and Interfaces*. 2016;8(45):31231-31238.
- FORNAGUERA C., FEINER-GRACIA N., CALDERO G., GARCÍA-CELMA M.J., SOLANS C. PLGA nanoparticles from nano-emulsion templating as imaging agents: Versatile technology to obtain nanoparticles loaded with fluorescent dyes. *Colloids and Surfaces B: Biointerfaces*. 2016;147:201-209.
- CALDERO G., MONTES R., LLINAS M., GARCÍA-CELMA M.J., PORRAS M., SOLANS C. Studies on the formation of polymeric nano-emulsions obtained via low-energy emulsification and their use as templates for drug delivery nanoparticle dispersions. *Colloids and Surfaces B: Biointerfaces*. 2016;145:922-931.

## Highlights


The research activities have been developed mainly in the frame of the intramural Project “Novel nanocarriers as delivery systems across the Blood-Brain barrier” (Nano3B) which objective is the design of new multifunctional polymeric nanoparticles targeting the blood-brain barrier (BBB) for the combined therapy of a neurodegenerative disease, X-linked adrenoleukodystrophy (X-ALD). PLGA nanoparticles with tunable characteristics, sizes below 100nm, high kinetic stability, encapsulating specific drugs have been prepared using non-toxic materials and low-energy methods. The nanoparticles have been functionalized with monoclonal antibodies and peptides specific to cross the BBB. The determination of drug concentration in tissues of murine models after treatment with the nanoparticles has shown that they are appropriate for the intended application. In addition, the group has developed research in the frame of two intramural projects started in 2016: “Novel functionalized contact lenses with anti-infective properties for the prevention of keratitis” (Funciolenses) y “Non-invasive blood-brain barrier opening by focused ultrasounds for the selective delivery of therapeutic nanocarriers against glioma” (Glio-Select). Moreover, the group has carried research in the frame of two I+D+I Spanish-funded projects “Design and applications of novel biocompatible micro/nanogels obtained by advanced condensation methods” (CTQ2014-52687-C3-1-P y “Strategies for preparation and stabilization of water-in-water emulsions for innovative pharmaceutical and food applications” CTQ2016-80645-R) and one funded by the EU “Biopolymer-Based Food Delivery Systems” (Bibafoods). The most important outcomes of the results obtained are reflected in 14 indexed publications and 2 book chapters, as well as in the presentation of 10 oral (1 Plenary Lecture and 1 Invited Lecture) communications and 9 poster presentations in national and international conferences. 3 PhD thesis and 2 Master theses have been presented. Other activities include the organization of FORMULA VIII Conference (Barcelona July 4-7, 2016) and the edition of an issue of “Current Opinion in Colloid and Interface Science” on Emulsions and Microemulsions.




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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- **Making cellular forces visible**

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

- **Cellular guidance by mechanical cues**

Directed cell migration is one of the earliest observations in cell biology, dating back to the late XIX century. Also known as taxis, directed cell migration has been commonly associated with chemotaxis, i.e. the ability of a broad variety of cell types to migrate following gradients of chemical factors. We recently demonstrated a new mode of collective cell guidance by mechanical cues, called collective durotaxis. This new migration mode emerges only in cell collectives and, strikingly, does not require isolated cells to exhibit gradient sensing.

- **Microfabrication and wound healing**

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

- **Fracking epithelial layers**

Epithelial sheets must be malleable enough to adopt functional shapes during morphogenesis and to quickly self-repair after damage. Yet, they must be resilient enough to ensure organ compartmentalization and to protect organisms against environmental pathogens. To study the



mechanisms that regulate this fine balance between malleability and integrity we develop tools to map epithelial tension during tissue stretching. By combining these tools with computational modeling, we determined the mechanisms of epithelial fracture. Intriguingly, one of such mechanisms is hydraulic fracturing or “fracking”.

## Most relevant scientific articles

- SUNYER R., CONTE V., ESCRIBANO J., ELOSEGUI-ARTOLA A., LABERNADIE A., VALON L. ET AL. Collective cell durotaxis emerges from long-range intercellular force transmission. *Science*. 2016;353(6304):1157-1161.
- LADOUX B., MEGE R.-M., TREPAT X. Front-Rear Polarization by Mechanical Cues: From Single Cells to Tissues. *Trends in Cell Biology*. 2016;26(6):420-433.
- ELOSEGUI-ARTOLA A., ORIA R., CHEN Y., KOSMALSKA A., PÉREZ-GONZÁLEZ C., CASTRO N. ET AL. Mechanical regulation of a molecular clutch defines force transmission and transduction in response to matrix rigidity. *Nature Cell Biology*. 2016;18(5):540-548.
- TEKELI I., AUJARD I., TREPAT X., JULLIEN L., RAYA A., ZALVIDEA D. Long-term in vivo single-cell lineage tracing of deep structures using three-photon activation. *Light: Science and Applications*. 2016;5(6).
- PLUTONI C., BAZELLIERES E., LE BORGNE-ROCHET M., COMUNALE F., BRUGUES A., SEVENO M. ET AL. P-cadherin promotes collective cell migration via a Cdc42-mediated increase in mechanical forces. *Journal of Cell Biology*. 2016;212(2):199-217.

## Highlights

### Funding

- TENSIONCONTROL: Multiscale regulation of epithelial tension (2015-2019). IP: Xavier Trepap, European Research Council - CoG.
- MICROGRADIENTPAGE: Micro Gradient Polyacrylamide Gels for High Throughput Electrophoresis Analysis (2014-2015). IP: Xavier Trepap, European Research Council - PoC.
- CAMVAS: Coordination and migration of cells during 3D Vasculogenesis (2014-2017). IP: Xavier Trepap, MARIE CURIE - IOF.
- ADHESIONFORCE: The mechanome of epithelial adhesion: unveiling the mechanisms of intercellular force detection, resistance, and transmission (2013-2015). IP: Xavier Trepap, MINECO.
- CAFFORCE: Physical forces driving fibroblast-led cancer cell migration (2014-2015). IP: Xavier Trepap, Marie Curie Intra-European Fellowships.
- Mechanics of Monolayer Migration (2011-2016). Co-Investigator: Xavier Trepap (PI: Jeffrey Fredberg, Harvard School of Public Health), National Institutes of Health, USA.
- Grup de recerca consolidat (2014-2016), IP: Xavier Trepap, Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Convocatòria d'ajuts per donar suport a les activitats dels grups de recerca de Catalunya.

### Scientific equipment and techniques

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

### Collaborations

- Julien Colombelli / Eduard Batlle Institute for Research in Biomedicine (IRB) Barcelona.
- Marino Arroyo Universitat Politècnica de Catalunya, Barcelona.
- Guillaume Charras / Roberto Mayor University College London, UK.
- Erik Sahai Cancer Research, UK.
- Benoit Ladoux Université Paris 7, France.
- Jim Butler / Jeff Fredberg Harvard University, Boston.



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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- Multifunctional nanoparticles for cancer, osteoporosis and infection therapy.
- Advanced bioceramics for bone tissue regeneration.
- Bacterial Anti-adherent biomaterials.
- Smart Biomaterials stimulus-response.

## Most relevant scientific articles

- DÍEZ-MARTÍNEZ R., GARCÍA-FERNÁNDEZ E., MANZANO M., MARTÍNEZ A., DOMENECH M., VALLET-REGÍ M. ET AL. Auranofin-loaded nanoparticles as a new therapeutic tool to fight streptococcal infections. *Scientific Reports*. 2016;6.
- IZQUIERDO-BARBA I., COLILLA M., VALLET-REGÍ M. Zwitterionic ceramics for biomedical applications. *Acta Biomaterialia*. 2016.
- RODRÍGUEZ-PALOMO A., MONOPOLI D., AFONSO H., IZQUIERDO-BARBA I., VALLET-REGÍ M. Surface zwitterionization of customized 3D Ti6Al4V scaffolds: A promising alternative to eradicate bone infection. *Journal of Materials Chemistry B*. 2016;4(24):4356-4365.
- VILA M., GARCÍA A., GIROTTI A., ALONSO M., RODRÍGUEZ-CABELLO J.C., GONZÁLEZ-VÁZQUEZ A. ET AL. 3D silicon doped hydroxyapatite scaffolds decorated with Elastin-like Recombinamers for bone regenerative medicine. *Acta Biomaterialia*. 2016;45:349-356.
- PARIS J.L., TORRE P.D.L., MANZANO M., CABANAS M.V., FLORES A.I., VALLET-REGÍ M. Decidua-derived mesenchymal stem cells as carriers of mesoporous silica nanoparticles. In vitro and in vivo evaluation on mammary tumors. *Acta Biomaterialia*. 2016.

## Highlights

The most important achievements during 2016 include; (i) the development, optimization of nanotechnological strategies to design multifunctional smart nanosystems for bone cancer, osteoporosis and infection diseases and (ii) the design, fabrication and implantation of 3D scaffolds based on bioceramics for bone tissue regeneration.

This year; Prof. Vallet-Regí has obtained an Advanced Grant from the European Research Council entitled “polyValent mEsopoRous nanosystem for bone Diseases” (VERDI). GIBI group has also developed diverse research lines in the frame of different national and international research projects including MAT2015-64831-R, MAT2013-43299-R, MAT2016-75611-R AEI/FEDER, PI15/00978 y CTQ2015-72605-EXP y H2020-Mozart 685872. Moreover, GIBI group has participated in different Intramural Projects (COATREG-3D, GOLIATH, SCAFFBONE, SPRING, MULTISCAFF, NanoPrevHIV) and translational CIBER-ECO project (SMART4NB).

GIBI group is member of the Research Institute of “Hospital 12 de Octubre (i+12)” and European Networking for prevention and treatment of osteoporotic fractures ([www.agening.net](http://www.agening.net)). GIBI group has also published 22 original research articles indexed in JCR, 1 PCT-patent, 3 book chapters, and 17 invited conferences in international research forums. GIBI group during 2016 has supervised 2 PhD Theses obtaining both the maximum qualification, being one of them awarded by RANF. GIBI group collaborates with many clinic institutions as Hospital Miguel Servet, Zaragoza, La Paz Hospital, Madrid, Alcalá de Henares University Hospital, Jimenez Diaz Foundation, Hospital del Mar Barcelona, University Hospital of Getafe, University Children’s Hospital Niño Jesus. Furthermore, Prof. María Vallet-Regí has coordinated the activity “Intelligent Materials. Are the new biomaterials science fiction?” within the framework of the European Night of Researchers. Finally, Prof. María Vallet-Register has received the Lilly Foundation Prize for the Distinguished Scientific Career in the specialty of Chemistry.





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PROGRAMMES  
**Nanomedicine**



## GROUP MEMBERS

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## Main lines of research

NANOMOL makes a valuable contribution to the advancement of knowledge in the field of molecular nanoscience and organic functional materials. The multidisciplinary research we carry out is aimed at the self-assembly, nanostructuring and processing of functional (bio- and electro-active) molecules as crystals, particles, vesicles, and structured or self-assembled monolayers on various substrates showing non-conventional chemical, physical and biological properties. We use several methodologies for such a processing but a special emphasis is made with supercritical fluids. The resulting molecular organizations/systems are studied and used in the fields of molecular and large-area electronics, molecular magnetism, nanomedicine and biomaterials as well as for environmental applications:

- Molecular electronics • Nanomedicine • Biomaterials • Materials processing • Molecular magnetism



## Most relevant scientific articles

- GRIMALDI N., ANDRADE F., SEGOVIA N., FERRER-TASIES L., SALA S., VECIANA J. ET AL. Lipid-based nanovesicles for nanomedicine. *Chemical Society Reviews*. 2016;45(23):6520-6545.
- YUAN L., FRANCO C., CRIVILLERS N., MAS-TORRENT M., CAO L., SANGEETH C.S.S. ET AL. Chemical control over the energy-level alignment in a two-terminal junction. *Nature Communications*. 2016;7.
- CABRERA I., ABASOLO I., CORCHERO J.L., ELIZONDO E., GIL P.R., MORENO E. ET AL.  $\alpha$ -Galactosidase-A Loaded-Nanoliposomes with Enhanced Enzymatic Activity and Intracellular Penetration. *Advanced Healthcare Materials*. 2016;5(7):829-840.
- SOUTO M., LLOVERAS V., VELA S., FUMANAL M., RATERA I., VECIANA J. Three Redox States of a Diradical Acceptor-Donor-Acceptor Triad: Gating the Magnetic Coupling and the Electron Delocalization. *Journal of Physical Chemistry Letters*. 2016;7(12):2234-2239.
- LEONARDI F., CASALINI S., ZHANG Q., GALINDO S., GUTIÉRREZ D., MAS-TORRENT M. Electrolyte-Gated Organic Field-Effect Transistor Based on a Solution Sheared Organic Semiconductor Blend. *Advanced Materials*. 2016;28(46):10311-10316.

## Highlights


- 28 scientific publications in JCR indexed journals with an average impact factor of 8,010.
- Application of 2 international patents (US and Europe).
- 16 invited lectures given in international conferences.
- Participation on the activities of EU FP7 and H2020 projects: NANO2FUN, COMMON SENSE, ACMOL, SAM-Tune GAIN, OSES-Int-Log, and i-SWITCH
- Participation in three RETOS COLABORACIÓN projects: TERARMET consortium to carry out the project “Desarrollo de terapias para el tratamiento de enfermedades raras metabólicas congénitas”, coordinated by the company PRAXIS PHARMACEUTICALS, UNDERLIPIDS consortium to carry out “Nanopartículas sólidas lipídicas para administración subcutánea de compuestos marinos antitumorales”, coordinated by PHARMAMAR, and NANO4DERM consortium to carry out “Nanocápsulas conteniendo activos para el tratamiento tópico de enfermedades dermatológicas”, coordinated by ALMIRALL.
- Approval of H2020 project SMART4FABRY – “Smart multifunctional GLA-nanoformulation for Fabry disease”, under the coordination of CIBER by NANOMOL group and with a total budget of 5.844.509€
- Implementation of scientific activities of ERC Starting Grant project “e-GAMES”.
- Execution of scientific activities of CIBER-BBN intramural projects: NANOLYSO, NANOMETS, BIOFILM-ATTACK, VASCUMAT, ORDECA
- Approval of two TECNIOspring fellowships funded by ACCIÓ-Generalitat where two experienced researchers join the group to carry out 2-year projects on biomedicine.
- Coordination of the CIBER-BBN Transfer Project: “Functionalized nanoliposomes for the development of therapies for intracellular-based diseases. Application to Fabry disease and homozygous familial hypercholesterolemia (LIPOCELL)” in collaboration with the company BIOPRAXIS RESEARCH AIE.
- Approval of RIS3CAT NANONAFRES project ““Estudis preclínics i clínics adreçats a l’aplicació de nano vesícules (quatsomes) amb EGF úlceres venoses cròniques” to be executed together with several clinical institutions in Catalonia.
- Implementation of scientific activities of EXPLORA projects “Engineering Cell Vessels on Surfaces using Dynamic Molecular Bio-Interfaces” and “Biosensors platform based on field effect organic transistors for diagnosis of Alzheimer”.
- Implementation of scientific activities of BE-WELL project under MINECO RETOS DE LA SOCIEDAD program. Approval of FANCY and MOTHER projects under same program 2016 call.
- Implementation of activities as Scientific Direction of the Large Scientific and Technical Facility NANBIOSIS.




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PROGRAMMES

**Biomaterials & Advanced Therapies**



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## Main lines of research

- Clinical research in implants for bone repair.
- Biocompatibility of new materials for potential use in implants for bone repair: cell and surface interactions, cell and particle interactions.
- Control of the expression of therapeutic genes using gene switches and nanoparticles.

## Most relevant scientific articles

- CRESPO L., HIERRO-OLIVA M., BARRIUSO S., VADILLO-RODRÍGUEZ V., MONTEALEGRE M.A., SALDANA L. ET AL. On the interactions of human bone cells with Ti6Al4V thermally oxidized by means of laser shock processing. *Biomedical Materials (Bristol)*. 2016;11(1).
- CIFUENTES S.C., BENSIAMAR F., GALLARDO-MORENO A.M., OSSWALD T.A., GONZÁLEZ-CARRASCO J.L., BENAVENTE R. ET AL. Incorporation of Mg particles into PDLLA regulates mesenchymal stem cell and macrophage responses. *Journal of Biomedical Materials Research - Part A*. 2016.
- BENSIAMAR F., OLALDE B., CIFUENTES S.C., ARGARATE N., ATORRASAGASTI G., GONZÁLEZ-CARRASCO J.L. ET AL. Bioactivity of dexamethasone-releasing coatings on polymer/magnesium composites. *Biomedical Materials (Bristol)*. 2016;11(5).
- LIEBLICH M., BARRIUSO S., MULTIGNER M., GONZÁLEZ-DONCEL G., GONZÁLEZ-CARRASCO J.L. Thermal oxidation of medical Ti6Al4V blasted with ceramic particles: Effects on the microstructure, residual stresses and mechanical properties. *Journal of the Mechanical Behavior of Biomedical Materials*. 2016;54:173-184.
- LIEBLICH M., BARRIUSO S., IBÁÑEZ J., RUIZ-DE-LARA L., DÍAZ M., OCANA J.L. ET AL. On the fatigue behavior of medical Ti6Al4V roughened by grit blasting and abrasiveless waterjet peening. *Journal of the Mechanical Behavior of Biomedical Materials*. 2016;63:390-398.

## Highlights

The group of Bone Physiopathology and Biomaterials has performed a thorough characterization of polymers and metallic alloys, including the study of their microstructure and mechanical properties. The group has studied the biocompatibility of polymer/Mg composites as well as coating on these materials which were designed to release bioactive molecules. The group has continued their studies on Ti6Al4V alloy modified by means of blasting, thermal treatments, laser shock processing or abrasiveless waterjet peening. The group has progressed in the development of gene switches for the spatial and temporal regulation of therapeutic transgenes. These molecular tools are being targeted for use in several biomedical applications such as vaccination, oncolytic therapy or regenerative medicine. The clinical scientists of the group have continued their participation in clinical trials for therapeutic interventions in bone-related diseases. The group funded its activities by means of grants from MINECO, ISCIII and research contracts with the industry.



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PROGRAMMES  
**Nanomedicine**



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**Contributors:** Saccardo, Paolo

## Main lines of research

The team is co-ordinately acting to exploit microbial and non-microbial platforms for the production of new generation protein-based drugs and materials, of interest in protein replacement therapies, gene therapy and regenerative medicine. In particular, we are interested in developing novel self-assembling, nanostructured materials in form of protein based drug delivery systems and of viral mimetics for the cell-targeted delivery of conventional drugs and nucleic acids. Associated activities are based in the improvement of biofabrication processes in different cell factories and in the use of non-protein nanomaterials such as magnetic particles.



## Most relevant scientific articles

- CANO-GARRIDO O., SÁNCHEZ-CHARDI A., PARES S., GIRO I., TATKIEWICZ W.I., FERRER-MIRALLES N. ET AL. Functional protein-based nanomaterial produced in microorganisms recognized as safe: A new platform for biotechnology. *Acta Biomaterialia*. 2016;43:230-239.
- GIANNOTTI M.I., ABASOLO I., OLIVA M., ANDRADE F., GARCÍA-ARANDA N., MELGAREJO M. ET AL. Highly Versatile Polyelectrolyte Complexes for Improving the Enzyme Replacement Therapy of Lysosomal Storage Disorders. *ACS Applied Materials and Interfaces*. 2016;8(39):25741-25752.
- PESARRODONA M., FERNÁNDEZ Y., FORADADA L., SÁNCHEZ-CHARDI A., CONCHILLO-SOLE O., UNZUETA U. ET AL. Conformational and functional variants of CD44-targeted protein nanoparticles bio-produced in bacteria. *Biofabrication*. 2016;8(2).
- CABRERA I., ABASOLO I., CORCHERO J.L., ELIZONDO E., GIL P.R., MORENO E. ET AL.  $\alpha$ -Galactosidase-A Loaded-Nanoliposomes with Enhanced Enzymatic Activity and Intracellular Penetration. *Advanced Healthcare Materials*. 2016;5(7):829-840.
- TORREALBA D., PARRA D., SERAS-FRANZOSO J., VALLEJOS-VIDAL E., YERO D., GIBERT I. ET AL. Nanostructured recombinant cytokines: A highly stable alternative to short-lived prophylactics. *Biomaterials*. 2016;107:102-114.

## Highlights

During 2016, the group has been carrying out several research activities on protein nanomaterials of biomedical interest, including two MINECO projects, one EU project, one NFFA project, one FIS project, two TV3 Fundació Marató projects on oncology, eight I + D agreements and twenty-six external service agreements associated with our Protein Production Platform.

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