ANNUAL REPORT 2014

ciber-bbn

Centro de Investigación Biomédica en Red

Bioingeniería, Biomateriales y Nanomedicina

Index

1. ORGANIZATION

Letter from the Scientific Director

Prof. Pablo Laguna
Scientific director.
CIBER-BBN.

CIBER-BBN IN 2014

When reviewing the main actions carried out and results achieved in year 2014 in CIBER-BBN, it is again very exciting to see how we have successfully maintained a clearly positive evolution. The milestones which I consider deserve being mentioned explicitly in this report are described below.

With respect to the annual evaluation of the groups in the centre based on data from 2013, we can again say that we are continuing in the line of continuous improvement, tending towards saturating our indicators in most groups, and this therefore translates into an overall improvement in CIBER-BBN. As a result of this evaluation and the evaluation carried out in the previous years, 2 groups left CIBER-BBN as of December 31, and at the time of writing this report the possibility of incorporating new groups into the different CIBER is open in the Strategic Health Action call for proposal.

As regards our day-to-day activity, the actions contemplated in the strategic plan approved in December 2013, including continuous actions, other reoriented actions and some completely new actions, were started this year.

It is worth pointing out that an international FORUM aimed at defining the proposals for H2020 in the field of "Brain Health & Neurorestoration" was held in Barcelona in September. The Forum was organized by CIBER-BBN, the consortium institutions Universidad Miguel Hernández de Elche, Universidad Autónoma de Barcelona and clinical partner Instituto Guttmann.

When reviewing the initiatives derived from these FORUMS that seek to open up paths towards clinical practice, the seminal and biannual projects that we started along with CIBERES and SEPAR will end early 2015. Given that all parties consider that the call for proposal has been a success within the modesty of its financial ambitions and seminal purposes, a decision was made to reissue said call for proposal in this year 2014, the new projects already under way. Similarly, another call for proposal has been made during 2014 together with Instituto de Investigación Sanitaria de Córdoba, IMIBIC, and this resulted in a collaboration project currently under development between the two institutions. In addition, 6 projects in collaboration with the Fundación ECO (Excellence in Oncology) are in the development phase.

Adding to this line of collaboration between CIBERs and at the initiative of the ISCIII, a new instrument consisting of funding multidisciplinary projects involving 4 different CIBERs has been designed. The first edition of this call for proposal took place in 2014 with the funding of 3 projects being proposed, including one of the proposals that involves CIBER-BBN participation as a coordinator. CIBER-BBN participates in this project along with our colleagues from CIBERDEM, CIBERNED and CIBERER. .

In aspects relating to training, mobility and research initiation programmes continued to be developed as usual and they are greatly appreciated and highly valued by the entire CIBER-BBN community. The year 2014 saw the grant of 39 "launching" grants for young researchers and 19 mobility grants.

With respect to the platform programme, the request submitted in the year 2013 for recognizing our platform programme as a Singular Scientific Infrastructure (ICTS), along with Centro de Cirugía de Mínima Invasión Jesús Usón de Cáceres (CCMIJU), has been resolved positively. This recognition is very good

news that will allow us to maintain and develop these singular infrastructures. A new path as an ICTS has begun. As always, a new beginning is usually filled with hopes and uncertainties, but we believe that ICTS has great potential to grow into competitive infrastructures.

Among the new initiatives put into action in 2014, the evaluation of researchers contracted by CIBER is featured in the development of the new strategic plan. 51 researchers with more than 3 years of contract in CIBER-BBN have been evaluated. Each researcher has been assessed by 2 external evaluators based on the CV of the researcher being evaluated, the report of said researcher and the report from the group PI. The aspects being considered include: scientific production, technology transfer, clinical transfer, leadership skill, alignment with CIBER-BBN strategic plan. 12 of the 51 researchers (24%) were categorized as excellent, 35 researchers (69%) were categorized as good, and finally 4 researchers (7%) were categorized as underperforming. These underperforming researchers will be subjected to a new evaluation after a period of 2 years so that it can be verified if the improvement actions have been fruitful, whereas the other researchers will again be evaluated after another period of 4 years.

At this moment, intramural projects are in the middle of the biannual period envisaged for said projects. 2 project categories have been established in this biennium: intramural projects of excellence which include 27 projects (8 in Bioengineering, 5 in Biomaterials and 14 in Nanomedicine), and which given their greater value with chances of succeeding, gain higher priority when resolving the mobility aid calls for proposal and launching grants or manager appointment; and intramural projects of recognized activity which include a total of 22 projects (7 in Bioengineering, 7 in Biomaterials and 8 in Nanomedicine) and in which elements for improvement were identified in the proposal, but they were not identified as insurmountable, in other words, they can quite probably be corrected.

For the first time ever, CIBER-BBN has a type of transfer projects in which CIBER works hand in hand with companies by funding 50% of projects in a state of maturity that makes them appealing for companies to get involved by providing funds. In order to move these projects further towards the end product, CIBER has decided to assign specific resources amounting to 250,000€ to these projects. The call for proposal was fairly successful and 4 projects were presented. All 4 projects obtained positive funding evaluation. Due to reasons not related to the project, one of them was subsequently withdrawn from the programme, so the transfer programme currently includes 3 projects under way with the participation of companies, namely, BRUKER (Germany), SYLENTIS (ZELTIA group) and PRAXIS, plus the project with the company, FERRER, which was already being developed a year ago. Seeing how positive this experience is, a new extraordinary call for proposal for such projects was opened at the end of 2014 and it has been resolved in the first months of 2015.

To finish with this actions review, it must be highlighted that CIBER-BBN has participated in key events such as BIO International Convention, BIO EUROPE or BIOSPAIN Conferences.

As a pilot experiment, a forum and seminar retransmission system has been approved this year. This retransmission system can now be considered robust enough to start allowing continuously planning the retransmission of events of great interest.

Annual conferences were held in Girona in November and time was dedicated to review the progress made in the different intramural projects which, in this occasion, were organized by their clinical application, such that cross fertilization may have much greater effect, and with a clinical moderator which allows better reflection oriented from that point of view. The resources for carrying out these projects continue to be assigned to the groups according to evaluation results, and they must be adjusted to some of the 4 main objectives of CIBER-BBN: 1-To continue generating science and knowledge of excellence; 2-To do so in collaboration, giving value to the multidisciplinary and complementary natures of the different groups; 3-To do so together with clinical partners to achieve better translation to clinical practice; and 4-To do so thinking about and together with the industrial sector to which any developments may be transferred and to give value to a society, who is ultimately funding and gives meaning to the results of our activity. Besides these presentations detailing the progress made in the projects, a session dedicated to presenting new ideas, usually presented by young researchers who, however, pre-

sent a degree of maturity that allows them to raise new challenges throughout their professional career, was held.

Finally, 2 plenary presentations on 2 very well-known subjects posing challenges which will be very interesting to solve in upcoming years were held in the conferences:

"Nanoparticulate biomaterials for gene and drug delivery", by Matthias Epple (Centre for Medical Biotechnology, Universität Duisburg-Essen) and "Overview of the development of nanomedicine in Europe and the next trends", by Patrick Boisseau (European Technology Platform on Nanomedicine).

Certificates of recognition were also given to researchers who obtained launching grants, co-sponsored by Caja de Ingenieros, during the year. This modest "initiation" grants allows us to be a bit more generous money wise with our programme to attract younger and more brilliant minds into research, giving them coverage in the final months of bachelor or masters studies in order to access other grants in regular competitive calls for proposal.

In summary, the year 2014 was a new year in which the results of the continued effort made by the centre since it was created started to become measurable realities and in which the reflections included in the strategic plan prepared in the previous year have been initiated simultaneously. 2014 also marked the first year with the integrated management office along with other 7 CIBERs. In my opinion, this is a great structuring effort that deserves acknowledgement. It must also be added that this experience must be used, advancing it in the years to come, without the initial haste, towards becoming the backbone for research in CIBER, which is the ultimate goal of CIBER-BBN.

RESEARCH GROUPS AND CONSORTIUM INSTITUTIONS

In 2014, CIBER-BBN was formed by 47 research groups, 45 of which were full member groups and 2 of which were associated groups:

PI	Institution	Region
Jordi Aguiló	Universidad Autónoma de Barcelona	Cataluña
Fernando Albericio	Inst. de Investigación Biomédica de Barcelona – IRB Barcelona	Cataluña
Carles Arús	Universidad Autónoma de Barcelona	Cataluña
José Becerra	Universidad de Málaga	Andalucía
Juan Manuel Bellón	Universidad de Alcalá	Madrid
Jerónimo Blanco	CSIC	Cataluña
Margarita Calonge	Universidad de Valladolid	Castilla y León
Bernardo Celda	Universidad de Valencia	Comun. Valenciana
Alberto de Leiva	Inst. de Investigación Hospital de Santa Cruz y San Pablo	Cataluña
Francisco del Pozo	Universidad Politécnica de Madrid	Madrid
Manuel Doblaré	Universidad de Zaragoza	Aragón
Elisabeth Engel	Instituto de Bioingeniería de Cataluña	Cataluña
Ramón Eritja	CSIC	Cataluña
Eduardo Fernández	Universidad Miguel Hernández de Elche	Comun. Valenciana
José Luis Gómez	Universidad Politécnica de Valencia	Comun. Valenciana
Rafael Gómez	Universidad de Alcalá	Madrid
Mª Luisa González	Universidad de Extremadura	Extremadura
Raimon Jané	Instituto de Bioingeniería de Cataluña	Cataluña
Pablo Laguna	Universidad de Zaragoza	Aragón
Laura Lechuga	CSIC	Cataluña
Ramón Mangues	Instituto de Investigación Hospital de Santa Cruz y San Pablo	Cataluña
M. Pilar Marco	CSIC	Cataluña
Ramón Martínez	Universidad Politécnica de Valencia	Comun. Valenciana
Isabel Obieta	Fundación TECNALIA	País Vasco
Javier Pavía	Universidad de Barcelona	Cataluña
José Luis Pedraz	Universidad del País Vasco	País Vasco
Soledad Penadés	CIC biomaGUNE	País Vasco
José Luis Peris	Instituto de Biomecánica de Valencia	Comun. Valenciana
Ángel Raya	Centro de Medicina Regenerativa de Barcelona	Cataluña
Félix Ritort	Universidad de Barcelona	Cataluña
Laura Roa	Universidad de Sevilla	Andalucía
José C. Rodríguez	Universidad de Valladolid	Castilla y León
Cristina Ruiz	Servicio Gallego de Salud - Hsp. Juan Canalejo	Galicia

PI	Institution	Region
Josep Samitier	Instituto de Bioingeniería de Cataluña	Cataluña
Julio San Román	CSIC	Madrid
Jesús Santamaría	Universidad de Zaragoza	Aragón
Andrés Santos	Universidad Politécnica de Madrid	Madrid
Fausto Sanz	Universidad de Barcelona	Cataluña
Simó Schwartz	Vall d'Hebron Institut de Recerca	Cataluña
Concepción Solans	CSIC	Cataluña
María Vallet-Regí	Universidad Complutense de Madrid	Madrid
Jaume Veciana	CSIC	Cataluña
Nuria Vilaboa	Servicio Madrileño de Salud / Hospital La Paz	Madrid
Antonio Villaverde	Universidad Autónoma de Barcelona	Cataluña
Mª Ángeles Muñoz Fernández(*)	Servicio Madrileño de Salud / Hospital General Universitario Gregorio Marañón	Madrid
Daniel Navajas(*)	Universidad de Barcelona	Cataluña

(*) Associated groups

ORGANIZATIONAL STRUCTURE

In 2014, CIBER-BBN, along with other CIBERs of the same nature, has been integrated in a common structure, with a single legal entity and under the legal status of a consortium formed by 90 institutions. Since 2014, CIBER-BBN continues to maintain its independence in terms of scientific management, although it constitutes a subject area within CIBER, a unique research structure in Spain in the field of biomedical research with great scientific potential.

The maximum decision-making body of CIBER is the Governing Board formed by 3 representatives from the ISCIII and 1 institutional representative from each of the Consortium Institutions. It is chaired by the Director of the ISCIII and meets on a half-yearly basis. The Permanent Commission is an appointed commission (formed by the ISCIII and 8 members of the Governing Board that are renewed every 6 months) that meets more often to make those decisions which, given their nature, cannot wait to be approved by the Governing Board, more swiftly.

Within the subject area of BBN (Bioengineering, Biomaterials and Nanomedicine), the basic and functional units are made up of 46 research groups (44 full member groups and 2 associated groups in 2014) described in detail in this report.

From the scientific point of view, the organisational structure is based on the member research groups, Research Programmes and Horizontal Programmes, with a coordinator for each Programme that is a Steering Committee member. Scientific decisions are made by the Scientific Director, counseled by the Steering Committee and the Scientific Advisory Board.

The **Steering Committee**, chaired by the Scientific Director comprises programme coordinators and the Managing Director.

STEERING COMMITEE 2014

Position	Name
Scientific Director	Pablo Laguna Lasaosa
Assistant Scientific Director and Industrial Transfer Coordinator	Simó Schwartz Navarro
Bioengineering Programme Coordinator	Jordi Aguiló Llobet
Biomaterials Programme Coordinator	José Luis Becerra Ratia
Nanomedicine Programme Coordinator	Mª Pilar Marco Colás
Clinical Translation Coordinator	Margarita Calonge Cano
Platform Programme Coordinator	Jesús Santamaría Ramiro
Training Programme Coordinator	Javier Pavía Segura
Managing Director	Manuel Sánchez Delgado
Scientific Director Assistant	Begoña Pérez Magallón

The members that are part of CIBER-BBN **Scientific Advisory Board** are ten renowned scientists from the disciplines that the Centre works in. There are two researchers in the Bioengineering Programme, three in the Biomaterials and Nanomedicine Programmes, and two in the Horizontal Programmes.

EXTERNAL SCIENTIFIC COMMITTEE 2014

Programme	Name	Institution
Bioengineering and Medical Imaging	Prof. Nilo Saranummi	VTT Technical Research Centre of Finland
	Prof. Leif Sörnmo	Biomedical Engineering Department, Univerity of Lund, Sweden
Biomaterials and Advanced Therapies	Prof. C. James Kirkpatrick	Institute of Pathology, Johannes Gutenberg University, Mainz
	Dra. Begoña Castro	Histocell, Spain
	Prof. Matthias Epple	Centre for Medical Biotechnology, Universität Duisburg-Essen, Germany
Nanomedicine	Prof. Mario Adolfo Barbosa	Instituto de Engenharia Biomédica, Laboratório de Biomateriais, Universidade do Porto
	Prof. Patrick Boisseau	Executive Board of European Technology Platform on Nanomedicine, France
	Wolfgang Parak	Philipps Universität Marburg, Germany
Transversal Programmes	Dr. Joan Bigorra	Director de Innovación del Hospital Clinic de Barcelona, España
	Dra. Pilar Calvo	PHARMAMAR, Spain

This year 4 new members have been incorporated in the External Advisory Scientific Committee (Leif Sörnmo, Matthias Epple, Patrick Boisseau and Wolfgang Parak) replacing Jean Louis Coatrieux, Roger Kamm, Ruth Duncan and Rogerio Gaspar.

A **Medical Advisory Committee** has been maintained since 2010 to reinforce the Translational Research Programme and to encourage CIBER-BBN research results to have a greater effect on society in general and on the National Health System in particular. The purpose is to advise management of the centre in the aspects relating to interactions between their scientific programme and clinical practice. The members of this Medical Advisory Committee are:

MEDICAL ADVISTORY COMMITTEE 2014

Area	Name	Institution
Traumatology and Orthopaedics	Enrique Gómez Barrena	Hospital Universitario La Paz, Madrid
Cardiology	Arcadi García Alberola	Hospital Universitario Virgen de la Arrixaca, Murcia
Oncology	Josep Tabernero Caturla	Hospital Vall d' Hebrón, Barcelona
Neurology	Mª. José Martí Domenech	Hospital Clínic, Barcelona
Ophthalmology	Jose María Ruíz Moreno	Complejo Universitario Hospitalario, Albacete
Pharmacology and Regulatory Affairs	Joan Bigorra Llosas	Hospital Clínic, Barcelona

As advisory bodies of CIBER-BBN, members of the External Advisory Scientific Committee and Medical Advisory Committee held a meeting with the Steering Committee on November 11 in Girona at the 8th Annual Conferences of CIBER-BBN. Aspects such as centre's activity in 2014, the implementation of several actions developed in the 2014-2017 Strategic plan, annual scientific evaluation results and projects which were presented in scientific sessions, were discussed during the work session.

Since 2014, administrative management falls entirely on the shoulder of the new Technical Unit located in Instituto de Salud Carlos III, Madrid.

After transferring administrative capacities to Madrid, the Scientific Direction has been supported by a person attached to it.

Furthermore, there is a team of professional managers for scientific programme management rendering their services in the following areas:

- Bioengineering Programme Manager: **Theodora Tsapikouni**
- Biomaterials Programme Manager: **Aída Castellanos**
- Nanomedicine Programme Manager: **Johanna Scheper**
- Transfer Programme Manager: **Fernando Santos**
- Platforms Programme Manager: **Jesús Izco**

2014 BUDGET

		Entry	Budget
CIBER-BBN PROGRAMMES	MANAGEMENT	Management	390.525 €
	BIOENGINEERING PROGRAMME	Intramural Bioengineering Projects	387.896 €
	BIOMATERIALS PROGRAMME	Intramural Biomaterials Projects	563.300 €
	NANOMEDICINE PROGRAMME	Intramural Nanomedicine Projects	801.737 €
	PLATFORMS	Platforms	212.000 €
	TRAINING PROGRAMME	Training Grants	202.697 €
		Mobility	32.000 €
		Qualification	1.529.071 €
	TRANSFER, TRASLATION & DISSEMINATION	Dissemination	20.000 €
		Technology Transfer	192.000 €
		Technology Transfer projects	250.000 €
		Translational Research Collaborations	50.000 €
	TOTAL		**4.631.226 €**

CIBER-BBN STAFF

Number of hires in the year ending December 31 classified by categories and genders.

	MEN			Total MEN
	Indefinite	Works & services	Postdoctoral	
CIBER-BBN	25	10	2	37
PhD	16	3	2	21
Degree Holder	8	7		15
Diploma Holder				
Technician	1			1
Grand total	25	10	2	37

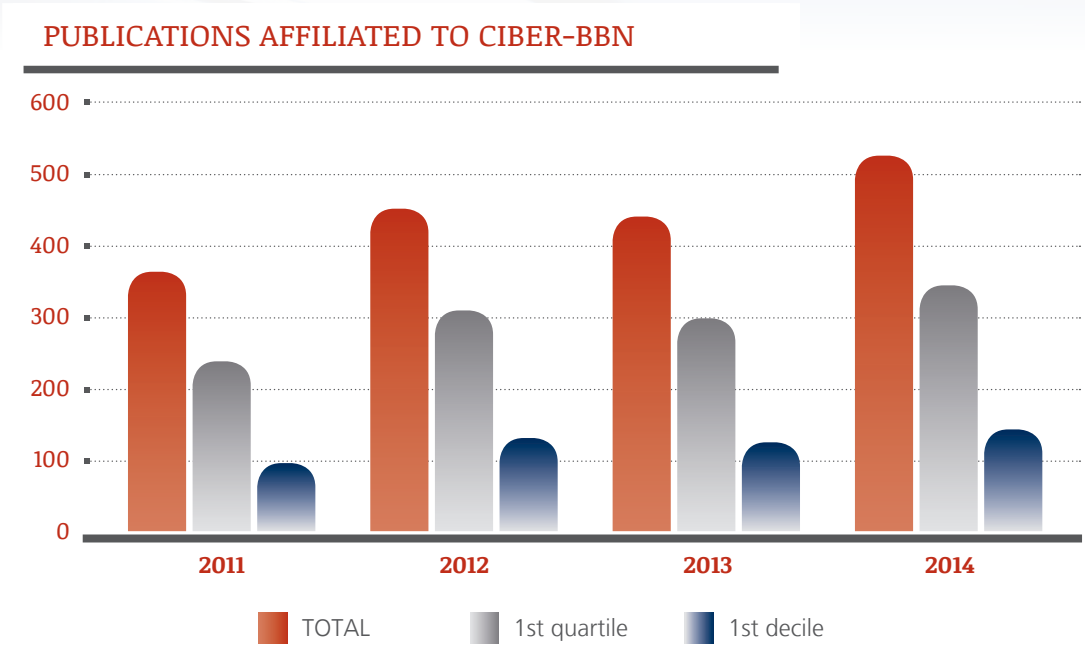
	WOMEN			Total WOMEN
	Indefinite	Works & services	Postdoctoral	
CIBER-BBN	41	30	2	73
PhD	26	12	2	40
Degree Holder	7	13		20
Diploma Holder	1			1
Technician	7	5		12
Grand total	41	30	2	73

	Indefinite	Works & services	Postdoctoral	Grand total
CIBER-BBN	66	40	4	110
PhD	42	15	4	61
Degree Holder	15	20		35
Diploma Holder	1			1
Technician	8	5		13
Grand total	**66**	**40**	**4**	**110**

Not all scientific production of the year 2014 suitably compiled and validated is available at the moment of preparing this report, so the scientific production of 2014 which is shown in this document is limited to the publications.

Quantitative and qualitative computing of publications per year

It can be seen that the number of publications affiliated to CIBER-BBN and their quality have been on the rise year after year.



The number of publications affiliated to CIBER-BBN, taking into account only articles, reviews and editorials in 2014 was 524, there being an increase of 85 publications compared to the previous year, i.e., an increase of almost 20%. At the same time, the quality of said publications also increases with 343 in the first quartile and 142 in the first decile compared to 287 and 124 in 2013:

Publications (articles, reviews and editorials) affiliated to CIBER-BBN by years

	2011	2012	2013	2014
Total	**362**	**450**	**439**	**524**
1st quartile	237	308	297	343
1st decile	95	130	124	142

The mean impact factor of the publications is 3.95 in 2014 with 17 publications with an impact factor greater than 10, 3 publications with an impact factor above 20 and 1 publication with an impact factor above 45.

Journals

The table below shows the journals in which most publications were made in 2014.

Journal	Impact Factor	Number of Publications
Acta Biomaterialia	5,684	13
Sensors and Actuators, B: Chemical	3,84	12
PLoS ONE	3,534	10
RSC Advances	3,708	9
Journal of the Mechanical Behavior of Biomedical Materials	4,287	8
Colloids and Surfaces B: Biointerfaces	4,287	7
Sensors	2,048	7
Biomaterials	8,312	5
Small	7,514	5
ACS Applied Materials and Interfaces	5,9	5
Chemistry - A European Journal	5,696	5

International publications

Collaborative publications with foreign institutions are increasing every year. Therefore, CIBER-BBN is gaining more international importance. In 2014 there were a total of 252 publications (articles, reviews and editorials) with CIBER-BBN affiliation and the participation of authors from foreign institutions.

Year	International Publications
2014	252
2013	179
2012	180
2011	144

IntraCIBER-BBN publications

Similarly, a significant increase in collaborative publications between CIBER-BBN groups can be seen. There are 64 publications with several groups participating in writing same compared to 44 in the previous year.

Year	intraCIBER Collaborations
2014	64
2013	44
2012	46
2011	29

2. SCIENTIFIC PROGRAMMES

BIOENGINEERING AND MEDICAL IMAGING

Coordinator:

Jordi Aguiló

Biomonitoring Group of the National Microelectronic Centre (GBIO-CNM)

The **assigned groups** to this programme in 2014 are:

BIOENGINEERING AND MEDICAL IMAGING GROUPS

PI	Name of the Group
Laura Roa	Biomedical Engineering Research Group, Universidad de Sevilla (GIB-US)
Pablo Laguna	Biomedical Signal Interpretation & Computational Simulation of the Aragon Institute for Engineering Research of the University of Zaragoza (BSICoS-I3A)
Alberto de Leiva	Endocrinology and Diabetes Research Group, Hospital Sant Pau -Univ. Autónoma de Barcelona (EDUAB-HSP)
Carles Arús	Research Group in Biomedical Applications of Nuclear Magnetic Resonance, Universidad Autónoma de Barcelona (GABRMN-UAB)
Francisco del Pozo	Bioengineering and Telemedicine Group, Universidad Politécnica de Madrid (GBT-UPM)
Bernardo Celda	Research group of Biomedical and Biophysical Applications of the NMR, Universidad de Valencia (GABBRMN-UVEG)
Javier Pavía	Biomedical Imaging Group, Universidad de Barcelona (GIB-UB)
Andrés Santos	Biomedical Imaging Technology Research Group, Universidad Politécnica de Madrid (BIT-UPM)
Raimon Jané	Biomedical Systems and Signals Research Group, Universidad Politécnica de Cataluña (SISBIO-UPC-IBEC)
Eduardo Fernández	Neuroprosthesis and Neuroengineering Research Group, Universidad Miguel Hernández de Elche (NN-UMH)

Strategic lines of research of the programme

BI 1. MULTIMODAL DIAGNOSTICS:

- Medical image's capture and processing optimization (TAC, NMR, PET, DTI)
- Biomedical signals' capture and processing improvement (ECG, EEG, EMG, Respiration, etc.)
- Morphological and functional modelling of tissues and organs.
- Pre-operative and intra-operative planning as well as creation of virtual surgery programs.

Imaging diagnosis is increasingly complemented by other types of diagnosis based on different biophysical elements such as: the combined use of different imaging techniques (CAT, MRI, PET, DTI, etc.), the prior treatment of the image (atlas, advanced segmenting and detection systems morphological co-registering etc.), very different types of signals (ECG, EEG, EMG, Respiration, etc.), as well as morphological and functional models derived from tissue and organ modelling.

The combination of these components would allow a more efficient, complete and rigorous diagnosis.

The objective of this line is therefore related to the combined analysis of all this information, promoting improvements in diagnosis systems, elaborating tools for aiding in making clinical decisions and encouraging pre- and inter-operatory planning systems, as well as simulation and control tools in virtual surgery.

This line is in turn complemented with others, such as Nanodiagnosis and Prostheses and Implants lines, in which similar or complementary techniques are used.

BI 2. INTELLIGENT DEVICES AND SYSTEMS:

- Creation of systems to monitor and control patients (sensoring, controlling and robotic systems)
- Software applications to improve systems for patient diagnosis.
- E-health and M-health Systems.

The introduction of more portable and efficient medical devices, affording a greater deal of autonomy from the clinical specialist (incorporating a certain degree of intelligence), would significantly increase the life quality. These devices include remote monitoring systems for high-risk patients, in conjunction with automatic telecommunication systems, automated drug delivery systems, even in a closed loop, controllably adaptable implants, among many other examples.

This implantation would entail a greater independence of the patients which in turn would reduce the burden on healthcare personnel. Additionally, research results coming from this line would offer more thorough and continuous control of the patients, since the evolution of their health condition could be tracked and different variables could be simultaneously monitored.

In these years a new line has emerged within this research area and it is related to E-health systems, which is a term used for healthcare supported by electronic processes and communication as well as m-health which is supported by mobile phones and other portable devices. CIBER-BBN has included this line to its current Research Programme since research of several groups point to this area.

The intramural projects of the Bioengineering and Medical Imaging programme during 2014 were:

Projects of excellence

DIAB-SUPPORT

Personalized Decision Support based on real-time monitoring of patients with type 1 diabetes
Coordinator researcher: Elena Hernando (F. del Pozo research group).
Participating PIs groups: L. Roa, A. Leiva.

OPTOGEN

A wide spectrum of bioengineered devices tailored to compliment and enhance optogenetic research with clinical implications
Coordinator researcher: Lawrence Humphreys (E. Fernández research group).
Participating PIs groups: J.L. Pedraz, J. Aguiló, external research groups.

MOLGLIO

Molecular Imaging strategies for development of surrogate biomarkers of early therapy response/ resistance detection in glioblastoma
Coordinator researcher: Carles Arús.
Participating PIs groups: J. Santamaría, A. Santos, S. Schwartz, external research groups.

MUDIRES-2PSD

Multimodal Diagnosis by Signal Interpretation of the Respiratory System oriented to Pulmonary Diseases and Sleep Disorders
Coordinator researcher: Raimon Jané.
Participating PIs groups: P. Laguna, D. Navajas.

NAVISURG

Intelligent support and navigation assistance for safer image-guided surgery in pancreatic interventions
Coordinator researcher: Enrique Gómez (F. del Pozo research group).
Participating PIs groups: M. Doblaré, J.L. Peris, external research groups.

TEA

New Therapeutic Approaches for Retinal Degenerative Diseases
Coordinator researcher: Eduardo Fernández.
Participating PIs groups: J.L. Pedraz, J. Aguiló, R. Eritja, F. del Pozo.

B-CUBE

Microfluidic blood-brain barrier model for screening of novel pharmacological drugs
Coordinator researcher: Rosa Villa (J. Aguiló research group).
Participating PIs groups: F. Albericio, E. Fernández, J.L. Pedraz.

ULTRASEN-4BIO-2MD

Characterization and evaluation of novel ultrasensitive piezoresistive all-organic sensors for biomedical signals applied to multimodal diagnosis
Coordinator researcher: Raimon Jané.
Participating PIs groups: J. Veciana, M. Doblaré.

Recognized activity projects

MITP

Development of multimodal imaging tools for Parkinson's disease diagnosis
Coordinator researcher: Albert Cot (J. Pavía research group).
Participating PIs groups: A. Santos, external research groups.

INTER-CARDIO

Computer-assisted interpretation of electrical signals: a step forward in understanding and treating cardiac diseases
Coordinator researcher: Esther Pueyo (P. Laguna research group).
Participating PIs groups: M. Doblaré, R. Jané, A. Santos, external research groups.

PLADEBACT

Platform for Detection of Bacteria in Human Fluids
Coordinator researcher: Javier Reina (L. Roa research group).
Participating PIs groups: F. del Pozo, J. Aguiló, external research groups.

NATRIP

Disposable microsensor for direct detection of BNP by surface conductivity measurements
Coordinator researcher: Elisabet Prats (J. Aguiló research group).
Participating PIs groups: F. Albericio, M.P. Marco, M. Doblaré.

NEUROMON

Organotypic culture platform for long–term monitoring and control of directed neuroregeneration
Coordinator researcher: Vicent Esteve (B. Celda research group).
Participating PIs groups: M. Doblaré, S. Penadés, R. Martínez, L. Roa, J. Aguiló, external research groups.

ROBERT

ROBotic arm and high density Electromyography for upper- limb Rehabilitation and Therapy
Coordinator researcher: Mónica Rojas (R. Jané research group).
Participating PIs groups: E. Fernández.

DEMVAS

Vascular Cognitive Impairment. Advance analysis using Diffusion weighted images
Coordinator researcher: Raúl Tudela (J. Pavía research group).
Participating PIs groups: A. Santos.

Further information at the CIBER-BBN website:

http://www.ciber-bbn.es/es/proyectos-cientificos

BIOMATERIALS AND ADVANCED THERAPIES

Coordinator:

José Becerra Ratia

Bioengineering and Tissue Regeneration Laboratory of the Universidad de Málaga (LABRET-UMA)

The groups involved in this programme in 2014 were:

BIOMATERIALS AND ADVANCED THERAPIES GROUPS

PI	Name of the group
Manuel Doblaré	Structural Mechanics and Material Modeling Group of the Engineering Research Institute of Aragón, Universidad de Zaragoza (GEMM-I3A)
Margarita Calonge	Ocular Surface Inflammation & Advanced Therapies Groups of the Applied Opfhthalmobiology Institute (IOBA), Universidad de Valladolid (IOBA-UVA)
Cristina Ruiz	Tissue Bioengineering and Cell Therapy Group, Complejo Hospitalario Universitario A Coruña (CBTTC-CHUAC)
Juan Manuel Bellón	Translational Research Group in Biomaterials and Tissue Engineering, Universidad de Alcalá (GITBIT-UAH)
Nuria Vilaboa	Research Group in Bone Physiopathology and Biomaterials, Hospital Universitario La Paz (FIOBI-HULP)
Julio San Román	Polymeric Biomaterials Group of the Polymer Science and Technology Institute, Consejo Superior de Investigaciones Científicas (GBP-CSIC)
Elisabeth Engel	Research Group in Biomaterials, Biomechanics and Tissue Engineering, Instituto de Bioingeniería de Cataluña (GBBIT-IBEC)
Jose Luis Peris Serra	Health Technology Group, Instituto de Biomecánica de Valencia (GTS-IBV)
Daniel Navajas	Respiratory and Cellular Biomechanics Group, Universidad de Barcelona (GBRC-UB)
José Luis Gómez	Biomaterials Center, Universidad Politécnica de Valencia (CBM-UPV)
Isabel Obieta	Tissue Engineering Research Group of the Health Unit, Fundación Tecnalia (TECNALIA)
Jerónimo Blanco	Cell Therapy Group, Instituto de Química Avanzada de Cataluña del CSIC (TC-CIC)
María Vallet Regí	Research Group in Intelligent Biomaterials, Universidad Complutense de Madrid (GIBI-UCM)
Jose C. Rodríguez	GIR BIOFORGE, Universidad de Valladolid (BIOFORGE-UVA)
Mª Luisa González	Research Group on Microbial Adhesion, Universidad de Extremadura (AM-UEX)
Ángel Raya	Regenerative Medicine Center of Barcelona (CMRB)

Strategic lines of research of the programme

BM 1. GENE THERAPY AND CELL THERAPY:

- Stem and progenitor cells. Cellular reprogramming.
- Development of non-viral vectors for gene therapy.

Gene therapy and cell therapy are overlapping fields of biomedical research with the goals of repairing the direct cause of genetic diseases in the DNA or cellular population, respectively.

These powerful strategies are also being focused on modulating specific genes and cell subpopulations in acquired diseases in order to re-establish the normal balance. In many diseases, gene and cell therapy are combined in the development of promising therapies.

In addition, these two fields have helped provide reagents, concepts, and techniques that are elucidating the finer points of gene regulation, stem cell lineage, cell-cell interactions, feedback loops, amplification loops, regenerative capacity, and remodelling.

Specifically, Gene therapy is defined as a set of strategies that modify the expression of an individual's genes or that correct abnormal genes. Each strategy involves the administration of a specific DNA (or RNA).

Within this framework, CIBER-BBN's research groups are focused on finding an appropriate use of this novel strategy to deliver new and improved therapies. Viral gene transfer is relatively efficient but there are concerns relating to the use of viral vectors in humans. Conversely, non-viral vectors appear safe but inefficient. Therefore, the development of an efficient non-viral vector remains a highly desirable goal and has been recently adopted as part of CIBER-BBN's Research Programme.

On the other hand, Cell therapy is defined as the administration of live whole cells or maturation of a specific cell population in a patient for the treatment of a disease.

This research line involves (1) technologies used in cell therapy, including direct cell injection systems; bioreactors and in vitro pre-differentiation; combined drug-cell systems; controlled release systems; noninvasive follow-up and in vivo monitoring systems; (2) analysis of cell biophysical properties (cell channels, membrane and cytoskeleton mechanics, etc.), and its response to biophysical stimuli (cellular mechanotransduction, adaptation and plasticity) and (3) modelling the behaviour of the individual cell and of cell populations, down to the organization of tissues and organs.

This line of research has a huge development potential due to the enormous current and future interest of Regenerative Medicine.

BM2. TISSUE ENGINEERING:

- Biomaterials for scaffolds.
- Signalling biomolecules.
- Cellular and molecular functionalisation of biomaterials.
- Mechanobiology and Microfluidics.
- Decellularisation and recellularisation of organs and tissues.
- Generation of organoids from stem cells: Towards artificial organs.

A paradigm shift is taking place in orthopaedic and reconstructive surgery from using medical devices and tissue grafts to a tissue engineering approach that uses biodegradable scaffolds combined with cells or biological molecules to repair and/or regenerate tissues.

CIBER-BBN studies scaffold-based tissue engineering which includes the development of new materials for scaffolds; the design and use of bioreactors for cell culture; the analysis of the processes involved and the effect of different tissue regeneration stimuli on scaffolds, both in vitro and in vivo; the functionalisation of the scaffold surface; or non invasive follow up and in vitro and in vivo monitoring systems, among many others.

Two new concepts have been added as they are leading research lines in this field: (1) Decellularisation and recellularisation of organs and tissues and (2) generation of organoids from stem cells.

(1) A promising tissue-engineering / regenerative-medicine approach for functional organ replacement has emerged in recent years. Decellularisation of donor organs such as heart, liver, and lung can provide a natural three-dimensional biologic scaffold material that can be seeded with selected cell populations. Preliminary studies in animal models have provided encouraging results for the proof of concept. Some of CIBER-BBN's research groups are focused on studying it as significant challenges for three-dimensional organ engineering approach still remain.

(2) Generation of transplantable organs using stem cells is a desirable approach for organ replacement and some of CIBER-BBN's basic and clinical scientist have great interest on it.

BM 3. PROTHESES AND IMPLANTS:

- Modelling and biomechanics.
- System of treatment and surface functionalisation.
- Custom prosthesis. 3D Printing.

The global objective of this line is to move forward in a new generation of patient-specific prostheses and implants, with greater control over their behaviour and over the evolution of the organ after implantation.

Therefore, this line includes all those elements contributing to the improvement of implant design and features such as: advanced modelling, considering the implant-organ interaction (osseointegration, tissue adaptation, influence of drugs, etc.); systems for supporting surgical decisions; surface mechanization and functionalization systems; local and controlled drug release systems operating from the surface of the implant; biomaterials for implantation; intelligent prostheses (active monitoring and control), etc.

The intramural projects of the Biomaterials and Advanced Therapies programme during 2014 were:

Projects of excellence

MICROREN

Development of regenerative therapies for acute kidney injuries based on microfluidic devices filled with microencapsulated cells

Coordinator researcher: Luis Fernández (M. Doblaré research group).

Participating PIs groups: J.L. Pedraz, J. Aguiló, J. Santamaría, external research groups.

BIOMIMESH

New abdominal biomimetic prostheses to improve adaptation to host tissue properties. Application in hernia repair

Coordinator researcher: Juan Manuel Bellón.

Participating PIs groups: M. Doblaré, J. Aguiló, external research groups.

HOT-SCAFF

Plasmonic scaffolds for deliberate regulation of transgene expression in bone tissue engineering

Coordinator researcher: Nuria Vilaboa.

Participating PIs groups: J. Santamaría, J. San Román, J.C. Rodríguez, external research groups.

BIOSURFACES

Biofunctionalization of titanium implant surfaces: protein conformation, osseointegration and antimicrobial activity

Coordinator researcher: J.L. Gómez Ribelles.

Participating PIs groups: E. Engel, J.C. Rodríguez, M.L. González, B. Celda, N. Vilaboa, external research groups.

PSVALVE

Patient-Specific image-based computational flow dynamic simulations for assessment of optimal biological aortic Valve replacement selection and delivery

Coordinator researcher: Miguel Ángel Martínez (M. Doblaré research group).

Participating PIs groups: L. Martí-Bonmatí (associated clinical group), external research groups.

Recognized activity projects

NANOANTILATHIV

Dendron decorated mesoporous silica nanoparticles: new drug/siRNA nanocarrier against HIV-1 latency

Coordinator researcher: Blanca González (M. Vallet research group).

Participating PIs groups: R. Gómez, M.Á. Muñoz, R. Eritja.

EYE-POC

Point Of Care Biosensor Devices to Detect Biomarkers As Evaluation End-Points For Therapeutic Clinical Trials In Ocular Surface Inflammation

Coordinator researcher: Amalia Enríquez de Salamanca (M. Calonge research group).

Participating PIs groups: M.P. Marco, L. Lechuga, R. Eritja.

NAVITE

New nanoparticles based on Vitamin E for antitumor and hearing loss treatment

Coordinator researcher: M.R. Aguilar (J. San Román research group).

Participating PIs groups: N. Vilaboa, M.L. González, S. Schwartz, external research groups.

BIOWOUND

Bioactive materials for wound healing based on controlled ion release
Coordinator researcher: Soledad Pérez-Amodio (E. Engel research group).
Participating PIs groups: J. Blanco.

BIOROTATOR

Tendon Tissue Engineering for Rotator Cuff Tears
Coordinator researcher: Miguel Ángel Mateos (E. Engel research group).
Participating PIs groups: M. Doblaré.

3D-TIMPTE

3D custom-made porous titanium endoimplants combined with tissue engineering elements for mandible reconstructive surgery
Coordinator researcher: Leonor Santos (J. Becerra research group).
Participating PIs groups: I. Obieta, J.L. Peris, J. Blanco, M. Vallet, external research groups.

ToGlioTHER

Towards Clinical Stem Cell Glioblastoma Therapy
Coordinator researcher: Jerónimo Blanco.
Participating PIs groups: C. Arús, E. Engel, J. Santamaría, external research groups.

Further information at the CIBER-BBN website:

http://www.ciber-bbn.es/es/proyectos-cientificos

NANOMEDICINE

Coordinator:

María Pilar Marco.

Nanobiotechnology for Diagnostics. Advanced Chemistry Institute of Catalonia, CSIC (Nb4D-IQAC)

The groups belonging to the programme in 2014 were:

NANOMEDICINE GROUPS

PI	Name of the group
Jesús Santamaría	Nanostructured Films and Particles Group of the Nanoscience Institute of Aragón, Universidad de Zaragoza (NFP-INA)
Antonio Villaverde	Nanobiotechnology research group of the Biotechnology and Biomedicine Institute, Universidad Autónoma de Barcelona (NBT-UAB)
Ramón Eritja	Nucleic Acid Chemistry Group of the Institute for Advanced Chemistry of Cataluña, CSIC (GQNA-CSIC)
Jaume Veciana	Molecular Nanoscience and Organic Materials Group of the Materials Science Institute of Barcelona, CSIC (NANOMOL-CSIC)
Simó Schwartz	Drug delivery and Targeting Group, Hospital Universitario Vall d'Hebrón (GDLF-HUVH)
Félix Ritort	Small System and Biomolecule Physics Group, Universidad de Barcelona (BIOSMALL-UB)
Josep Samitier	Nanomedicine Group, Instituto de Bioingeniería de Cataluña (NANOMED-IBEC)
Fernando Albericio	Nanoparticle and Peptide Chemical Group, Instituto de Investigación Biomédica - IRB Barcelona
Fausto Sanz	Nanomembrane Group, Universidad de Barcelona (NANOMEMB-UB)
Laura M. Lechuga	Nanobiosensors and Bioanalytical Applications, Centro de Investigación en Nanociencia y Nanotecnología del CSIC ((CIN2)CSIC-ICN)
Soledad Penadés	Glyconanotechnology Laboratory, Biofunctional Nanomaterials Unit, CIC-Biomagune (LNB-CICBIOMAGUNE)
Rafael Gómez	Dendrimer Group for Biomedical Applications, Universidad de Alcalá (GDAB-UAH)
José Luis Pedraz	Micro and Nano technologies, Biomaterials and Cells Research Group (NANOBIOCEL)
Ramón Mangues	Oncogenesis and Antitumor Group of the Research Institute, Hospital de la Santa Cruz y San Pablo (GOA-HSCSP)
Mª Ángeles Muñoz	Molecular immunobiology laboratory, Hospital General Universitario Gregorio Marañón (LIBM-HGUGM)
Concepción Solans	Colloidal and Interfacial Chemistry Group of the Advanced Chemistry Institute of Cataluña, CSIC (QCI-CSIC)
Ramón Martínez	Applied Molecular Chemistry Group, Centro de Reconocimiento Molecular y Desarrollo Tecnológico de la Universidad Politécnica de Valencia (IQMA-IDM-UPV)

Strategic lines of research of the programme

NM 1. NANODIAGNOSIS:

- Development of biosensor devices based on micro / nanotechnologies to detect specific biomarkers of disease.
- Evaluation and validation of new biomarkers of disease through new strategies and devices based on micro / nanotechnologies.
- Development of new contrast agents.

Nanodiagnosis consists on developing systems and image analysis techniques both in vivo and in vitro for the early detection of disease, at cellular or molecular level.

One of the detection systems developed to date is based on diagnosis with nanoparticles (semiconductor, or magnetic metal) such as quantum dots that are used as cell labeling, identification of tumors or diseased areas.

Another line of action within this field is the diagnosis with nanobiosensors. These integrated nanoscale devices for a biological receptor (proteins, DNA, cells) are prepared to specifically detect a substance and a transducer or sensor, capable of measuring biomolecular recognition reaction and translate it into a measurable signal.

The use of these techniques would allow diagnosis with a more solid biological base and more reliable results, which would translate into greater precision in the diagnosis of different pathologies.

NM 2. THERAPEUTIC NANOSYSTEMS:

- Study and development of new agents (enzymes, proteins, nucleic acids...) and nanostructures with therapeutic properties.
- Development of nanosystems to improve pharmacokinetics and pharmacotherapy of therapeutic agents.

This line will concentrate on the development of new pharmacological therapies based on the intelligent design of guided nanoconjugates.

Therapeutic nanosystems research line includes both the development of pharmacological release systems optimized to traverse the blood-brain barrier, and the specific release of enzymes, proteins or gene inhibition strategies by means of siRNA.

The line must assure that toxicological and therapeutic activity data are obtained in all the newly designed nanoconjugates. The basic objective is to obtain suitable proofs of concept for therapy.

The development of therapeutic nanoconjugates and of local and controlled release systems for these nanoconjugates, would allow guiding the treatment to the area of action, in the attempt to achieve perfect control of the therapy, thereby preventing the action of the drug or therapeutic particle in areas that might entail a potential risk for the patient.

NM 3. NANOBIOTECHNOLOGY:

- Study of biocompatibility and toxicity of therapeutic nanosystems and nanodevices.
- Biological processes research (physiology, cell adhesion or communication, cell biophysics and epigenetic) and development of techniques for their study.
- Theranostic systems development.

Finally, NanoBiotechnology is a cross area focused on both basic and applied nanotechnology knowledge research to be used within Nanodiagnosis and Therapeutic nanosystems areas.

This research line includes the study of biocompatibility and toxicity of therapeutic nanosystems and nano-devices, the development of theranostic systems and the analysis of biological processes as physiology, cell adhesion or communication, cell biophysics or epigenetic.

The intramural active projects of the Nanomedicine programme during 2014 were:

Projects of excellence

NANOHYPERTHERMIA

Development of new nanoparticles and protocols for enhanced hyperthermia
Coordinator researcher: José Javier Serrano (F. del Pozo research group).
Participating PIs groups: R. Martínez, E. Fernández, external research groups.

MAGNETO-NH IA

Multiplexed determination of pathogenic bacteria in sepsis by novel magneto-nanohollows immunoassay
Coordinator researcher: Juan Pablo Salvador (M.P. Marco research group).
Participating PIs groups: J. Santamaría, F. Albericio.

TBIO-GATE

New nanoparticles containing bio-gated scaffoldings for tuberculosis diagnosis
Coordinator researcher: Ramón Martínez.
Participating PIs groups: M.P. Marco, R. Eritja.

OLIGOCODES

A universal Diagnostic Platform Based On Oligonucleotide Codified Nanoparticles and DNA Microarray Sensor Devices
Coordinator researcher: María Pilar Marco.
Participating PIs groups: J. Samitier, F. Albericio, R. Eritja, I. Obieta.

GLYCOHIV-3

Gold glyconanoparticles as non-viral platform for HIV vaccine candidates
Coordinator researcher: Soledad Penadés.
Participating PIs groups: B. Celda, external research groups.

NANOXEN++

Xenopus Tropicalis as a platform to test light-regulated drugs with applications in nanomedicine
Coordinator researcher: Pau Gorostiza (F. Sanz research group).
Participating PIs groups: R. Eritja, external research groups.

NANOMETS

Drug nanconjugates and nanovesicles for the treatment of metastatic colorectal cancer
Coordinator researcher: Ramón Mangues.
Participating PIs groups: A. Villaverde, R. Eritja, J. Veciana.

E-LEUKEMIA

The nanoconductance of redox proteins of the respiratory chain and its physiopathological implication in leukemia
Coordinator researcher: Pau Gorostiza (F. Sanz research group).
Participating PIs groups: J. Samitier, R. Mangues, external research groups.

NANOPROTHER

Cell-targeted nanomedicines base on therapeutic, protein-only nanoparticles
Coordinator researcher: Antonio Villaverde.
Participating PIs groups: J. Veciana, S. Schwartz, R. Eritja, R. Mangues, external research groups.

COLOCOMB

Combinatory and targeted nanomedicines for the treatment of advanced colorectal cancer
Coordinator researcher: Simó Schwartz.
Participating PIs groups: F. Albericio, M.P. Marco.

NANO-OPHTHAL

New si-RNA-nanoparticle conjugates for the treatment of ocular surface inflammations
Coordinator researcher: Santiago Sala (J. Veciana research group).
Participating PIs groups: R. Gómez, R. Eritja, M. Calonge, external research groups.

PCP-SENS

Development of a biosensing diagnostic tool for the fast identification of infection by Pneumocystis
Coordinator researcher: Laura Lechuga.
Participating PIs groups: R. Eritja.

DYNAMIC-VASC

Dynamic Molecular Bio–Interfaces for Controlled Environments Towards Vascular Morphogenesis
Coordinator researcher: Inma Ratera (J. Veciana research group).
Participating PIs groups: A. Villaverde, F. Albericio, N. Vilaboa, external research groups.

ORDECA

Organic Radicals and Radical Dendrimers as Contrast Agents in Magnetic Resonance Imaging
Coordinator researcher: José Vidal (J. Veciana research group).
Participating PIs groups: R. Gómez, F. Albericio, C. Arús, M. Á. Muñoz, external research groups.

Recognized activity projects

PENTRI

Personalized nanomedicine for triple negative breast cancer stem
Coordinator researcher: Simó Schwartz.
Participating PIs groups: A. Villaverde, F. Albericio, F. Ritort, external research groups.

SPRING

Gated Scaffolds for the PRevention of implant Infection
Coordinator researcher: Ramón Martínez.
Participating PIs groups: M. Vallet, J.L. Peris, I. Obieta.

NANO3B

Novel nanocarriers as delivery systems across the Blood-Brain barrier
Coordinator researcher: Concepción Solans.
Participating PIs groups: R. Eritja, F. Albericio, R. Gómez, F. Sanz, external research groups.

NANOLYSO

Nanomedicine-based enzyme replacement therapy for the treatment of lysosomal storage disorders
Coordinator researcher: Simó Schwartz.
Participating PIs groups: F. Albericio, F. Sanz, J. Veciana, A. Villaverde, R. Mangues, external research groups.

CHONDRONANONET

Nanopatterned Cell Carriers for Improved Architectural Communication Networks in Chondrogenesis towards Osteoarthritic Joint Repair
Coordinator researcher: Josep Samitier.
Participating PIs groups: F. Sanz, J. Becerra, J.L. Gómez, C. Ruiz, external research groups.

LINATO

Lipid nanoemulsions for therapeutic oligonucleotides
Coordinator researcher: Ramón Eritja.
Participating PIs groups: M.J. Alonso (grupo clínico vinculado), external research groups.

HEPATO-POC

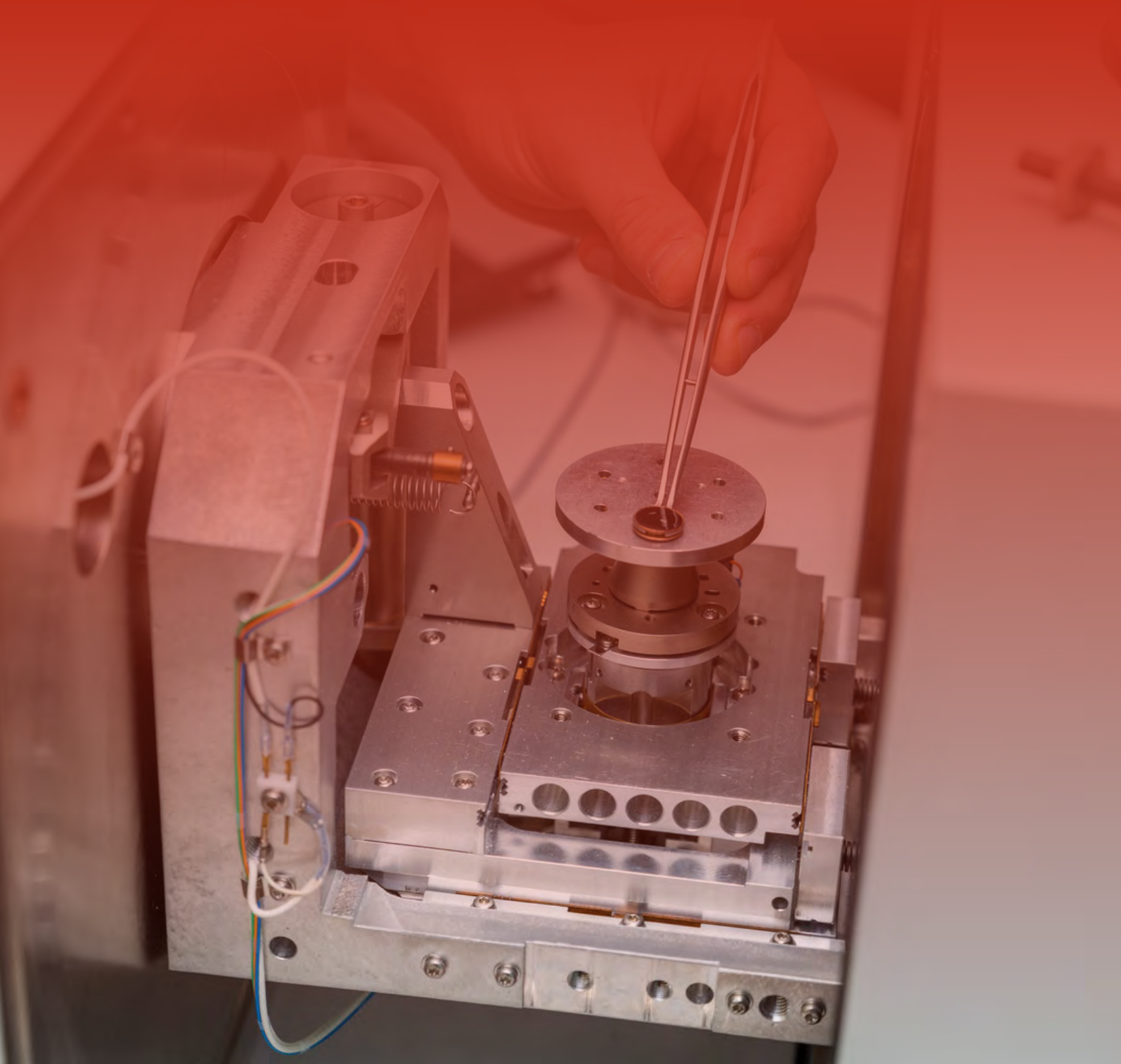
Advanced Diagnostic Tool for Early Identification of liver diseases and infections in intensive care units
Coordinator researcher: Laura Lechuga.
Participating PIs groups: M.P. Marco, M. Doblaré, external research groups.

NANOSENFIBRO

New Nanomaterials For Diagnosis And Treatment Of Idiopathic Pulmonary Fibrosis (IPF)
Coordinator researcher: Ramón Martínez.
Participating PIs groups: S. Penadés, S. Schwartz, J.L. Pedraz, external research groups.

Further information at the CIBER-BBN website
http://www.ciber-bbn.es/es/proyectos-cientificos

3. TRANSVERSAL PROGRAMMES



Patents and transfer results

In the year 2014, a license for the patent "Functionalized liposomes useful for the delivery of bioactive compounds" (PCT/EP2013/063646) has been granted to a pharmaceutical company.

Furthermore, 4 patentability studies were conducted in 2014. In addition, CIBER-BBN has also filed, throughout 2014, 1 Spanish patent application, 2 European patent applications, 4 PCT extension applications, and 1 application in 4 countries/regions (USA, Japan, China and Brazil) through patent entry into national phases. 2 Spanish patents were granted.

SPANISH PATENT APPLICATION:

- *Biovidrios y andamiajes bioactivos, procedimientos de preparación y usos de los mismos. P201400570 (10/07/2014).*

EUROPEAN PATENT APPLICATIONS:

- *Bioreactor for cell co-culture (EP14157145.5) (28/02/2014).*
- *Device for measuring the trans-layer electrical impedance in an in vitro model of a cell barrier) (EP 14170509.5) (29/05/2014).*

INTERNATIONAL PATENT APPLICATIONS PCT, CORRESPONDING TO FIRST (SPANISH OR EUROPEAN) PATENT APPLICATIONS MEETING YEAR OF PRIORITY:

- *Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa. PCT/ES2014/070161, fecha de solicitud: 04/03/2014.*
- *Hidrogeles plasmónicos basados en fibrina para la generación de hipertermia controlada. PCT/ES2014/070484 fecha de solicitud: 11/06/2014.*
- *Método de activación química superficial de un soporte sólido en base silicio mediante anclaje covalente directo de al menos una biomolécula de ácidos nucleicos. PCT/ES2014/070813 fecha de solicitud: 29/10/2014.*
- *Sensor Inteligente de bioimpedancia para aplicaciones biomédicas. PCT/ES2014/070822 070813 fecha de solicitud: 4/11/2014.*

INTERNATIONAL APPLICATIONS IN NATIONAL/REGIONAL PHASES:

- *Functionalized liposomes useful for the delivery of bioactive compounds. Applications filed in 4 countries/regions: USA (14/411,097; 23/12/2014), China (201380034806.6; 29/12/2014), Brazil (BR112014032919-2; 29/12/2014) Japan (25/12/2014, pending application number, to be issued by the Japanese Office).*

GRANT OF SPANISH PATENTS:

- *Péptido biomimético RGD con dominio de afinidad por el colágeno tipo i y sus usos como factor osteogénico. ES2417705B1 (20/05/2014).*
- *Medio de cultivo celular útil para la proliferacion in vitro de células del epitelio del limbo esclerocorneal. ES2409537B1 (24/04/2014).*

CIBER-BBN-Industry Forums and Clinical Forums

CIBER-BBN periodically organizes forums with companies and clinical forums to facilitate the identification of common interest and favor collaborations between companies, research groups and clinical professionals. An international CIBER-Company forum was held in 2014:

- "Brain Health and Neurorestoration" (Barcelona, 10/9/2014) organized with the collaboration of Instituto Guttmann, Universidad Autònoma de Barcelona and Universidad Miguel Hernández de Elche. 15 companies, 13 health care centres and 31 engineering/biomedicine/bioengineering academic centres participated in this international forum. From the 15 presentations, there were 2 keynote presentations by invited speakers, one concerning the next calls for proposal of the H2020 programme and the other concerning funding opportunities in H2020. The latter presentation was conducted by the European project, CoWin, coordinator. 15 bilateral interviews were held in the evening session.

Work for defining a clinical forum to be held in 2015 with Hospital Nacional de Parapléjicos de Toledo has been started.

Transfer project call for proposal

A new action already contemplated in the 2014-2017 Strategic Plan which consists of a technology transfer project call for proposal has been set in motion. Said technology transfer essentially requires the presented projects to include the participation of at least 2 CIBER-BBN groups along with a company. This company must provide 50% of the funding for the project to be carried out (the company must provide monetary contribution and not contribution in kind) while CIBER-BBN provides the remaining 50%.

In 2014, the projects of the call for proposal launched in 2013 have been resolved (based on the evaluation by the ANEP) and 3 of the 4 presented projects have been set in motion. For this reason, a collaboration agreement has been negotiated for every project between CIBER and the company regulating the participation conditions of each party. The funding provided by CIBER-BBN for carrying out the 3 projects is 270,000€ in 2 years. For reasons of confidentiality, no further information will be provided for these transfer projects.

A new call for proposal, resolved in 2015, was opened at the end of 2014. 6 new proposals were presented in said call for proposal.

Technology prioritization and assessment

A new process for prioritization and assessment of 11 CIBER-BBN technologies (patents and intramural projects) considering their transfer potential has been started in 2014. This process will end in 2015 and has 3 phases:

Phase I: Analysis of 11 technologies, prioritization by transfer potential and selection of 5 technologies with greatest potential for an in-depth evaluation.

Phase II: Comprehensive analysis of the 5 prioritized technologies, evaluating the main key factors of the 5 projects with greater market transfer potential in order to select the project having the greatest transfer potential.

Phase III: Preparation of a development plan so that the selected technology successfully reaches significant milestones which allow licensing it to an industrial partner.

Each technology will be evaluated from the technological offer viewpoint (evaluating the degree of development and technological competitiveness) and from the business demand viewpoint (evaluating the market needs, market size and value generating potential).

This process is being carried out with advice from a consultant specializing in strategic consultancy and project assessment.

Technological offer and congresses

Informative material in the form of leaflets, posters, patent and project flyers, etc., has been maintained with updated information of our technological offer and with all the service units grouped into a single infrastructure.

CIBER-BBN has participated in the following forums in which our technological offer was disseminated, establishing relations that may lead to future collaborations:

- European Infrastructure Conference, ESFRI, ISCIII, Madrid, January 2014.
- OFTARED-Cluster4eye Forum. ISCIII, Madrid, January 2014.
- ARTEMIS Pre-Brokerage Event 2014, Brussels, February 2014.
- H2020NMP Conference, Madrid, February 2014.
- 7th Annual Conference of Biomedical Research Technological Platforms: Innovative Drugs, Nanomedicine, Health Technology and Biotechnology Markets, Barcelona, March 2014.
- Market Access Topic Group Meeting, ASEBIO, Madrid, April 2014.
- Annual CEBR Meeting, Coimbra, April 2014.
- Internal CTLS Congress, Paris, June 2014.
- Life Sciences Introduction Conference: Investment opportunities, SF Biotech, Barcelona, June 2014.
- Life Sciences Workshop. Madrid Network–US Davis Research. CSIC, Madrid, June 2014.
- BIO International Convention, San Diego, USA, June 2014.
- Advanced Therapy Legislation Meeting, AEMPS, Madrid, July 2014.
- European Biomedical Investor Day, Biocat, Barcelona, September 2014.
- BIOSPAIN, Santiago de Compostela, September 2014.
- Advanced Therapy Conference, ISCIII, Madrid, October 2014.
- Flag-ERA Graphene Networking Event, Barcelona, October 2014.
- ETP Nanomedicine Annual Event and General Assembly 2014, San Sebastián, October 2014.
- Bio-Europe, Frankfurt, Germany, November 2014.
- Brockerage Event Nanofutures, Brussels, November 2014.
- CAT-Hearing with Interested Parties, EMA, London, UK, December 2014.

Other transfer actions

An agreement was signed in 2014 with the company, B-ABLE, which dedicates itself to the creation of spin-off companies based on potentially marketable technologies obtained in research centres.

Universidad Politécnica de Valencia (UPV) is currently negotiating the grant of a license for a patent co-owned by CIBER (of which UPV holds majority of the rights) with a company that Fundación Botín invested in as it has been chosen in the *Mind the Gap* selective programme promoted by this entity.

A new transfer initiative has been launched in 2014 in order to seek sponsorship for more mature technologies identified in the previous year during the CIBER-BBN patent and project portfolio prioritization process.

6 confidentiality agreements have been signed with several companies which are interested to learn more about the many different technologies and projects of CIBER-BBN.

Collaborative projects with clinical entities

A joint initiative between CIBER-BBN and Fundación para la Investigación Biomédica de Córdoba/Instituto Maimónides de Investigación Biomédica de Córdoba (FIBICO-IMIBIC) has been launched in 2014 to create new translational projects in different areas of interest for Hospital Reina Sofía de Córdoba. 2 multidisciplinary collaboration proposals were received of which funding is being given to the proposal rated best based on the opinion of independent specialists making up the evaluation panel.

As a continuity to the first collaboration initiative in the scope of respiratory pathologies (in the year 2012), the 2nd edition of this collaboration between CIBER-BBN, CIBERES (Respiratory Diseases) and Fundación SEPAR (Sociedad Española de Neumología y Cirugía Torácica) has been promoted in 2014, to support collaborative projects with the participation of research groups from the 3 entities. Of the 7 eligible projects, the 3 best evaluated projects (based on evaluation made by evaluators from the 3 institutions without any conflict of interest) have been selected to obtain funding.

The CIBER-BBN training programme seeks to increase research capabilities of personnel integrated in the groups by means of improving professional competency of technical and research personnel as a factor of change, transforming attitudes, knowledge and skills according to needs arising while conducting their research activity.

The CIBER-BBN training programme is based on three actions: aid for research initiation training, aid for mobility and the researcher qualification sub-programme.

Grants for research initiation training

The purpose of this "launching" grant is to cover the transitional period from the end of studies until the resolution of the public grant calls for pre-doctoral grants or other professional itineraries which involve recruiting a recent graduate into the work force.

In 2014 there were two grant calls in the months of March and September. There is still a large number of applications in each of the grant calls due to the interest this aid provokes in the research groups. Between the two grant calls, a total of 37 grants were awarded to the candidates with the best academic record and whose proposals were most consistent with the priority lines of research of the CIBER-BBN.

Year	No. of aid packages for "research initiation" granted
2011	19
2012	12
2013	15
2014	37

Grants for mobility

The purpose of this training programme is to encourage short internships in other research groups to aid in transferring experience and technology and to potentiate collaboration between different CIBER-BBN groups. These internships must be within the priority and strategic lines of work for our subject area.

In 2014 there were two calls for proposals for mobility (March and September) and a total of 17 grants were awarded for internships in groups outside CIBER-BBN.

With respect to grant packages for mobility for research personnel between CIBER-BBN groups, which has a permanent, year-round calls for proposal, two grants were awarded.

Year	No. of aid packages for intra-CIBER-BBN "mobility" granted	No. of aid packages for external "mobility" granted	Total no. of aid packages for "mobility" granted
2011	6	10	16
2012	6	9	15
2013	1	20	21
2014	2	17	19

Qualification 2014

Qualification Subprogramme implementation and management within the CIBER-BBN Training Programme, which seeks to potentiate research methodologies involving several groups in the priority lines for CIBER-BBN established in the 2014-2017 Master Plan, continued in 2014.

It is done through the provision of human resources to the groups in order to enhance the creation of said methodologies, seeking to complement the activity currently being conducted by the groups for fomenting collaboration possibilities and increasing consortium competitiveness. There is one person per group who belongs to this line of work.

The process comprises identifying senior researcher profiles that are already trained or are currently under training in fields complementary to the "know-how" of the group. Their integration will allow stepping into a multidisciplinary environment. This circumstance is considered key for obtaining relevant advances in the CIBER-BBN work areas and establishing the basis for forming long- and mid-term competitive groups.

8th Annual CIBER-BBN Conference

The 8th Annual CIBER-BBN Conference was held on 9, 10 and 11 November 2014 in Gerona.

The main objective of the conference was, once again, to favour the meeting of the groups, the identification of synergies and shared knowledge between members of the consortium, and to show the results of the collaborative research conducted in the framework of intramural projects.

About 200 people attended the conference, essentially members of CIBER-BBN groups, but also from other research institutions and centres.

The day before the conference started (November 9), the Scientific Director held a prior meeting with the PIs of the consortium at the same location where the conference was held. They discussed some of the ongoing actions of the CIBER-BBN launched within the new strategic plan, budget aspects, etc.

Two plenary sessions conducted by internationally relevant researchers were held. These two sessions were:

- *Overview of the development of nanomedicine in Europe and the next trends. Patrick Boisseau, European Technology Platform on Nanomedicine.*
- *Nanoparticulate biomaterials for gene and drug delivery. Matthias Epple, Centre for Medical Biotechnology, Universität Duisburg-Essen*.

As a novelty this year, presentations for projects and lines of research were grouped by pathologies. Therefore, there were sessions on neurology, respiratory diseases, infectious diseases, musculoskeletal diseases, ophthalmology, cardiology, implants, rare diseases, chronic diseases and oncology. Each session was moderated by a clinical specialist who analyzed the capability of translating and transferring the results to the clinical practice, indicating in some cases possible realignments of the project for the purpose of improving these aspects.

Furthermore, members of our Advisory Committees (External Scientific Committee and Advisory Medical Committee), with whom the Steering Committee held a meeting at the end of the event, also attended. The conference also included a poster session and a special session for showing new lines of research conducted by young researchers.

Events and activities

In 2014, CIBER-BBN attended a large number of internationally relevant scientific forums and meetings, some of the most representative of which are shown below.

- ARTEMIS Pre-Brokerage Event 2014 Brussels, February 2014.
- CEBR Annual Meeting, Coimbra, April 2014.
- Internal CTLS Congress, Paris, June 2014.
- Life Sciences Workshop. Madrid Network–US Davis Research. CSIC, Madrid, June 2014.
- BIO International Convention, San Diego, USA, June 2014.
- BIOSPAIN, Santiago de Compostela, September 2014.
- Flag-ERA Graphene networking event, Barcelona, October 2014.
- ETP Nanomedicine Annual Event and General Assembly 2014, San Sebastián, October 2014.
- Bio-Europe, Frankfurt, Germany, November 2014.

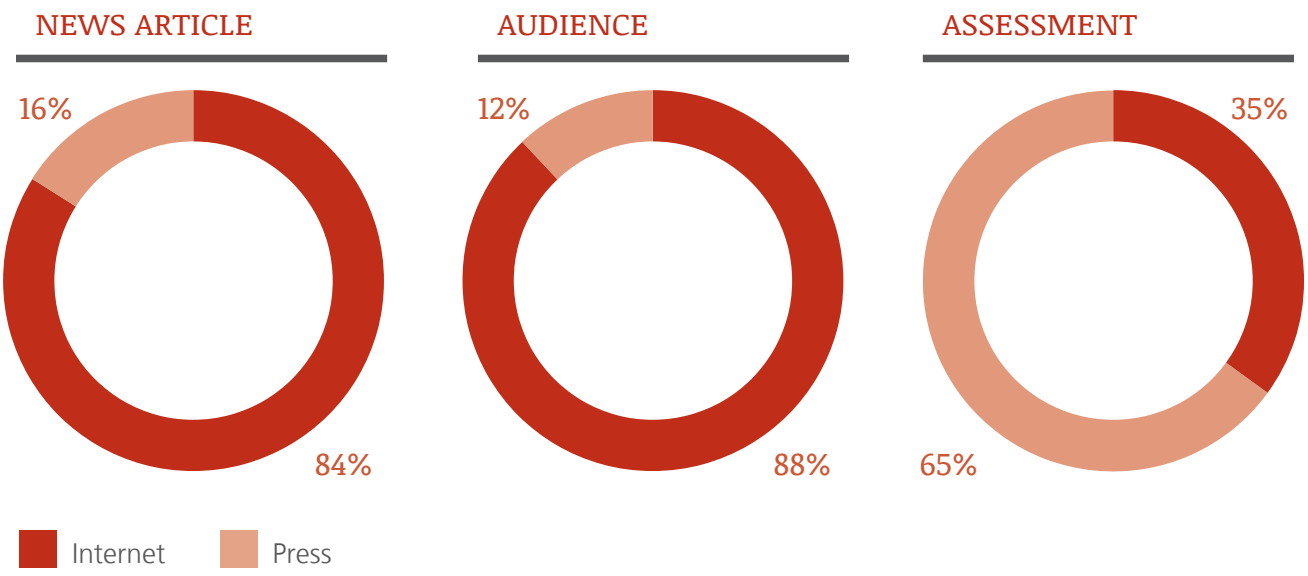
- Brokerage Event Nanofutures, Brussels, November 2014.
- CAT-Hearing with Interested Parties, EMA, London, UK, December 2014.

CIBER-BBN in the Press:

The following press releases were sent from CIBER-BBN in 2014, and 268 hits in the media, fundamentally online, were recorded.

- 14/04/2014 - "La Fundación ECO y el CIBER-BBN destinan 50.000 euros a proyectos de investigación oncológica" (Fundación ECO and CIBER-BBN give 50,000 Euros to cancer research projects)
- 10/09/2014 - "El primer Foro en Salud Mental y Neurorrehabilitación pone en común los proyectos más innovadores en este ámbito" (The first Mental Health and Neurorehabilitation Forum brings together the most innovative projects in this field)
- 10/10/2014 - "La plataforma del CIBER-BBN, NANBIOSIS, se incorpora al mapa actualizado de ICTS" (CIBER-BBN platform, NANBIOSIS, is incorporated in the updated ICTS map)
- 10/11/2014 - "Presentan un proyecto para identificar mecanismos comunes de las enfermedades neurodegenerativas y la diabetes en las jornadas del CIBER-BBN" (A project for identifying common mechanisms of neurodegenerative diseases and diabetes is presented at the CIBER-BBN conference)

	News Article	Audience	Economic Assessment*
INTERNET	226	33482200	335.032 €
PRESS	42	4605000	180.790 €
total	**268**	**38087200**	**515.822 €**



* Consists of the monetary value of each appearance in a media outlet. It is calculated according to the space of the news article in the media according to a publicity rate.

Most striking appearances in the media:

Date	Headline / topic approached	Mentioned member	No. of hits
03/01/2014	Nanomaterials will help to reduce cancer treatments	Juan Parra	27
08/09/2014	The first Mental Health and Neurorehabilitation Forum brings together the most innovative projects in this field.		27
05/12/2014	The loss of a gene contributes to colon cancer progression.	Diego Arango	25
14/04/2014	Fundación ECO and CIBER-BBN give 50,000 Euros to projects for potentiating translational research.	Pablo Laguna	17
10/10/2014	CIBER-BBN platform, NANBIOSIS, is incorporated in the updated ICTS map.		15
27/06/2014	"1,000 million Euros needed to compete with Korea in graphene".		12
11/10/2014	Centro de Cirugía de Mínima Invasión Jesús Usón joins the Scientific Infrastructure network in Spain.		12
11/11/2014	Search for common mechanisms between diabetes and neurodegenerative diseases.		12

Press clipping comprising all appearances in the press monthly can be consulted on the CIBER intranet.

Presence in Twitter (https://twitter.com/CIBERBBN) was maintained, the number of followers increasing up to more than 1,600.

	January 2014	December 2014
Updates	645	830
Followers	1267	1607
Klout (level of influence, values between 1 and 100)	42	45

Participation in dissemination events

SEMANA DE LA CIENCIA. ACTIVITY: *TAPACONCIENCIA.*

CIBER-BBN participated in the dissemination activity "TapaConCiencia" in the Semana de la Ciencia in Madrid with 250 participants. Eight research projects corresponding to the subject areas of the CIBER were disclosed in the activity and used as a source of inspiration for Chef Jorge Cuéllar to design 8 elaborate "tapas".

Researcher María Vallet-Regí represented CIBER-BBN presenting the project "Smart nanoparticles for attacking neuroblastoma cancer in children", which was accompanied by chocolate "nanoparticles" prepared by the chef.

The act raised a lot of interest among the general public as well as among the general media, scientific specialists and gastronomy specialists who interviewed the researchers participating in the activity.


ACTUALIDAD

Auténtica divulgación científica

Sardinas marinadas para la diabetes

Los beneficios del aceite de oliva en forma de gazpachuelo

Jorge Cuéllar preparó las propuestas

La noche de los Investigadores. *COMMHERE project*

The European project COMMHERE (Communicating European Health Research) organized a disseminating activity in the context of "La noche europea de los investigadores" (European Researchers Night http://www.madrimasd.org/lanochedelosinvestigadores/activities). Under the title "Cerveciencia", the activity consisted of a directed artisan beer tasting to go along with the presentation of three European projects in the health area.

Fernando Salvador Vélez, researcher on the European project called BERENICE -coordinated at the Hospital Vall d'Hebron of Barcelona and in which CIBER-BBN is a partner- shared with the attendees the work conducted in this project to develop a new drug for the treatment of Chagas disease that is more effective, less expensive and less toxic than the treatment currently used, making use of nanotechnology.

Other activities

2013 ANNUAL REPORTS

The CIBER-BBN Annual Report for the preceding period was written in 2014 and is available on the web page in an interactive format (Flipbook) and in pdf, both in English and in Spanish.

http://www.ciber-bbn.es/es/quienes-somos

http://www.ciberisciii.es/comunicacion/memorias-anuales

NEWSLETTERS

The CIBER newsletter was started in mid-2014, and it includes content relevant to both CIBER-BBN and to the other subject areas. The newsletter is sent every two months through the Mailchimp platform to a total of 4,240 subscribers. Three CIBER newsletters were written and distributed in 2014.

http://www.ciberisciii.es/comunicacion/boletines

NEWS UPDATE ON THE WEBSITE OF THE CIBER-BBN

The web page has been periodically updated from time to time to reflect the consortium's activity and news. http://www.ciber-bbn.es The most noteworthy news and events have been included on the web page www.ciberisciii.es along with those that stand out among the rest of the CIBER subject areas.

4. PLATFORMS

One of the global objectives of CIBER-BBN is to share resources and infrastructures between groups.

CIBER-BBN platforms are clusters of technical-scientific equipment with a specific functionality, intended for offering high-level technological resources to CIBER-BBN research groups and external groups, under the established conditions.

CIBER-BBN Platforms

HIGH-PERFORMANCE COMPUTING PLATFORM

Units:	• High-performance computing, massive storage and software unit for biomedical applications.
General Objective:	To provide technical support and advising for projects, especially those related to the line of Multimodal Diagnostics, allowing remote access to all users.
Purpose and functionality:	This platform provides service by means of remote access to run numerical model simulations requiring high-powered calculation: mesh processing, image segmenting, data and image or model simulation recording, finite elements simulation, 3D modelling.

BIOMOLECULE PRODUCTION PLATFORM

Units:	• Protein production • Antibody production • Peptide synthesis
General Objective:	To advise and provide a sufficient amount of biological molecules to correctly carry out intramural projects, provide external value-added services without creating a conflict with the existing business network, to keep activity outside the research activity of the coordinating group.
Purpose and functionality:	This platform provides biological molecules which are currently peptide and protein in nature and necessary for carrying out projects relating to the strategic lines of Smart Devices, Prostheses and Implants, Tissue Engineering, and especially Nanodiagnostics and Therapeutic Nanosystems. They offer services for the customized design and production of these elements for: • Functionalizing nanosystems • Functionalizing implants and prostheses • Providing essential elements in regenerative and angiogenic processes • Functionalizing surfaces

BIOMATERIAL AND NANOPARTICLE PRODUCTION PLATFORM

Units:	• Biodeposition and biodetection • Rapid prototyping • Molecular Biomaterial Processing and Nanostructuring • Nanolithography / E-beam • Micro/nanoelectronics • Nanoparticle synthesis • Drug formulation.
General Objective:	To advise and provide materials for correctly carrying out projects requiring them, keeping activity outside the research activity of the coordinating group and to provide external high value-added services, taking advantage of the experience of the groups to provide solutions to technological problem solving.

Purpose and functionality:	This platform provides both 2D and 3D materials and constructions that provide support to projects primarily comprised in the Biomaterials and Advanced Therapies Programme, specifically in the lines of Prostheses and Implants and Tissue Engineering, and in the line of Nanomedicine, especially in Therapeutic Nanosystems. It provides services for: • Functionalizing devices and biosensors by means of dispensing solutions • Surface treatments to favour integration; coating implants and prostheses with bioactive factors • Creating 3D matrices with materials such as polymers, ceramics and composites; preparing scaffolds or prototypes for testing; or even functionalizing by adding stem cells • Production and characterization of pure nanometric-sized drug substances, vesicular systems, nanosuspensions or compounds formed by a biocompatible polymer and a drug substance • Synthesis of particles and functionalized surfaces • Pilot-scale preparation and characterization of molecular materials with a controlled micro-nano- and supramolecular structure with different functionalities • Repeatedly stamping dies of various composites to study the behaviours of cells or other elements given these situations; implant integration assays; prototyping and manufacturing micro/nano arrays of electrodes for implants • Growth of materials on surfaces improving the bio-electronic interface in recording biomonitoring signals • Producing micro-/nano-structures present in microelectronic devices and surface characterization

TISSUE, BIOMATERIAL AND SURFACE CHARACTERIZATION PLATFORM

Units:	• Nanostructured liquid characterization • Tissue characterization • Magnetic nanoparticle characterization, guiding and locating • Surface characterization and calorimetry • Confocal microscopy • Nanotoxicology
General Objective:	To provide characterization services for materials, biological tissues and nanosystems developed in intramural projects and within CIBER-BBN groups.
Purpose and functionality:	This platform provides characterization support for the materials obtained in the Material Production Platform, among others. Its functions are: • Characterization of the functional behaviour of 2D and 3D constructions as tissue scaffolds from the mechanical, structural and microstructural point of view • Morphological and mechanical-structural characterization of biological tissues • Characterization of the surface composition and structure of materials and biological solutions (containing bioactive factors or cells). • Real time in vitro and ex vivo study of cell and tissue behaviour, respectively, in response to the potential therapeutic agents identified, as well as to identify and locate the targets of said agents • Characterization of intermolecular interactions, material functionalization quality control • Conducting the in vitro and in vivo toxicological studies necessary for assuring that the new materials are innocuous

BIOIMAGING PLATFORM

Units:	• In vivo experiments • NMR: Biomedical applications I • NMR: Biomedical applications II
General Objective:	To provide support to the preclinical development of research projects for identifying new therapeutic compounds by means of validation studies of new therapeutic targets and/or nanotherapies by means of NMR and optical imaging technologies, in addition to collaborating with hospitals and other centres of the National Health System and with pharmaceutical companies in diagnostic research activities.
Purpose and functionality:	The functions of this platform include: • Analysing the phagocytic behaviour and interactions of cells in response to therapeutic magnetic nanoparticulate agents; establishing possible infections due to magnetotactic bacteria • Spectroscopies for in vivo applications; applications in fluids, tissues, and biomaterials • Validating, viewing, following up on and quantifying, in vivo and in real time, the therapeutic factors used, as well as analysing treatment-induced tissue regeneration • Validating new therapeutic targets using NMR and optical imaging technologies • Viewing, following up on and quantifying cellular and genetic activities relating to pathologies in a living organism in real time

COLLABORATION WITH OTHER PLATFORMS:

- Platform of the Instituto Universitario en Nanociencia de Aragón (INA)
- Centro de Cirugía de Mínima Invasión Jesús Usón
- Unidad de Imagen de CIC biomaGUNE
- BIONAND (Centro Andaluz de Nanomedicine y Biotecnología)

Internal evaluation of the units continued in 2014 to assign economic incentives according to the activity performed in the preceding year. The internal evaluation protocol was maintained and also applied 2014.

A year later, the search for external funding from both public and private sources was a priority in 2014. The Platform Programme was presented in international partnering events and entities, as well as in national companies, private research foundations and public research entities. Promotional material was distributed at different company visits, research centres and industrial associations, as well as through participation in the Spanish Technological Platform MATERPLAT, the Spanish Biotechnology Platform, the Council for European Bioregions (CEBR) and the recently created European project called IN2LifeSciences (IN2LS), which promotes new relationships between small- and mid-sized enterprises on one hand, and research entities on the other. Participation in international infrastructures, such as Eurobioimaging, was also promoted. Meetings were held with the manager of Eurobioimaging in Spain for a more in-depth study of how we fit in and we signed the Memorandum of Understanding, expressing our interest in the creation of same.

We attended the following events:

- European Infrastructure Conference, ESFRI, ISCIII, January 2014, Madrid.
- H2020 NMP Conference, February 2014, Madrid.
- Annual Meeting of Biomedicine Platforms, March 2014, Barcelona.
- Annual CEBR Meeting, April 2014, Coimbra (Portugal).
- Internal CTLS Congress, June 2014, Paris.
- Biospain, September 2014, Santiago de Compostela.
- ETPN Annual Meeting, October 2014, San Sebastián.
- Brokerage Event Nanofutures, November 2014, Brussels.

The process for becoming an ICTS (Singular Scientific and Technological Infrastructure) was successfully culminated. A response to allegations with respect to a series of comments about the request submitted by CIBER-BBN together with the Centro de Cirugía de Mínima Invasion Jesús Usón (Cáceres) for recognition of research service infrastructure of both entities as a Singular Scientific and Technological Infrastructure (ICTS) was prepared in 2014. Said request was favourably resolved in October 2014, and NANBIOSIS (Infrastructure for the Production and Characterization of Nanomaterials, Biomaterials and Systems for application in Biomedicine) was recognized as an ICTS. Furthermore, several meetings were held with MINECO. The Consolidation Agreements as an ICTS between both Centres was written, and work is being done on said consolidation process. Actions were instituted to create a web page, informative dossier, etc.

Information about the programme on the web page has been permanently updated such that the most recent information about the services and conditions are available for internal and external research groups and companies.

Follow up on collaborations that started with companies was performed. Some examples are the PHYTECH project (INNPACTO programme), in which two Spanish companies and a unit (Surface Characterization and Calorimetry) are involved, the European project called BERENICE (Benznidazole and triazole nanoformulation for treating Chagas disease), involving 2 units (Molecular Biomaterial Processing and Nanostructuring Unit and the Drug Formulation Unit), or the project called TERET (RETOS-COLABORACIÓN programme), which includes the participation of two companies (Sylentis and LeadArtis) together with the Drug Formulation Unit and two more CIBER-BBN groups, among others.

The new strategic action launched in 2011 to improve equipment platforms for developing collaboration projects with companies and with the participation of one or more Programme units continued in 2014.

In an attempt to promote collaborations with companies, making our services more appealing, the line for supporting ISO 9001 standard certification for interested units was continued. It was consolidated in 2014 with the certification process of two units (Protein Production Platform and In vivo Experiment Unit) and the process for Nanostructured Liquid Characterization Unit and Surface Characterization Unit began.

Participation in European initiatives was maintained. Some examples are:

- ETP Nanofutures (www.nanofutures.eu)
- IN2LifeSciences (IN2LS)
- ARBRE (Association of Resources for Biophysical Research in Europe)

5. TECHNOLOGICAL OFFER

TECHNOLOGICAL OFFER

Following the process for protecting inventions, abstracts were prepared with non-confidential information of these patent applications, updating the technological offer of the CIBER-BBN:

DELIVERY OF SUBSTANCES TO SENESCENT CELLS

Spanish Patent Application P201231370

International Patent Application PCT/ ES2013/070581

This invention refers to nanodevices for controlled and specific delivery of substances (drugs, bio-actives, markers, cosmetics) to senescent cells. The nanodevice comprises a carrier enclosing the cargo and allowing its liberation when targeted cells are reached, by means of the interaction with senescence-associated beta-galactosidase (SA-ß-Gal). Therefore, it is useful for senescence studies, prevention and treatment of senescent-associated diseases. Besides others where ß-Gal is specifically present or increased.

The invention also comprises preparation procedures and uses of the nanodevice. The invention belongs to the pharmaceutical and cosmetic fields.

FUNCTIONALIZED LIPOSOMES USEFUL FOR THE DELIVERY OF BIOACTIVE COMPOUNDS

Licensed patent

International Patent Application PCT/EP2013/063646

National phase in Europe, USA, Japan, China, Russia and Brazil

The present invention is related to a new kind of functionalized liposome, for the selective delivery of active agents. This liposome carries a conjugate, by means of functionalizing the sterol present in its lipid bi-layer with a polymer, linked by a no-carbamate bond (differing from the state of the art). Besides, the polymer is also functionalized with a guiding ligand. This conjugate improves the physical-chemical properties of its carrying vesicles, making these more stable and homogeneous. A procedure for their preparation, a pharmaceutical composition containing these liposomes, and their therapeutic use are described as well.

AMPHIPHILIC COPOLYMERS WITH ANTITUMORAL PROPERTIES

Spanish Patent Application P201230679

International Patent Application PCT/ES2013070287

The present invention describes the use of a family of amphiphilic co-polymers that form micro- or nano-micelles, with intrinsic anti-tumoral activity, and also serving as vehicles for other anti-tumoral agents.

BIOMIMETIC PEPTIDE AND ITS USE AS OSTEOGENIC FACTOR

Spanish Patent ES 2417705 B1

International Patent Application PCT/ES2013/000007

The present invention comprises a peptide with osteogenic capacity, the sequence of nucleotides codifying for this peptide, as well as a genetic construction containing said sequence, a vector containing said construction or sequence, and a host cell containing this vector. The invention also comprises the use of the peptide, or its pharmaceutical compositions, for bone regeneration or coating of implants and prostheses.

COMPOUND MATERIAL BY POLYMER AND METALLIC PARTICLES FOR BIOMEDICAL APPLICATIONS

Spanish Patent ES 2372341 B1

The present invention refers to a material with a polymeric matrix and metallic particles. It provides a biocompatible and bio-degradable material for the manufacturing of useful devices for medical applications such as material for bone-synthesis and tissue engineering for the regeneration of bone tissue.

A first aspect of the present invention refers to a material comprising a biodegradable polymer and metallic particles. A second aspect of the present invention refers to a procedure for obtaining the biomaterial. A third aspect of the present invention refers to the use of this biomaterial for the manufacture of an implant or biomedical device for the repair and regeneration of bone tissue.

DEVICE AND METHOD FOR INTAKE MONITORING

Spanish Patent ES 2353711 B2

The invention consists in a method of transparent monitoring of the intake, a monitoring device and a method to associate overall weight variations to individual containers. Transparent monitoring is that where the guest has meals in the most possible similar way to a situation in the absence of monitoring. This is a historical challenge for intake monitoring.

The present invention proposes a method and a device for the transparent intake monitoring. A solution for the transparent monitoring of the intake is achieved because the method can, at any moment, automatically associate the weight variation, detected by a sole measurement in a containers bearing surface, to the container where it was originated.

The invention also comprises a monitoring device specifically designed for this kind of measurements and association.

LIPOPHILIC DERIVATIVES OF NUCLEIC ACIDS

Spanish Patent ES2368300B1

In this invention, new siRNA derivatives are described, which facilitate siRNA cellular administration, and are more stable to nucleases, what makes them more effective for the inhibition of gene expression. These siRNA duplex can be transfected into human cells, efficiently entering the cells where they triggers the siRNA mechanism, in a similar way to the unmodified ones, including the specific inhibition of the gen with the complementary sequence to the siRNA.

Synthesis procedures are described as well. Moreover, another aspect of the invention is the pharmaceutical compositions containing, at least, an excipient or pharmaceutical vehicle. An excipient comprises any inert material used in the preparation of a form for dosage. A particular kind of excipients is the transfection agents, which improves the vector properties.

The administration of these compounds can be oral, parenteral, intravenous, intramuscular subcutaneous, intra-duodenal, etc.

MAGNETIC-LUMINESCENT PARTICLES FOR BIO-MEDICALS APPLICATIONS

Spanish Patent ES 2367959 B1

The authors have developed a system of magnetic-luminescent particles, with a size inferior to three microns, and the procedure for its preparation. They can present a luminescence of high efficacy in the near infrared spectrum and in the whole visible one, from 400 to 1500 nm (blue to near IR). The luminescence can last until one week after the synthesis. The particle surface can be modified by linking

molecules or functional groups, forming a biocompatible coating. In vitro assays have shown that both types of particle functionalized or not, are not cytotoxic. These studies also shown that these particles can be efficiently internalized into the cells, through interaction with specific membrane receptors. The viability rate of the cells, in the presence of these particles, was 95-98%, after 72 hours in culture. This invention also provides pharmaceutical formulations including active biological molecules in these particles.

MESENCHYMAL CELLS AND A COMPOUND MEMBRANE FOR THE TREATMENT OF OSTEOCHONDRAL LESIONS

Spanish Patent ES2380674 B1

The present invention provides and efficient product for the cellular therapy of articular cartilage lesions, which is prepared in vitro, and is based in autologous adult mesenchymal stem cells and a biomaterial with a new fibrillar organization in the shape of a compound membrane.

Thanks to this product, in the chondro-osteo-articular lesion a regenerative tissue is formed equal to the adjacent cartilage in the three cartilaginous strata, and equal to the subchondral bone in the organization of the cells, and in the amount and quality of either the cartilaginous or the bone surrounding matrix. The generated tissue integrates in a permanent way in the receptor tissue, and, besides, it is functional regarding its response to loads.

The authors of the present invention have demonstrated that this product allows the formation of cartilage in a natural way, therefore the new tissue is formed de novo, and integrates in the treated tissue, allowing a stable, long-lasting, and functional regeneration. That is, the product allows a intra-tissue, rather than a lesion, repair.

Therefore, a first aspect of the present invention refers to a composition comprising mesenchymal stem cells and a compound membrane. The term "compound" make reference to that the membrane presents at least two layers with different structure. A second aspect of the present invention refers to the use of the pharmaceutical composition to prepare a drug for the treatment of a cartilage lesion, for the regeneration of the cartilage, for the treatment of a bone lesion, for the regeneration of the bone, for the treatment of a osteochondral lesion, for the treatment of osteoarthritis, for the regeneration of the cartilage. A third aspect of the present invention refers to an obtaining method for the pharmaceutical composition of the invention.

MODIFIED OLIGONUCLEOTIDES AS REGULATORS OF GENE EXPRESSION

Spanish Patent ES2372237B1

In the present invention, new siRNA compounds are described, which are more stable and efficient in inhibiting gene expression. The synthesis procedures for oligoribonucleotides containing chemical groups are also described.

The presence of these groups improves the thermodynamic stability of the siRNA duplex. These duplexes can transfect human cells, and the conjugates efficiently enter in the RNA mechanism of interference, in a similar way to the unmodified ones, inducing specific inhibition of the gene with the complementary sequence to the siRNA. Besides, the modified siRNA have a higher stability to nucleases present in serum than the unmodified ones. Therefore, those described in this invention can keep the gene silencing for a longer time than those unmodified. Another aspect is the pharmaceutical compositions containing these siRNA compounds and, at least, an excipient or pharmaceutical vehicle, and the use of these compounds or their pharmaceutical compositions for the preparation of drugs.

The excipients include any inert material used for the preparation of a composition for pharmaceutical dosage. A particular excipient is the transfection agents that increase the vector properties of the composition. The preferred administration of the pharmaceutical compositions of this invention is oral or parenteral.

NEW DELIVERY SYSTEM OF THERAPEUTICS TO COLORECTAL CANCER CELLS

European Patent Application EP2011382005.4

International Patent Application PCT/EP2012/050513

National phase in Europe, USA, Japón, China, India, Australia, and Israel

A new drug delivery system for the selective treatment of colorectal tumor cells has been developed. So far, in vivo delivery tests have been successful, showing specific and receptor mediated cell internalization of payload vehicles in tumor and metastasis tissues at low doses.

Furthermore, carriers have shown high stability into the animal, without apparent toxicity.

OCULAR DEVICE

Spanish Patent ES 2370014 B2

International Application PCT/ES2012/070474

US Application number 13/534,583

The present invention describes a device useful for retinal re-attachment and its post-surgery treatment. It belongs to the micro- and nano-technologies for health and biomedical applications, particularly to the optimization of ophthalmological surgery, as well as to patient post-surgery conditions.

The device, provided by this invention, keeps the retinal hole closed and improves the well-being of patient after surgery. Its components are intra-ocularly injected and placed in the tear zone closing the retinal holes causing the detachment.

It was tested in rabbits. Results showed a 90% success in the retina re-attachment after one week. Furthermore, no side effects have been detected.

The high incidence of retinal detachment places this pathology as a priority for ophthalmologists, particularly the technological challenge of achieving an efficient system to close the break due to retinal hole.

OPTIMIZED HISTOLOGICAL METHOD FOR THE PRESERVATION OF EPITOPES AND CELLULAR ARCHITECTURE OF VERTEBRATE TISSUES

Spanish Patent ES 2363551 B2

This invention develops an optimized new method for the histological and histochemical preservation of tissue. This method is compatible with any staining method for histological sections, as well as for immuno-localization and in situ hybridization.

The optimization with respect to the present techniques is achieved by the combination of fixing and inclusion conditions, and the use of the appropriate chemicals and materials for fixation and inclusion, allowing a very high preservation of the morphology and reactive properties of the tissue. Sections have been processes for immuno-staining and in situ hybridization, and the results compared with control techniques. The method in this invention improves most of the present histological methods designed for optical microscopy, and constitutes a good alternative to classical histological methods.

PROCEDURE FOR OBTAINING A BIOMATERIAL WITH METALLIC COATING

Spanish Patent ES 2372340 B1

The present invention refers to a procedure for obtaining a biomaterial with biocompatible metallic coating, by means of a metallurgic method. Besides, the present invention refers to the use of this biomaterial for medical applications.

A first aspect of the present invention refers to a procedure for obtaining the biomaterial, the parameters influencing the final properties of the biomaterial and coating. The parameters are optimized according to the desired final composition and properties of the material. A second aspect of the present invention

refers to the biomaterial itself obtainable by the procedure of the invention. A third aspect of the present invention refers to the use of the biomaterial for the manufacture of an implant or biomedical device, such as dental or orthopaedic implant, knee, shoulder, or elbow prostheses.

PROCEDURE TO SHAPE THE SURFACE OF CURABLE MATERIALS

Spanish Patent ES 2370690 B2

Lens, optical cavities, and curve mirrors, from millimetric to nanometric size, to be apply in industries such as optic, photonic, electronic, communication, optoelectronic, etc.

Cell cultures substrates: Substrates topographically modified have shown a better cellular behaviour, improving adhesion, growth or differentiation.

Chemical and biochemical micro-reactors: Confinement systems, from millimetric to nanometric size, for processes requiring space restrictions, such as crystallization, chemical or biochemical reactions, biological, cellular or bacterial systems, etc. microchips and micro-arrays, for biology, biochemistry, medicine, biotechnology, etc.

ANTIBODIES FOR THE DETECTION AND QUANTIFICATION OF ANTICOAGULANTS

Spanish Patent Application P201231836

International Patent Application PCT/ES2013/070816

The present invention is related to the design of haptens structurally related to oral coumarin-like anticoagulants, (CAC) in order to be used for the production of specific antibodies against such substances. Furthermore, to be used for the development of point-of care (PoC) devices. Particularly, a diagnostic tool has been developed for the quantification of plasma levels of CAC in treated patients.

CELL CULTURE DEVICE

Spanish Patent Application P201230911

International Patent Application PCT/ES2013/000141

The present invention refers to an encapsulated device (lab-on-chip) useful to study cell cultures. It is preferably made of a plastic material where several culture wells are located. Bottoms of wells are covered with a gelled material, differing from mechanical properties in each well. The objective of the invention is the production of high throughput analytical systems capable of studying the cellular response depending on the gelled substrate rigidity.

MICRO-CHAMBER DEVICE FOR CELLULAR CULTURE MONITORING BY NUCLEAR MAGNETIC RESONANCE

Spanish Patent ES2365282B1

The present invention comprises a micro-chamber device for cell culture allowing longitudinal long-term monitoring of the cellular system by nuclear magnetic resonance (NMR) and other image techniques. Image analysis and metabolic studies can be performed.

Effect of active agents, such as drugs, nanoparticles or biological factors, can be assessed. By using it, a better knowledge of physiological and pathological conditions will be acquired, helping for diagnosis and therapy.

CHAMBER DEVICE FOR DYNAMIC CELL CULTURE ON BIOMATERIALS

Spanish Patent Application P201330040

International Patent Application PCT/ES2013070819

This new device is composed by a chamber where 2D or 3D biomaterials can be immobilized. Cells from

different sources can be cultured on these materials using different flow conditions allowing the manipulation of cell behavior as a function of physical stimulation, and mimicking the physiological conditions.

The chamber is made of a transparent material allowing the visualization of cultured cells by microscopic techniques. Furthermore, the chamber is hermetically sealed thereby keeping controlled conditions.

The present invention has application in the tissue engineering field, as well as for the characterization of the cell response to a wide range of biocompatible materials.

HAPTENS, ANTIBODIES, AND METHOD TO DETECT PSEUDOMONAS AERUGINOSA INFECTIONS

Spanish Patent Application P201330312

International Patent Application PCT/ES2014/070161

The present invention is related to the design of haptens, structurally related to pyocyanin, a toxin secreted by the Gram negative bacterium Pseudomonas aeruginosa, and its derivatives. It is also related to the hapten conjugates used for the production of specific antibodies against such substances. Furthermore, the invention refers to a method and a kit for the detection and quantification of pyocyanin and its derivatives, using the mentioned antibodies, to detect infections due to *Pseudomonas aeruginosa*.

FIBRIN HYDROGELS WITH PLASMONIC NANOPARTICLES

Spanish Patent Application P201330894

International Patent Application PCT/ES2014/070484

The invention relates to a photothermal device comprising plasmonic nanoparticles embedded in a hydrogel made of fibrin matrix that in addition may entrap thermosensitive effectors. Irradiation of the device with near infrared light of specific wavelength and energy level increases the temperature of the composite. This photothermal device can be implanted and then irradiated on demand, providing a reliable source of heat in biological tissues. Localized photothermia can be used to remotely control the delivery of therapeutic agents from the device. The invention is useful for the application of hyperthermia-based therapies and controlled delivery of therapeutic agents in biological tissues.

METHOD FOR DIRECT COVALENT ANCHORING OF NUCLEIC ACIDS TO SOLID STANDS

Spanish Patent Application P201331587

International Patent Application PCT/ES2014/070813

Development of efficient superficial chemical functionalization for the production of DNA microarrays on solid stands has become essential for the improvement of DNA chip technology.

The present invention is related to a method for the superficial chemical activation of a silicon base solid stand by means of direct covalent anchoring of oligonucleotides, with no use of crosslinkers or catalysts. To date, chips where oligonucleotides and stand surface are directly linked without intermediary have not been reported. The product obtained by this method is the first one.

The invention focuses on the use of click chemistry reactions to both immobilize covalently and spatially locate nucleic acid probes on a silicon base stand. Also it focuses on the method to modify these probes in order to allow the anchoring.

INTELLIGENT BIO-IMPEDANCE SENSOR FOR BIOMEDICAL APPLICATIONS

Spanish Patent Application P201301062

International Patent Application PCT/ES2014/070822

It is a portable sensor that measures bio-impedance in a part of the body, an organ, a tissue or a fluid, allowing continuous monitoring of physiological variables and health condition.

The sensor is in contact with the biological environment to be measured through four electrodes, in a way that both, injects electrical current inside the biological environment and measures the tension produced by the said current circulation. It is capable of taking bio-impedance measurements for multiple frequencies, processing data to obtain both magnitude and phase of bio-impedance for every frequency, and transmitting the results wirelessly, according to the whole operation of the (1) sensing, (2) processing data, (3) wireless communication, (4) timing (5) data storage, and (6) energy subsystems.

This device is useful in the areas of mHealth, eHealth, information and communications technology, biomedical engineering and medical technology.

BIOREACTOR FOR CELL CO-CULTURE

European Patent Application EP14157145.5

The invention relates to a cell co-culture bioreactor comprising at least first and second cell culture chambers, said chambers being separated by a porous membrane for cell culture. Said membrane forms a single part with its sealing gasket which, in turn, defines a closed perimeter demarcating a first cell culture area.

The bioreactor can bring together several membranes parallel to one another to form additional culture chambers. In this invention the concept of "cell co-culture" is not limited to two different cell types but rather relates to two, three or more cell types. The bioreactor allows the separate analysis of each cultured cell type, in addition to the paracrine influence between them.

The bioreactor is compact, versatile and allows cell co-culture in an easy and simple manner, optimising both cultured cell viability and the time required for conducting assays.

DEVICE FOR MEASURING TRANSCELLULAR ELECTRICAL IMPEDANCE IN IN VITRO CELL BARRIER MODELS

European Patent Application EP14170509.5

Cell (endothelial or epithelial) barrier dysfunction is a characteristic of a number of diseases. A common technique for quantitatively evaluating cell barrier integrity without affecting cell physiology is based on the study of passive electrical properties of cells. Measuring transcellular electrical impedance provides a quantifiable value of the state of the barrier.

The present invention allows studying different in vitro cell barrier models by means of a device comprising two chambers, where cells are cultured, and an interdigitated electrode array on the inner surfaces of the chambers. It also comprises elements for the electrical connection to an impedance measurement apparatus and to an electroporation apparatus.

BIOACTIVE GLASS AND SCAFFOLDS, METHODS OF PREPARATION AND USES THEREOF

Spanish Patent Application P201400570

This invention relates to bioactive materials for being used in biomedical technologies for tissue regeneration and engineering. It particularly relates to bioactivo glass and to three-dimensional networks or bioactive glass scaffolds. Furthermore, the invention relates to methods of preparation and to uses thereof in regeneration, particularly in bone tissue engineering.

The primary objective of this invention is the design and preparation of a new bioactivo glass that is able to provide active biological signals to favour cell adhesion, migration, proliferation and differentiation by creating better cell stimuli and a better capability of detecting biological needs or changes in the environment.

6. RESEARCH GROUPS

Biomonitoring Group

Programme: Bioengineering and Medical Imaging

Lead Researcher: Aguiló Llobet, Jordi

Group Members

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Main lines of research

GBIO Research Group: New technologies, devices and systems for biomonitoring.

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

- Ventayol M., Vinas J.L., Sola A., Jung M., Brune B., Pi F. et al. MiRNA let-7e targeting MMP9 is involved in adiposederived stem cell differentiation toward epithelia. Cell Death and Disease. 2014;5(2).
- Del Campo F.J., Abad L., Illa X., Prats-Alfonso E., Borrise X., Cirera J.M. et al. Determination of heterogeneous electron transfer rate constants at interdigitated nanoband electrodes fabricated by an optical mix-and-match process. Sensors and Actuators, B: Chemical. 2014;194:86-95.
- Silve A., Guimera Brunet A., Al-Sakere B., Ivorra A., Mir L.M. Comparison of the effects of the repetition rate between microsecond and nanosecond pulses: Electropermeabilization-induced electro-desensitization?. Biochimica et Biophysica Acta - General Subjects. 2014;1840(7):2139-2151.
- Guimera X., Moya A., Dorado A.D., Villa R., Gabriel D., Gabriel G. et al. Biofilm dynamics characterization using a novel DO-MEA sensor: mass transport and biokinetics. Applied Microbiology and Biotechnology. 2014;99(1):55-66.
- Esteve V., Berganzo J., Monge R., Martinez-Bisbal M.C., Villa R., Celda B. et al. Development of a three-dimensional cell culture system based on microfluidics for nuclear magnetic resonance and optical monitoring. Biomicrofluidics. 2014;8(6).

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Nanoparticle and Peptide Chemical Group

Programme: Nanomedicine

Lead Researcher: Albericio Palomera, Fernando

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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 olidoethylene 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) or OEG dendrimers, as nanomedicine for the advanced colorectal cancer treatment. Study of the use of these platforms on monotherapy and combined therapy .
- Multiple ligands as chemical tools to study various biological processes, for example: G protein-coupled receptors (GPCRs) oligomerization.
- Design and synthesis of a bicomponent thermoreversible hydrogel platform which combines the bioactive peptide dendrimer decorated hyaluronic acid with the thermoresponsive hyaluronic acid for developing scaffolds for tissue engineering with application to regenerative medicine (bone and cartilage regeneration).
- Development of protein drug delivery systems (PEGylation, peptide functionalized nanovesicles) for substitutive therapy (ie: Fabry disease).
- Design and synthesis of gamma peptides with capacity to cross biological barriers, such as the cytoplasmatic membrane of eukaryotic cells and parasites (Leishmania) and the blood brain barrier (BBB).
- Development of new 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

- Góngora-Benitez M., Tulla-Puche J., Albericio F. Multifaceted roles of disulfide bonds. peptides as therapeutics. Chemical Reviews. 2014;114(2):901-926.
- Pulido D., Albericio F., Royo M. Controlling multivalency and multimodality: Up to pentamodal dendritic platforms based on diethylenetriaminepentaacetic acid cores. Organic Letters. 2014;16(5):1318-1321.
- Fransen P., Pulido D., Sevrin C., Grandfils C., Albericio F., Royo M. High control, fast growth OEG-based dendron synthesis via a sequential two-step process of copper-free diazo transfer and click chemistry. Macromolecules. 2014;47(8):2585-2591.
- Just-Baringo X., Albericio F., Álvarez M. Thiopeptide engineering: A multidisciplinary effort towards future drugs. Angewandte Chemie - International Edition. 2014;53(26):6602-6616.
- De la Torre C., Casanova I., Acosta G., Coll C., Moreno M.J., Albericio F. et al. Gated mesoporous silica nanoparticles using a double-role circular peptide for the controlled and target-preferential release of doxorubicin in CXCR4-expresing lymphoma cells. Advanced Functional Materials. 2014.

Highlights

In 2014, the peptide and nanoparticles group has published a total of 60 publications in international journals, some of them are high impact factor publication (Angewandte Chemie, Chemical Reviews, Advanced Functional Materials, Macromolecules...) Some of these publications described the synthesis of diverse marine-derived drugs with potent antitumoral properties. Others describe the use of a new family of oligoethylene glycol based dendrimers on diverse applications. In addition, Fernando Albericio Palomera, IP of the group, was honored with the "Premio a la Excelencia Investigadora 2014" from RSEQ and the "Premio a la Excelencia en Investigación" GEPRONAT 2013, in recognition of his career research.

During this year, financial resources have been provided by various national and international agencies that include four national grants and a private foundation project. The group has three collaborative projects with pharmaceutical and biotech companies founded by competitive grants (NANOCARDIOCOCO, HUMANFARMA and MARINMAB, INNPACTO-MINECO). The group also applied and granted other two national collaborative project (RETOS-COLABORACION RTC-2014-2557-1 and TERARMET) that were initiated in 2014. Furthermore, in 2014 has began the PENTRI project focused on the development of personalized nanomedicine for breast cancer founded by the La Marató de TV3 2012 call. In addition, the group was granted with Technology Transfer Project from the CIBERBBN,(LIPOCELL), focused on the development of a protein delivery system for Fabry disease. In the frame of the LIPOCELL project, a patent from our group, in collaboration with other CIBER BBN groups, was licensed to Biopraxis.

Collaborations have been established and continued at the national environment (IBEC, IRB, Hospital Vall d'Hebró, CIB-CSIC, Universitat Autònoma de Barcelona, Universitat de Barcelona, Universidad de Santiago de Compostela) and international levels (Chile, Argentina, Brasil, Portugal, Netherlands, Belgium, South Africa and Denmark) ,as well as, several collaborative projects being carried out with companies from the pharmaceutical and biotechnology sectors.

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Research Group in Biomedical Applications of Nuclear Magnetic Resonance

Programme: Bioengineering and Medical Imaging

Lead Researcher: Arús Caraltó, Carles

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Main lines of research

The major research interest of our group is the improvement of non-invasive diagnosis and prognosis of anomalous brain masses by nuclear magnetic resonance (NMR), as well as the development of non-invasive therapy response monitoring tools for cerebral tumors. Within this major goal, several sublines with connections to the MR methodology or other pathologies are being investigated, which include:

- 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).
- Classifier development and their implementation into decision-support systems (DSS) for helping in clinical decision making in an evidence-based medicine context.
- Search for molecular biomarkers of in vivo tumor progression/therapy response with the help of ex vivo and in vitro studies of cell models, animal models and their biopsies.
- In vivo molecular phenotyping of tumor progression and therapy response.

Most relevant scientific articles

- Candiota A.P., Acosta M., Simoes R.V., Delgado-Goni T., Lope-Piedrafita S., Irure A. et al. A new ex vivo method to evaluate the performance of candidate MRI contrast agents: A proof-of-concept study. Journal of Nanobiotechnology. 2014;12(1).
- Julia-Sape M., Majos C., Camins A., Samitier A., Baquero M., Serrallonga M. et al. Multicentre evaluation of the INTERPRET decision support system 2.0 for brain tumour classification. NMR in Biomedicine. 2014;27(9):1009-1018.
- Delgado-Goni T., Julia-Sape M., Candiota A.P., Pumarola M., Arús C. Molecular imaging coupled to pattern recognition distinguishes response to temozolomide in preclinical glioblastoma. NMR in Biomedicine. 2014;27(11):1333-1345.
- Mora P., Majos C., Castaner S., Sanchez J.J., Gabarros A., Muntane A. et al. 1H-MRS is useful to reinforce the suspicion of primary central nervous system lymphoma prior to surgery. European Radiology. 2014;24(11):2895-2905.
- Chavarría L., Romero-Giménez J., Monteagudo E., Lope-Piedrafita S., Córdoba J. Real-time assessment of 13C metabolism reveals an early lactate increase in the brain of rats with acute liver failure. NMR in Biomedicine. 2014;28(1):17-23.

Highlights

Among the most relevant achievements of 2014, we would like to highlight that we have had 50 user groups of the "Unidad de RMN aplicaciones Biomédicas I. Plataforma de Bioimagen", among them, CIBER groups, users of the consortiated institution, as well as public and private research centers and hospitals. The platform has generated a revenue of 104.896,91 €. The platform has the scientific support of the GABRMN-UAB (http://gabrmn.uab.es/).

With respect to research projects, the GABRMN-UAB participates in the European Union Marie Curie ITN TRANSACT (http://www.transact-itn.eu/), and during 2014 we have organised the Mid-term review meeting (1st-2nd December) as well as the"Scientific Workshop on Spectra classification and decision-support tools in the clinic", on the 3rd and 4th of December, at the Campus Hotel of the UAB (http://gabrmn.uab.es/transact_workshop), with the participation of renowned international experts from the area of pattern recognition and decision-support applied to magnetic resonance data.

With respect to the training capacity of the group, one PhD thesis was completed (Myriam Dávila Huerta) and we hosted one PhD student from the University of Bern (Sreenath Pruthvi Kyathanahally), in the frame of the TRANSACT project. One of our PhD students (Nuria Arias Ramos), obtained a fellowship "Estancias Breves MINECO", to visit the research group of Prof. Ralph Mason, at the UT Southwestern, in Dallas.

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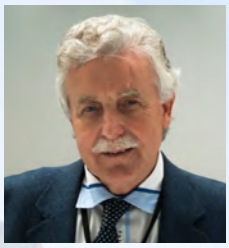
Tissue Bioengineering and Regeneration Laboratory, LABRET-UMA

Programme: Biomaterials and Advanced Therapies



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CONTRIBUTORS: Belmonte Urbano, Rosa Mª | Cosano Moncada, Ángel | López-Puerta González, Jose Mª

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 functionalizatión 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

- Visser R., Arrabal P.M., Santos-Ruiz L., Fernández-Barranco R., Becerra J., Cifuentes M. A collagen-targeted biomimetic RGD peptide to promote osteogenesis. Tissue Engineering - Part A. 2014;20(1-2):34-44.
- Rivera P., Arrabal S., Cifuentes M., Grondona J.M., Pérez-Martín M., Rubio L. et al. Localization of the cannabinoid CB1 receptor and the 2-AG synthesizing (DAGLα) and degrading (MAGL, FAAH) enzymes in cells expressing the Ca2+-binding proteins calbindin, calretinin, and parvalbumin in the adult rat hippocampus. Frontiers in Neuroanatomy. 2014;8(JUN).
- Algarra M., Pérez-Martín M., Cifuentes-Rueda M., Jiménez- Jiménez J., Esteves Da Silva J.C.G., Bandosz T.J. et al. Carbon dots obtained using hydrothermal treatment of formaldehyde. Cell imaging in vitro. Nanoscale. 2014;6(15):9071-9077.
- Tomé M, Sepúlveda JC, Delgado M, Andrades JA, Campisi J, González MA et al. miR-335 correlates with senescence/aging in human mesenchymal stem cells and inhibits their therapeutic actions through inhibition of AP-1 activity.Stem cells (Dayton, Ohio). 2014;32(8):2229-44.
- Ramiro-Gutiérrez M.L., Will J., Boccaccini A.R., Diaz-Cuenca A. Reticulated bioactive scaffolds with improved textural properties for bone tissue engineering: Nanostructured surfaces and porosity. Journal of Biomedical Materials Research - Part A. 2014;102(9):2982-2992.

Highlights

During 2014, the group has published a total of 11 papers, with several in Q1 and 3 of them in D1. Papers belong to basic and preclinical research. One of them is an international collaboration, two are intraCIBER colaboration, other two are interCIBER colaboration and several are national colaboration. Several members of the group have been authors of several articles in international books. We have sent one patent for registration concerning a new biomaterial for bone regeneration.

Regarding to the research projects, we got several new competitive projects from public national and regional agencies. We maintain partnerships within the intramural projects, particularly intense with the groups led by J Blanco, JA Planell, JL Peris, Samitier and JL Gomez. In the context of the intramural projects our group is leading one of them, 3D-TImpTE, and we have got funding associated with such project from the Junta de Andalucia in the call of 2014. The group has attended to the call for TECHNOLOGY TRANSFER PROGRAM in two of them, recently approved. We have sent a EUROPEAN PROYECT entitle: STEMRELEASE – The biomaterials-based toolkit of scaffolds enabling effective MSCs therapies. This project has recently passed the first review.

The group maintains the following international collaborations: A. H. Reddi, University California, Davis, P. Ferretti, London University College, E. Lucarelli, Istituti Ortopedici Rizzoli, Bologna, Italy (EU project appllication), A. Bader, BBZ Leipzig, Germany.

Several members within our group are promoter, coordinator and teacher of Masters and PhD Program "Advanced Biotechnology", are speakers at international forums, members of international scientific associations, etc.

The leader of the group has been asked by the media and appeared in newspapers, radio and TV as the coordinator of the Biomaterials Program of the CIBER-BBN or related to the research of their own group.

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Translational Research Group in Biomaterials and Tissue Engineering

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Bellón Caneiro, Juan Manuel

Group Members

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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 bioprostheses as well as composites meshes and prosthetic materials with polymeric coatings that can reduce inflammation, accelerate healing process or prevent contamination are currently being assayed.
- 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.
- Vascular repair. Work has been conducted within this line in healing/ restenosis, with special interest in the modulation thereof, concluding that intimal hyperplasia is a result of the vascular wall healing process, which has the objective of maintaining homeostasis of the damaged vessel. 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.

- Osteogenic regeneration. This research line was introduced in our department recently as a result of collaboration with the group COFIBIC, coordinating group, of an autonomic project BIOINTEL, that has continued with another project, "BITI" award in 2010 until 2014. We have worked on the regeneration of bone defects using tissue engineering techniques and on the biocompatibility of bone substitutes in different experimental models.

Most relevant scientific articles

- Pascual G., Pérez-Kohler B., Rodríguez M., Sotomayor S., Bellón J.M. Postimplantation host tissue response and biodegradation of biologic versus polymer meshes implanted in an intraperitoneal position. Surgical Endoscopy and Other Interventional Techniques. 2014;28(2):559-569.
- García-Moreno F., Sotomayor S., Pérez-López P., Pérez-Kohler B., Bayon Y., Pascual G. et al. Intraperitoneal behaviour of a new composite mesh (Parietex™ Composite Ventral Patch) designed for umbilical or epigastric hernia repair. Surgical Endoscopy. 2014.
- Simon-Allue R., Pérez-López P., Sotomayor S., Pena E., Pascual G., Bellón J.M. et al. Short- and long-term biomechanical and morphological study of new suture types in abdominal wall closure. Journal of the Mechanical Behavior of Biomedical Materials. 2014;37:1-11.
- Maldonado A.A., Cristóbal L., Martín-López J., Mallen M., García-Honduvilla N., Buján J. A novel model of human skin pressure ulcers in mice. PLoS ONE. 2014;9(10).
- Pérez-Rico C., Pascual G., Sotomayor S., Asunsolo A., Cifuentes A., García-Honduvilla N. et al. Elastin development-associated extracellular matrix constituents of subepithelial connective tissue in human pterygium. Investigative Ophthalmology and Visual Science. 2014;55(10):6309-6318.

Highlights

The third year of the coordinated national project DPI2011-27939-C02-02, "Diseño de prótesis biomiméticas con adaptación a las propiedades del tejido receptor", included in our main line of research in abdominal wall hernia repair, as part of the CIBER intramural project ABDOMESH/BIOMIMESH, has been carried out successfully during 2014. One contract of transfer (Art. 83), related to prosthetic infection, with the company Covidien, has finished and another project signed with LifeCell, on the behavior of different biological collagen prostheses, has been developed. This research line has had a significant scientific productivity during 2014, with a total of ten publications (three of them included in 1st JCR quartile (Q) and 5 in the 2nd Q). In connection with this research line, several communications have been presented to the 16th Annual Hernia Repair and 36th International Congress of the European Hernia Society, held in Las Vegas and Edinburgh and to the III International Conference on Antimicrobial Research held in Madrid.

Regarding our research line in repair of skin defects, a paper in PLoS One (1ºQ) on a new pressure ulcer model in mice was published. During this year a major contract of transfer with the company Novartis, in the field of drug healing, has been developed.

Respect to the research line of vascular repair, during 2014 the first year of the National Research Project on venous insufficiency, funded by the Instituto de Salud Carlos III (PI13 / 01513) was carried out successfully. Several communications have been presented to the 30th Meeting on Vascular Research LIAC held in Valladolid.

In November 2014 a national patent application (P201431678) entitled "Methods of cell removal" has been presented in collaboration with the National Institute for Research and Agricultural and Food Technology (INIA).

Additionally, an article in the IOVS journal (1ºQ) has been published and a communication has been presented to the 8th European Elastin Meeting, related to ocular pathology.

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Cell Therapy Research Group

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Blanco Fernández, Jerónimo

Group Members

STAFF MEMBERS: Garrido López, Cristina Pilar

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CONTRIBUTORS: Aguilar Bohorquez, Elisabeth | Alieva Kraseninnikova, María | Meca Cortés, Óscar

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.
- SYSTEMS BIOLOGY AND THERAPEUTIC TARGET IDENTIFICATION OF METASTATIC CANCER STEM CELLS In this line of research, we generate and characterize cell models through the manipulation of genes known or suspected to confer metastatic cancer stem cell (CSC) properties to tumor cells. The characterizations include phenotypic analysis in vitro and in mouse xenograft models, whole transcriptomic analysis (microa-

rray and RNAseq), metabolomics, glycolytic flux balance analysis and integrative data analysis. The goals are the identification of new biomarkers of tumor progression, tested on human samples, and new therapeutic targets, validated by RNAi or specific drugs, with emphasis on metabolic regulators that are differentially activated in metastatic CSCs or non-CSCs.

- 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

- Aguilar E., Bago J.R., Soler-Botija C., Alieva M., Rigola M.A., Fuster C. et al. Fast-Proliferating adipose tissue mesenchymal-stromal-like cells for therapy. Stem Cells and Development. 2014;23(23):2908-2920.
- Vila O.F., Martino M.M., Nebuloni L., Kuhn G., Pérez-Amodio S., Muller R. et al. Bioluminescent and micro-computed tomography imaging of bone repair induced by fibrin-binding growth factors. Acta Biomaterialia. 2014;10(10):4377-4389.
- Reyes D., Ballare C., Castellano G., Soronellas D., Bago J.R., Blanco J. et al. Activation of mitogen-and stress-activated kinase 1 is required for proliferation of breast cancer cells in response to estrogens or progestins. Oncogene. 2014;33(12):1570-1580.
- Habel N., Vilalta M., Bawa O., Opolon P., Blanco J., Fromigue O. Cyr61 silencing reduces vascularization and dissemination of osteosarcoma tumors. Oncogene. 2014.
- Cuenca-López M.D., Andrades J.A., Gómez S., Zamora-Navas P., Guerado E., Rubio N. et al. Evaluation of posterolateral lumbar fusion in sheep using mineral scaffolds seeded with cultured bone marrow cells. International Journal of Molecular Sciences. 2014;15(12):23359-23376.

Highlights

The Cell Therapy Group is involved in two general aspects of cell therapy: regenerative medicine and cell based tumor therapy, as well as, in the advancement of our understanding of the interactions between stem cells and tumor cells. The main advances of the team during 2014 were: in cell therapy, the completion of the work characterizing a new cell type, "Fast Proliferating Mesenchymal Stem Cells" (FP-MSCs) derived from human mesenchymal cells from adipose tissue (hAMSCs), whit a replication capacity 3,5 fold faster than that of the parental type. Such cells are expected to be useful in therapeutic strategies requiring large numbers of cells. In tumor therapy, it has been shown that FP-MSCs expressing HSV thymidin kinase have a capacity equivalent to that of hAMSCs for bystander killing of tumors. Moreover, a project showing that the repeated application of FP-MSCs is able to "chronify" or keeps inhibited, a glioblastoma tumor implanted in the mouse brain. In support of our hypothesis that hAMSCs nest in the tumor vascular system, more precisely, in the tumor stem cell niche, we have completed a project showing that the selective elimination of CD133+ tumor stem cells is sufficient to inhibit a tumor of human glioma implanted in the brain of an immune depressed mouse.

During 2014 the research team has been supported by a project from MINECO, the Cell Therapy Network "TerCel" and an internationalization project with India for the use of photodynamic therapy against tumors. Additional support has been provided by a "Retos Colaboración" project with Instituto Químico de Sarria and the SAGETIS company.

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Ocular Surface Inflammation & Advanced Therapies Groups

Programme: Biomaterials and Advanced Therapies

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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

- Benito M.J., González-García M.J., Teson M., García N., Fernández I., Calonge M. et al. Intra- and inter-day variation of cytokines and chemokines in tears of healthy subjects. Experimental Eye Research. 2014; 120:43-49.
- López-Miguel A., Teson M., Martín-Montánez V., Enríquez-De-Salamanca A., Stern M.E., Calonge M. et al. Dry eye exacerbation in patients exposed to desiccating stress under controlled environmental conditions. American Journal of Ophthalmology. 2014;157(4).
- Arranz-Valsero I., Soriano-Romani L., García-Posadas L., López-García A., Diebold Y. IL-6 as a corneal wound healing mediator in an invitro scratch assay. Experimental Eye Research. 2014; 125:183-192.
- Martín-Montánez V., López-Miguel A., Arroyo C., Mateo M.E., González-Meijome J.M., Calonge M. et al. Influence of environmental factors in the in vitro dehydration of hydrogel and silicone hydrogel contact lenses. Journal of Biomedical Materials Research - Part B Applied Biomaterials. 2014; 102(4):764-771.
- García-Posadas L., Contreras-Ruiz L., Arranz-Valsero I., Lopez-Garcia A., Calonge M., Diebold Y. CD44 and RHAMM hyaluronan receptors in human ocular surface inflammation. Graefe's Archive for Clinical and Experimental Ophthalmology. 2014;252(8):1289-1295.

Highlights

PROYECTOS INTRAMURALES

- BioScaff-EYE: "Bio-engineered stem cell niches in ocular surface reconstruction for corneal blindness: from basic research to clinical trials", coordinated by IOBA-UVa was transferred to Ferrer Advanced Biotherapeutics (FAB). Three groups: IOBA-UVa, Valladolid (PI M.Calonge), IBEC-Barcelona (PI E.Engel), and NanoBioCel (PI JL.Pedraz), are closely working with CIBER-BBN and FAB to lead this project to the desired end at maximum speed. As a result in vitro studies concluded and animal studies were well advanced in 2014, and the project is ready to apply for a POC clinical trial along 2015. Additionally, IOBA-UVa finished in 2014 the first double-masked randomized clinical trial to report safety and efficacy of mesenchymal stem cells (MSC) in human ocular surface. The positive results of this trial facilitate immensely the clinical translation of this project. Due to the signed non-disclosure agreement, dissemination of results is not yet allowed. Patents are being prepared but not released during 2014.
- EYE-PoC: "Point-of-care biosensor devices to detect biomarkers as evaluation end-points for therapeutic clinical trials in ocular surface inflammation" was granted in 2014. It's coordinated by IOBA-UVa, the clinical group (PI A. Enríquez-de-Salamanca) and teamed with NB4D-CISC (PI R. Galve, E. Valera), CIN2-CISC (PI L. Lechuga) and GQNA-CISC (PI A. Aviñó). During 2014, a selection of 4 candidate molecules to be placed in PoC devices was possible by analyzing a broad database of previous clinical studies. Time to disseminate results has been insufficient.
- NANO-OPHTHAL: "New si-RNA-nanoparticle conjugates for the treatment of ocular surface inflammations", granted as "excelent project" during 2014, is coordinated by Nanomol-CISC (PI S. Sala/ J. Veciana) and teamed with GDAB-UAH (PI J.de-la-Mata), GQNA-CISC (PI R. Eritja), IOBA-UVa as clinical group (PI M. Calonge) and external group (R. Herrero). Experimental work has just begun trying to conjugate siRNA targeting TNFalpha using tears. Time to disseminate results has been insufficient.

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Bioengineering and Telemedicine Group

Programme: Bioengineering and Medical Imaging

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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

- Riera J., Cabanas F., Serrano J.J., Bravo M.C., López-Ortego P., Sánchez L. et al. New time-frequency method for cerebral autoregulation in newborns: Predictive capacity for clinical outcomes. Journal of Pediatrics. 2014;165(5):897-902.e1.
- Oropesa I., Sánchez-González P., Chmarra M.K., Lamata P., Pérez-Rodríguez R., Jansen F.W. et al. Supervised classification of psychomotor competence in minimally invasive surgery based on instruments motion analysis. Surgical Endoscopy and Other Interventional Techniques. 2014;28(2):657-670.
- Capel I., Rigla M., García-Sáez G., Rodríguez-Herrero A., Pons B., Subías D. et al. Artificial pancreas using a personalized rule-based controller achieves overnight normoglycemia in patients with type 1 diabetes. Diabetes Technology and Therapeutics. 2014;16(3):172-179.
- Sánchez C., Ramos J.A., Fernández T., del Pozo F., Serrano J.J. Photoacoustics of gold nanorods under low frequency laser pulses in optical hyperthermia. IFMBE Proceedings. 2014;41:868-871.
- Félix-Gonzalez N., Urbano-Bojorge A.L., Sánchez-L de Pablo C., Ferro-Llanos V., del Pozo-Guerrero F., Serrano-Olmedo J.J. Power absorption measurements during NMR experiments. Journal of Magnetics. 2014; 19(2):155-160.

Highlights

- Development of a pancreatic ex vivo in a porcine animal model for registration of preoperative imaging and laparoscopic ultrasounds within the surgical navigation environment NAVISurg
- Development of a prototype for freehand laparoscopic ultrasound 3D image reconstruction.
- Publication of the results of the artificial pancreas clinical trial (NCT01614496) demonstrating that the pRBA (Predictive Rule-Based) algorithm maintains normoglycemia over 95% during the night time without an increased risk of hypoglycemia in T1DM patients.
- Design of transcranial magnetic stimulation actuators, approved by the AGEMED and CE marking for clinical use in fibromyalgia.
- Development of a model of focal cerebral ischemia in mice by occlusion of the middle cerebral artery. Study of alterations in the somatosensory cortex using evoked potentials.
- Development of an injectable system based on fibroin hydrogels for stereotactic implantation of stem cells in the brain parenchyma

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G. Structural Mechanics and Materials Modeling

Programme: Biomaterials and Advanced Therapies

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Main lines of research

- Modeling and simulation of the functional behavior 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 remodeling, bone healing and bone morphogenesis, implant osteointegration and wound healing, taking into consideration the effect of the mechanical environment in cell response.
- Tissue engineering, analyzing the design of ceramic, polymeric and biological scaffolds and meshes in tissue regeneration, including the interaction scaffold-tissue.
- Cell biophysics, studying cell transduction and signaling 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, etc. for the study of cell biology under in vitro biomimetic enviroments.
- Design, fabrication and development of novel in vitro diagnostic systems based on microfluidic systems.
- Microtechnology for life science applications.

Most relevant scientific articles

- Esteve V., Berganzo J., Monge R., Martínez-Bisbal M.C., Villa R., Celda B. et al. Development of a three-dimensional cell culture system based on microfluidics for nuclear magnetic resonance and optical monitoring. Biomicrofluidics. 2014;8(6).
- Mousavi S.J., Doblaré M., Doweidar M.H. Computational modelling of multi-cell migration in a multi-signalling substrate. Physical Biology. 2014;11(2).
- Cilla M., Peña E., Martínez M.A. Mathematical modelling of atheroma plaque formation and development in coronary arteries. Journal of the Royal Society Interface. 2014;11(90).
- Chiastra C., Migliavacca F., Martinez M.T., Malve M. On the necessity of modelling fluid-structure interaction for stented coronary arteries. Journal of the Mechanical Behavior of Biomedical Materials. 2014;34:217-230.
- Arana M., Gavira J.J., Peña E., González A., Abizanda G., Cilla M. et al. Epicardial delivery of collagen patches with adipose-derived stem cells in rat and minipig models of chronic myocardial infarction. Biomaterials. 2014;35(1):143-151.

Highlights

Researchers of our group are leading competitive research projects during 2014:

- Incidencia de los fenómenos de transporte en la hidrólisis enzimática y aplicación de mecánica de fluidos computacional en problemas de escalado (MIXING). RTC-2014-1826-3. Investigador responsable: Luis J. Fernández Ledesma • Diseño y mejora de dispositivos intravasculares recubiertos de farmaco mediante una herramienta computacional. Aplicación al diseño de stent y balones en lesiones estenóticas. DPI2013-44391-P. Investigador responsable: Miguel Angel Martínez Barca / Estefanía Peña Baquedano • Desarrollo de una herramienta computacional para el estudio de problemas de interacción fluido-estructura aplicada a problemas cardiovasculares. DPI2010-20746-C03-01. Investigador responsable: Miguel Angel Martínez Barca • Modelado y Simulación del envejecimiento de arterias debido a Aterosclerosis. PRI-AIBDE-2011-1216. Investigador responsable: Estefanía Peña Baquedano. • MODELADO BIOMECANICO DEL TEJIDO MUSCULO-ESQUELETICO ABDOMINAL. CICYT. DPI2011-27939-C02-01. Investigador responsable: Begoña Calvo Calzada • POPCORN / Development of corneal biomechanical model. Dynamic topographical characterization based on 3D plenoptic imaging. FP7-SME-2013 606634. Unión Europea. Investigador/es responsable/es en UNIZAR: María Begoña Calvo Calzada

One of the main achievements of 2014 was the award of two multidisciplinary projects CIBER called MICROANGIOTHECAN and Micropod. These projects, both have collaborative nature with various institutions are public call obtained in 2014. Principal Investigator Ochoa Ignacio Garrido.

Coordinator of the line of Biomedical Engineering and Nanoscience at the IIS (Institute for Health Research) of Aragon.L. J. Fernández Ledesma. 2014.

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Research Group in Biomaterials, Biomechanics and Tissue Engineering

Programme: Biomaterials and Advanced Therapies

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Main lines of research

- Biomechanics and computer simulation.
- Development of new functional biomaterials for tissue engineering, based on calcium phosphate, glasses, ceramics and composites.
- Cell bioengineering: interactions between cells and biomaterials for manufacturing biocompatible materials for tissue regeneration and repair.
- Metallurgy and coatings: obtaining and characterizing metals and alloys for applications in traumatology, orthopedics, odontology and cardiovascular surgery.

Most relevant scientific articles

- Álvarez Z., Castano O., Castells A.A., Mateos-Timoneda M.A., Planell J.A., Engel E. et al. Neurogenesis and vascularization of the damaged brain using a lactate-releasing biomimetic scaffold. Biomaterials. 2014; 35(17):4769-4781.
- Mas-Moruno C., Fraioli R., Albericio F., Manero J.M., Gil F.J. Novel peptide-based platform for the dual presentation of biologically active peptide motifs on biomaterials. ACS Applied Materials and Interfaces. 2014; 6(9):6525-6536.
- Castano O., Sachot N., Xuriguera E., Engel E., Planell J.A., Park J.-H. et al. Angiogenesis in bone regeneration: Tailored calcium release in hybrid fibrous scaffolds. ACS Applied Materials and Interfaces. 2014; 6(10):7512-7522.
- Unosson E., Rodríguez D., Welch K., Engqvist H. Reactive combinatorial synthesis and characterization of a gradient Ag-Ti oxide thin film with antibacterial properties. Acta Biomaterialia. 2014.
- Vila O.F., Martino M.M., Nebuloni L., Kuhn G., Pérez-Amodio S., Muller R. et al. Bioluminescent and micro-computed tomography imaging of bone repair induced by fibrin-binding growth factors. Acta Biomaterialia. 2014;10(10):4377-4389.

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Nucleic Acid Chemistry Group

Programme: Nanomedicine

Lead Researcher: Eritja Casadellà, Ramón

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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

- Puras G., Mashal M., Zarate J., Agirre M., Ojeda E., Grijalvo S. et al. A novel cationic niosome formulation for gene delivery to the retina. Journal of Controlled Release. 2014; 174(1):27-36.
- Escorihuela J., Banuls M.-J., Grijalvo S., Eritja R., Puchades R., Maquieira A. Direct covalent attachment of DNA microarrays by rapid thiol-ene "click" chemistry. Bioconjugate Chemistry. 2014; 25(3):618-627.
- Grijalvo S., Alagia A., Puras G., Zarate J., Pedraz J.L., Eritja R. Cationic vesicles based on non-ionic surfactant and synthetic aminolipids mediate delivery of antisense oligonucleotides into mammalian cells. Colloids and Surfaces B: Biointerfaces. 2014; 119:30-37.
- Avino A., Portella G., Ferreira R., Gargallo R., Mazzini S., Gabelica V. et al. Specific loop modifications of the thrombin-binding aptamer trigger the formation of parallel structures. FEBS Journal. 2014; 281(4):1085-1099.
- Tintoré M., Eritja R., Fabrega C. DNA nanoarchitectures: Steps towards biological applications. ChemBioChem. 2014;15(10):1374-1390.

Highlights

In collaboration with other CIBER-BBN (NANOBIOCEL, NN-UMH) groups we have developed formulations for transfection of nucleic acids that are effective for gene therapy of ocular diseases. With these results we have obtained a project (Retos-Colaboración, TERET). Also in collaboration with other CIBER-BBN (NBT-UAB, GOA-HSCSP) groups we have obtained nanoconjugates directed against cancer stem cells that are able to effectively remove metastatic cells. We have requested several projects based on these results that are under evaluation. Also in collaboration with a group of the Polytechnic University of Valencia (UPV) we have achieved a method for immobilizing DNA probes based on the radical reaction between thiols and alkenes. This methodology allows the preparation of devices for the detection of mutations. The results have been protected by a patent application. An important part of scientific activity has been focused on the evaluation of small RNA (siRNA) duplexes that are capable of silencing genes specifically. We have studied the introduction of small chemical modifications that increase the stability of siRNAs in serum and the ability to use nanostructured materials (prepared by other groups CIBER-BBN) for the development of new formulations that increase the efficiency of transfection . In collaboration with the group of CIBER-BBN (ICN2-CSIC) we have studied the detection of microRNA by SPR using capture probes with high efficiency which are able to form triple helices with the target miRNA. We have also studied a series of compounds for their potential ability to inhibit DNA repair enzymes that can be used to increase the efficacy of chemotherapy. Finally structural details and possible applications of G-quadruplex forming oligonucleotides have been studied.

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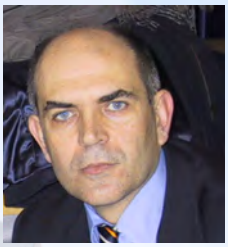
Neuroprosthesis and Neuroengineering Research Group

Programme: Bioengineering and Medical Imaging



Lead Researcher: Fernández Jover, Eduardo

Group Members

STAFF MEMBERS: Humphreys, Lawrence | Soto Sánchez, Cristina

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CONTRIBUTORS: Pérez Vidal, Carlos

Main lines of research

- Genetic therapy:
  - Genetic therapy directed for reprogramming cells in vivo and in vitro for the regeneration of the retina.
  - Development of new nanoparticles to perform as vehicles for genes in genetic therapies.
- Development of biomedical technologies:
  - Development of robots to assist in surgery and surgery simulations.
  - Development of devices for neurorehabilitation and robot assisted rehabilitation.
  - Development of non-invasive brain-computer interfaces (BCI) based on electroencephalography (EEG) electrooculography (EOG) for disabled people.
  - Development of technology for the detection of breast cancer.
  - Development of new generations of multifunctional intraocular lenses.
  - Development of software for neural signal analysis.
- Functional optimization and improvement of biocompatibility of long term neural interfaces.
- Study of cortical reorganization and associated changes to neural plasticity in the blind.

Most relevant scientific articles

- Puras G., Mashal M., Zarate J., Agirre M., Ojeda E., Grijalvo S. et al. A novel cationic niosome formulation for gene delivery to the retina. Journal of Controlled Release. 2014;174(1):27-36.
- Bongard M., Micol D., Fernández E. NEV2lkit: A new open source tool for handling neuronal event files from multi-electrode recordings. International Journal of Neural Systems. 2014;24(4).
- Fernández E., Greger B., House P.A., Aranda I., Botella C., Albisua J. et al. Acute human brain responses to intracortical microelectrode arrays: Challenges and future prospects. Frontiers in Neuroengineering. 2014; 7(JUL).
- Wark H.A.C., Mathews K.S., Normann R.A., Fernández E. Behavioral and cellular consequences of high-electrode count Utah Arrays chronically implanted in rat sciatic nerve. Journal of Neural Engineering. 2014; 11(4).

Highlights

Our main interest is to develop innovative solutions to the problems raised by interfacing the human nervous system and on this basis, develop a two-way direct communication with neurons and ensembles of neurons which could be applied to enhance the life of people that are affected by visual impairments or to treat several brain diseases more specifically and effectively. Along 2014 we have been working on: 1) Better understanding of cortical plasticity in the blind, 2) Biocompatibility and overall consequences of high-electrode count multielectrode arrays on the brain and peripheral nerves, 3) Development of new therapeutic approaches for retinal degenerative diseases, 4) Development of new tools and protocols for optogenetic applications, 5) New adaptive multimodal human-machine interfaces and robotic systems for neuro-rehabilitation.

The group is coordinating a multidisciplinary project which aims to develop new therapeutical approaches for retinal visual diseases, belong to the panel of experts of the working group on patient-reported outcomes of the International Task Force on Methods for Phsychophysical Testing and Reporting of Visual function of patients involved in the development of visual prosthesis and other new vision restoration technologies, and host the Bidons Egara Research Chair in Degenerative Eye Diseases of the University Miguel Hernandez, which supports research to end blindness and promote public awareness and programs to improve the quality of life for those with vision loss. Furthermore the group is coordinating the H2020 AIDE project, that has been funded with 3,5 MEUR by the European Commission and is focused on the development of novel adaptive multimodal interfaces to assist disable people in daily activities.

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Dendrimer Group for Biomedical Applications

Programme: Nanomedicine

Lead Researcher: Gómez Ramírez, Rafael

Group Members

STAFF MEMBERS: Ortega López, Paula | Sánchez-Nieves Fernández, Javier

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CONTRIBUTORS: Arnáiz Garrido, Eduardo | Fuentes Paniagua, Elena | Galán Herranz, Marta | García Gallego, Sandra | Lozano de la Cruz, Tania | Peña González, Cornelia Emeritrina

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 anti-prion dendrimers and for the treatment of Alzheimer's disease.
- Development of dendrimers in vaccines.
- Development of metal complexes for their antiviral, antibacterial and/or anti-cancer use.

Most relevant scientific articles

- Sepúlveda-Crespo D., Lorente R., Leal M., Gómez R., De la Mata F.J., Jiménez J.L. et al. Synergistic activity profile of carbosilane dendrimer G2-STE16 in combination with other dendrimers and antiretrovirals as topical anti-HIV-1 microbicide. Nanomedicine: Nanotechnology, Biology, and Medicine. 2014;10(3):609-618.
- Perise-Barrios A.J., Jiménez J.L., D' Ominguez-Soto A., De La Mata F.J., Corbi A.L., Gómez R. et al. Carbosilane dendrimers as gene delivery agents for the treatment of HIV infection. Journal of Controlled Release. 2014; 184(1):51-57.
- Vacas-Córdoba E., Galán M., de la Mata F.J., Gómez R., Pion M., Munoz-Fernández M.A. Enhanced activity of carbosilane dendrimers against HIV when combined with reverse transcriptase inhibitor drugs: Searching for more potent microbicides. International Journal of Nanomedicine. 2014; 9(1):3591-3600.
- Vacas-Córdoba E., Climent N., De La Mata F.J., Plana M., Gómez R., Pion M. et al. Dendrimers as nonviral vectors in dendritic cell-based immunotherapies against human immunodeficiency virus: Steps toward their clinical evaluation. Nanomedicine. 2014; 9(17):2683-2702.
- Fuentes-Paniagua E., Hernández-Ros J.M., Sánchez-Milla M., Camero M.A., Maly M., Perez-Serrano J. et al. Carbosilane cationic dendrimers synthesized by thiol-ene click chemistry and their use as antibacterial agents. RSC Advances. 2014; 4(3):1256-1265.

Highlights

The activity of the group during 2014 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 and anticancer agents, funded by european (IRSES), national (CTQ2011-23245 (MINECO)) and regional (Consorcio NANODENMED-CM) projects. The research carried out, focused in the search of a new therapeutic approach towards the HIV treatment based on the combined therapy of anionic dendrimers and retroviral drugs, achieving 100% of inhibition both in CCR5 and CXCR4 strains. In addition, new cationic dendritic systems have been developed based on the dendronization of soft and hard nanoparticles to carry short nucleic acid (antisense oligonucleotides or siRNA) within different intramural CIBER-BBN projects.

Results of the research have been presented in several conferences, notably in the 4 th Biodendrimers held in Lugano (Switzerland) and published works consisted of 13 publications and 1 book chapter. The group has continued intensifying its activities related to technology transfer applying for a national Spanish patent based on the use in biomedicine of thiol-terminated dendrimers. Also, along with other research group, we have achieved a proof of concept in humanized mice for the use of a topic microbicide against HIV prevention with an efficacy higher than 85% with a high relevance in the media.

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Biomaterials Centre

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Gómez Ribelles, José Luis

Group Members

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CONTRIBUTORS: Araque Monrós, Carmen

Main lines of research

- Scaffolds for regenerative medicine and tissue engineering of biodegradable and biostable materials and customized characteristics providing a suitable environment in which cells and live tissue can carry out their function.
- Modified surfaces and bioactive coatings.
- Microparticles and combined platforms for the delivery of drugs and growth factors.
- Synthesis and manufacture of special materials— copolymers, nanohybrids, membranes, tubules, gels, microfilaments.

Most relevant scientific articles

- Neto A.I., Cibrao A.C., Correia C.R., Carvalho R.R., Luz G.M., Ferrer G.G. et al. Nanostructured polymeric coatings based on chitosan and dopamine-modified hyaluronic acid for biomedical applications. Small. 2014;10(12):2459-2469.
- Valles-Lluch A., Arnal-Pastor M., Martínez-Ramos C., Vilarino-Feltrer G., Vikingsson L., Castells-Sala C. et al. Erratum: Combining self-assembling peptide gels with three-dimensional elastomer scaffolds (Acta Biomaterialia (2013) 9 (9451-9460)). Acta Biomaterialia. 2014;10(3):1487.
- Costa C.M., Gomez Ribelles J.L., Lanceros-Méndez S., Appetecchi G.B., Scrosati B. Poly(vinylidene fluoride)-based, co-polymer separator electrolyte membranes for lithium-ion battery systems. Journal of Power Sources. 2014;245:779-786.
- Correia D.M., Goncalves R., Ribeiro C., Sencadas V., Botelho G., Ribelles J.L.G. et al. Electrosprayed poly(vinylidene fluoride) microparticles for tissue engineering applications. RSC Advances. 2014;4(62):33013-33021.
- Lozano Picazo P., Perez Garnes M., Martínez Ramos C., Valles-Lluch A., Monleon Pradas M. New Semi-Biodegradable Materials from Semi-Interpenetrated Networks of Poly(-caprolactone) and Poly(ethyl acrylate). Macromolecular Bioscience. 2014.

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Research Group on Microbial Adhesion

Programme: Biomaterials and Advanced Therapies

Lead Researcher: González Martín, Mª Luisa

Group Members

STAFF MEMBERS: Fernández Calderón, Mª Coronada | Hierro Oliva, Margarita | Pacha Olivenza, Miguel Ángel

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CONTRIBUTORS: Delgado Rastrollo, María | Perera Núñez, Julia Mª | Rodríguez Cano, Abraham | Vadillo Rodríguez, Virginia

Main lines of research

- Microbial adhesion to biomaterials.
- Characterization of microbial surfaces.
- Characterization of biomaterial surfaces.
- Formation of biofilms and effect of antibiotics and/or antiseptics on them.
- Genetic bases for biofilm production.
- In vivo infectious processes related to the presence of implants or prostheses (in collaboration with the Orthopedic Surgery and Traumatology Service of Hospital Universitario Infanta Cristina of Badajoz).
- Characterization of explanted (in collaboration with the Oral and Maxillofacial Surgery Service of Hospital Universitario Infanta Cristina of Badajoz).

Most relevant scientific articles

- Rodríguez-Cano A., Pacha-Olivenza M.-T., Babiano R., Cintas P., González-Martín M.-L. Non-covalent derivatization of aminosilanized titanium alloy implants Silver-enhanced coating of antibacterial organics. Surface and Coatings Technology. 2014;245:66-73.
- González-García R., Monje A., Fernández-Calderón M.C., Hierro-Oliva M., Gonzalez-Martin M.L., Monje F. Three-dimensional and chemical changes on the surface of a 3-year clinically retrieved oxidized titanium dental implant. Journal of the Mechanical Behavior of Biomedical Materials. 2014;34:273-282.
- Perera-Costa D., Bruque J.M., González-Martín M.L., Gómez-García A.C., Vadillo-Rodríguez V. Studying the influence of surface topography on bacterial adhesion using spatially organized microtopographic surface patterns. Langmuir. 2014;30(16):4633-4641.
- Braceras I., Pacha-Olivenza M.A., Calzado-Martín A., Multigner M., Vera C., Broncano L.L.-. et al. Decrease of Staphylococcal adhesion on surgical stainless steel after Si ion implantation. Applied Surface Science. 2014;310:36-41.
- Hierro-Oliva M., Gallardo-Moreno A.M., González-Martín M.L. XPS Analysis of Ti6Al4V Oxidation Under UHV Conditions. Metallurgical and Materials Transactions A: Physical Metallurgy and Materials Science. 2014;45(13):6285-6290.

Highlights

Throughout the year 2014 our research group has conducted its investigation on surface modifications and processes in order to achieve a better response against bacterial colonization. It is to mention those contributions related to metal prosthetics materials addressed to both, the behavior of its passive layer in anaerobic conditions and the modification of their electrochemical properties, due the latter to a bacterial biofilm growth on their surface. Also, new surface modifications have been tested to decrease microbial colonization on metal materials; these tasks were carried out in collaboration with other CIBER groups to assess the biocompatibility of these modifications against various cell lines. In a different issue related to the topic, we were particularly involved in the study of those degradable materials able to release metal ions into the surrounding medium, since it can represent an advantage against infections on these materials. Additional studies, at a fundamental level, were focus on the relationship between surface textural and morphological aspects and protein adsorption, mainly on the unfolding of proteins.

With regards to the translation area we have collaborated with various companies. These works were in the field of microbial contamination and the thorough analysis of modified surfaces. These activities were performed either by direct agreements with our group or through the Surface Characterization nodule of the Equipment Platform. Finally, we should highlight the collaboration with the Maxillofacial Surgery Unit of the Infanta Cristina University Hospital in Badajoz, particularly on the damage and alterations of different osteosynthesis elements after explantation.

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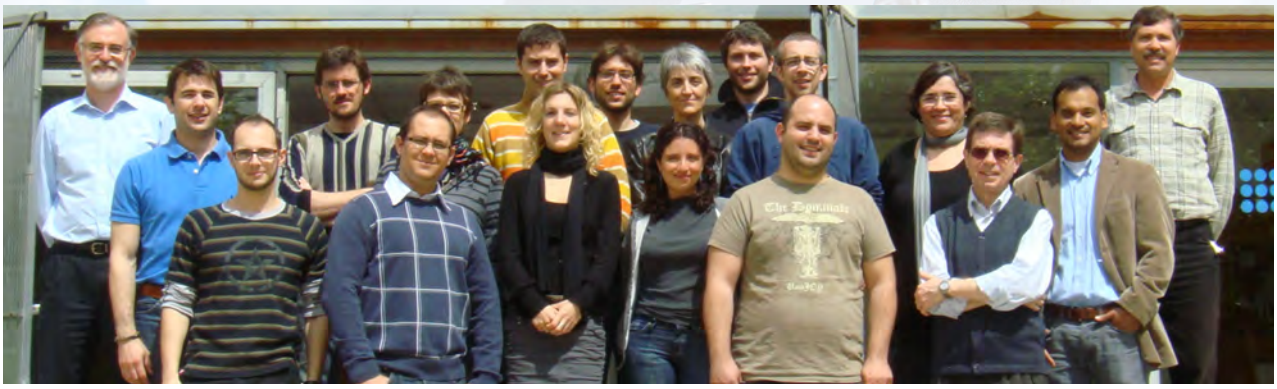
Biomedical Systems and Signals Research Group

Programme: Bioengineering and Medical Imaging



Lead Researcher: Jané Campos, Raimon

Group Members

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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

- Martínez-Horta S., Riba J., de Bobadilla R.F., Pagonabarraga J., Pascual-Sedano B., Antonijoan R.M. et al. Apathy in parkinson's disease: Neurophysiological evidence of impaired incentive processing. Journal of Neuroscience. 2014;34(17):5918-5926.
- Fernández-Albert F., Llorach R., Andrés-Lacueva C., Perera-Lluna A. Peak aggregation as an innovative strategy for improving the predictive power of LC-MS metabolomic profiles. Analytical Chemistry. 2014;86(5):2320-2325.
- Ziyatdinov A., Fonollosa J., Fernández L., Gutiérrez-Gálvez A., Marco S., Perera A. Bioinspired early detection through gas flow modulation in chemo-sensory systems. Sensors and Actuators, B: Chemical. 2014;206:538-547.
- Sarlabous L., Torres A., Fiz J.A., Jane R. Evidence towards improved estimation of respiratory muscle effort from diaphragm mechanomyographic signals with cardiac vibration interference using sample entropy with fixed tolerance values. PLoS ONE. 2014;9(2).
- Fiz J.A., Jane R., Lozano M., Gómez R., Ruiz J. Detecting unilateral phrenic paralysis by acoustic respiratory analysis. PLoS ONE. 2014;9(4).

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Biomedical Signal Interpretation & Computational Simulation

Programme: Bioengineering and Medical Imaging

Lead Researcher: Laguna Lasaosa, Pablo

Group Members

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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 photopletismography (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

- Demidova M.M., Martin-Yebra A., Van Der Pals J., Koul S., Erlinge D., Laguna P. et al. Transient and rapid QRS-widening associated with a J-wave pattern predicts impending ventricular fibrillation in experimental myocardial infarction. Heart Rhythm. 2014;11(7):1195-1201.
- Sánchez C, Bueno-Orovio A, Wettwer E, Loose S, Simon J, Ravens U et al. Inter-subject variability in human atrial action potential in sinus rhythm versus chronic atrial fibrillation.PloS one. 2014;9 (8):e105897.
- Meijs L.P.B., Galeotti L., Pueyo E.P., Romero D., Jennings R.B., Ringborn M. et al. An electrocardiographic sign of ischemic preconditioning. American Journal of Physiology - Heart and Circulatory Physiology. 2014;307(1).
- Lázaro J., Alcaine A., Romero D., Gil E., Laguna P., Pueyo E. et al. Electrocardiogram Derived Respiratory Rate from QRS Slopes and R-Wave Angle. Annals of Biomedical Engineering. 2014;42 (10):2072-2083.
- Alcaine A., Soto-Iglesias D., Calvo M., Guiu E., Andreu D., Fernández-Armenta J. et al. A wavelet-based electrogram onset delineator for automatic ventricular activation mapping. IEEE Transactions on Biomedical Engineering. 2014;61(12):2830-2839.

Highlights

- Award of a ERC "Starting grant" from H2020 program led by Esther Pueyo entitled: MODELAGE: Modeling and characterization of cardiac aging.
- Funding of a project from Spanish national research plan, led by Juan Pablo Martínez: TEC2013-42140-R: procesado de señales guiado por la fisiologia para la estratificacion del riesgo cardiovascular y guiado de la terapia: herramientas para mejorar la toma de decisiones
- Funding of a project from Spanish national research plan, led by Esther Pueyo: TIN2013-41998-R: el sistema nervioso autonomo como modulador de la funcion cardiaca: investigación integral mediante procesado de señal y modelado computacional
- Funding of a project from the program: proyectos colaborativos multidisciplinares de transferencia tecnológica en patologías respiratorias CIBER-BBN-CIBERES-SEPAR: PVI-ANS-NCOG: Effects of an early neurocognitive intervention on patient-ventilator interaction and stress in critically ill patients receiving mechanical ventilation
- Assumption of the presidency of the Board of Directors from "Computing in Cardiology" by the PI of the group Pablo Laguna, for the period 2014-2017.

Additionally the group has published a total of 21 papers and 24 conference proceedings, From those it is worthy to highlight three reviews on signal processing applied in Physiology:

- A. Bueno-Orovio, C. Sánchez, E. Pueyo, B. Rodriguez (2014). Na/K pump regulation of cardiac repolarization: insights from a systems biology approach. Eur J Physiol. INVITED REVIEW. 466:183–193 doi: 10.1007/s00424-013-1293-1
- A Roebuck, V Monasterio, E Gederi, M Osipov, J Behar, A Malhotra, T Penzel, G D Clifford (2014), A review of signals used in sleep analysis. Physiological Measurement. vol. 35 R1–R57 doi:10.1088/0967-3334/35/1/R1.
- P. Laguna, L. Sörnmo (2014). The STAFF III ECG Database and its Significance for Methodological Development and Evaluation, Journal of Electrocardiology, n.47; pp. 408–417 doi:10.1016/j.jelectrocard.2014.04.018.

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NanoBiosensors and Bioanalytical Applications Group

Programme: Nanomedicine

Lead Researcher: Lechuga Gómez, Laura Mª

Group Members

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CONTRIBUTORS: Dante, Stefania | González Guerrero, Ana Belén | Maldonado Váquez, Jesús Manuel | Márquez Villalobos, Salomón Elieser | Otte Ortiz, Bert | Sánchez Huertas, César | Solís Tinoco, Verónica Irais

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 optonanomechanics 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

- Carrascosa L.G., Sina A.A.I., Palanisamy R., Sepúlveda B., Otte M.A., Rauf S. et al. Molecular inversion probe-based SPR biosensing for specific, label-free and real-time detection of regional DNA methylation. Chemical Communications. 2014;50(27):3585-3588.
- Estévez M.-C., Otte M.A., Sepúlveda B., Lechuga L.M. Trends and challenges of refractometric nanoplasmonic biosensors: A review. Analytica Chimica Acta. 2014;806:55-73.
- Mauriz E., Carbajo-Pescador S., Ordónez R., García-Fernández M.C., Mauriz J.L., Lechuga L.M. et al. On-line surface plasmon resonance biosensing of vascular endothelial growth factor signaling in intact-human hepatoma cell lines. Analyst. 2014;139(6):1426-1435.
- Olguin Y., Carrascosa L.G., Lechuga L.M., Young M. The effects of lipids and surfactants on TLR5-proteoliposome functionality for flagellin detection using surface plasmon resonance biosensing. Talanta. 2014;126:136-144.
- Soler M., Estévez M.C., Alvarez M., Otte M.A., Sepúlveda B., Lechuga L.M. Direct detection of protein biomarkers in human fluids using site-specific antibody immobilization strategies.Sensors (Basel, Switzerland). 2014;14(2):2239-2258.

Highlights

In the research line of integrated silicon nanophotonic biosensors, important milestones have been reached for the implementation of a sensitive, affordable, hand-held and portable point-of-care device. The ultrasensitive limit of detection of this technology at the pM-fM level is far beyond the state-of-the-art and we have demonstrated the detection of a few number of infectious microorganisms directly in patient´s samples. A technological transfer plan with a private company has been developing during 2014. Several new projects have been granted in 2014 related to this research line:

- COLONTEST: Diseño y puesta a punto de kits para el diagnóstico del cáncer de colon en sangre basados en plataformas multiplex. (RTC-2014-1518-1)
- RAIS: Scalable, point-of-care and label free microarray platform for rapid detection of Sepsis (UE. H2020-ICT-2014-1-644956)

The utility of our nanophotonic biosensing techniques for real bioanalytical applications has been successfully demonstrated. We are focusing in the point-of-care detection of diseases as for example Malaria (collaboration with FIND diagnostics Foundation) or Tuberculosis (POCKET EU project), early detection of several types of cancer as colorectal cancer (COLONTEST national project); early detection of liver complications (CIBER internal project); monitoring of celiac or allergic patients directly in their human fluids, among others (most of them in collaboration with private companies). In the environmental field, we are focusing in the early detection of toxic pollutants as pesticides, antibiotics or alga toxins (BRAAVOO EU project).

We have successfully developed in 2014 the fundamental research line in Molecular Biology using our nanobiosesing technology for the deciphering of alterations in the cellular pathways, including alternative splicing of RNA, and epigenetics modifications (DNA metylation or microRNA release).

2014 indicators to be noted: 7 international publications, 1 industrial contract, 21 invited contributions to conferences and courses.

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Endocrinology and Diabetes Research Group

Programme: Bioengineering and Medical Imaging

Lead Researcher: Leiva Hidalgo, Alberto

Group Members

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CONTRIBUTORS: Cubero Marcos, Jose María | González Blanco, Cintia

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 gen and the aggressiveness of the TPC-1human 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 a an original thyroid chemotherapy. PGLA nanoparticles, loaded with an inhibitor of tyrosinkinase, 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 Therapeutical 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

- González C., Aulinas A., Colom C., Tundidor D., Mendoza L., Corcoy R. et al. Thyroglobulin as early prognostic marker to predict remission at 18-24 months in differentiated thyroid carcinoma. Clinical Endocrinology. 2014;80(2):301-306.
- Vinagre I., Sánchez-Quesada J.L., Sánchez-Hernández J., Santos D., Ordonez-Llanos J., De Leiva A. et al. Inflammatory biomarkers in type 2 diabetic patients: Effect of glycemic control and impact of ldl subfraction phenotype. Cardiovascular Diabetology. 2014;13(1).
- Hawa M.I., Kolb H., Schloot N., Beyan H., Paschou S.A., Buzzetti R. et al. Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7 (Diabetes Care (2013) 36, (908-913). Diabetes Care. 2014;37(5):1494.
- Mato E., González C., Moral A., Pérez J.I., Bell O., Lerma E. et al. ABCG2/BCRP gene expression is related to epithelial-mesenchymal transition inducer genes in a papillary thyroid carcinoma cell line (TPC-1). Journal of Molecular Endocrinology. 2014;52(3):289-300.
- Aulinas A., Ramírez M.-J., Barahona M.-J., Valassi E., Resmini E., Mato E. et al. Telomere length analysis in Cushing's syndrome. European Journal of Endocrinology. 2014;171(1):21-29.

Highlights

- ENDOCRINE CANCER. In our research on differentiated thyroid carcinoma (DTC) we recorded serum bank and private collection of 200 tumors.We have discovered by proteomics the involvement of genes (ABCG2/BCRP, VDAC2) in epithelial-mesenchymal transition processes, undifferentiation and aggressiveness, and differential expression of 120 proteins (2D-DIGE) in these tumors. We have published that the determination of basal thyroglobulin may predict remission of DTC. We have shown that PGLA nanoparticles loaded with the chemotherapy agent inhibitor of tyrosine kinase are recognized by monoclonal antibodies against VEGFR-FGFR in human poorly DTC cell lines (potential therapeutic target). We evaluated telomerase activity in Cushing's syndrome, demonstrating the beneficial effect of treatment on processes associated with aging.
- DIABETES, OBESITY, DYSLIPIDEMIA AND BIOMEDICAL TECHNOLOGY**.** We have observed, for the first time, by ultrasound, preclinical atherosclerosis markers (vascular intima-media thickness, IMT) at different stages of gestation, finding a relationship between gestational age and IMT in the umbilical artery, and between BMI and IMT in the maternal common carotid artery. We have completed and published the immunological, metabolic and clinical characterization of diabetes LADA in the Spanish population (EU Project). A Doctoral Thesis – PhD candidate Irene Vinagre – demonstrated the impact of glycemic control on inflammation biomarkers and LDL-c. The technological platform PREDIRCAM, CIBER-BBN original, is being subject to a Spanish multicenter clinical trial (3 university hospitals-FIS).
- FUNDED RESEARCH PROJECTS**.** The projects DALI (Prevention of Gestational Diabetes in Europe) and CONCEPTT (first clinical trial worldwide about the continuous monitoring of glycemic control in pregnancy; we are Co-IP and members of the Steering Committee) keep going, as well as national projects (with GBT-UPM), investigating open/ closed loop and semi-automation of insulin therapy. In 2014, we were granted the SGR 2014-16 with maximum score (6.66/7.0) of those obtained by the IIB-HSP.

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Oncogenesis and Antitumour Drug Group

Programme: Nanomedicine

Lead Researcher: Mangues Bafalluy, Ramón

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Main lines of research

- Development of animal models of disseminated human solid tumors and hematological neoplasias for the molecular study of metastatic stem cells, metastasis and resistance to therapy
- 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

- Urosevic J., García-Albéniz X., Planet E., Real S., Cespedes M.V., Guiu M. et al. Colon cancer cells colonize the lung from established liver metastases through p38 MAPK signalling and PTHLH. Nature Cell Biology. 2014;16(7):685-694.
- Céspedes M.V., Unzueta U., Tatkiewicz W., Sánchez-Chardi A., Conchillo-Sole O., Alamo P. et al. In vivo architectonic stability of fully de novo designed protein-only nanoparticles. ACS Nano. 2014;8(5):4166-4176.
- De la Torre C., Casanova I., Acosta G., Coll C., Moreno M.J., Albericio F. et al. Gated mesoporous silica nanoparticles using a double-role circular peptide for the controlled and target-preferential release of doxorubicin in CXCR4-expresing lymphoma cells. Advanced Functional Materials. 2014.
- Unzueta U., Saccardo P., Domingo-Espin J., Cedano J., Conchillo-Sole O., García-Fruitós E. et al. Sheltering DNA in self-organizing, protein-only nano-shells as artificial viruses for gene delivery. Nanomedicine: Nanotechnology, Biology, and Medicine. 2014;10(3):535-541.
- Alamo P., Gallardo A., Pavón M.A., Casanova I., Trías M., Mangues M.A. et al. Subcutaneous preconditioning increases invasion and metastatic dissemination in mouse colorectal cancer models. DMM Disease Models and Mechanisms. 2014;7(3):387-396.

Highlights

The continuity of the NanoMets CIBER-BBN intramural Project of Excellence has been approved. We have obtained funding from Fundació La Marató de TV3 for this project, which is carried out in collaboration with Antonio Villaverde and Ramon Eritja groups and focuses on the development of a targeted genotoxic nanoconjugate as antimetastatic drug for colorectal cancer. The renewal fo the recognition of our Group as Consolidated has been granted by the Generalitat de Catalunya AGAUR agency. We have become members of the COST Action (EU-RTD) on antitumor resistance and cancer stem cells and of the European Technology Platform on Nanomedicine (EATRIS) in the area of advanced therapies and Biologicals. The CIBER-BBN Nanotoxicology Unit coordinated by our group has been incorporated to the NANBIOSIS Platform, which has been recognized as singular ICTS by the Spanish MINECO, having also obtained a contract for an infrastructure support technician associated with this Unit. In collaboration with Roger Gomis, of the Institut de Recerca Biomédica in Barcelona we have identified the molecular mechanism of re-metastasis from liver to lung in colorectal cancer. In collaboration with Villaverde's group we have demonstrated stability and long re-circulation time in the bloodstream of the nanoparticles we are using for targeted drug delivery. The researcher Lourdes Farré and its post-doctoral fellow Marcelo Magalhaes, from the FIOCRUZ Center at Salvador de Bahia (Brasil), have performed a stage in our laboratory to complete a join bilateral project. We have obtained a Sara Borrell post-doctoral contract and defended one doctoral dissertation. We have also been granted a US patent on focal adhesion inhibitors as antitumor drugs. Our Group continues its industrial transference activity through contracts with the pharmaceutical industry for the preclinical development of new antitumor drugs within an INNPACTO project of the Spanish MINECO.

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Nanobiotechnology for Diagnostics

Programme: 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 Catalonian 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 the research addresses three fundamental specific objectives:

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

The scientific activity of the group began in 1996 and was particularly focused on the development of antibodies and on the establishment of immunochemical methods. In this respect, the group has an important collection of immunoreagents for environmental pollutants including endocrine disruptors, pesticides or pharmaceuticals. The group is running the CAbS (Custom Antibody Service), a facility that provides internal and external services addressed at developing immunoreagents and providing scientific support in the immunodiagnostic field. For more than eight years the scientific objectives have been expanded to the biosensor and nanobiotechnology fields. The associated increase of the know-how, expertise and capabilities of the Nb4D group has been achieved through its participation in a significant number of Spanish and FP European research projects (FP4-FP7: INEXsPORT- ENV4-CT97-0476, TECACOR- FAIR-CT98-9586; RADAR-GLK1-CT-2001-01670, ELISHA- NMP2-CT-2003-505485, GOODFOOD- IST-2003-508774, Conffidence-KB-BE-2008-211326, CAJAL4EU- ICT-ENIAC-2012-120215) and through contracts with companies. The output of this scientific activity has been reflected in an increasing number of publications (more than 160 scientific publications in high impact international journals), participation in international conferences, patents and scientific training activities perfor-

med through the supervision of doctoral theses (more than 15 theses read) or the giving of courses to PhD students and specialized technical personnel.

From a practical point of view, the research group 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

- Valera E., García-Febrero R., Pividori I., Sánchez-Baeza F., Marco M.-P. Coulombimetric immunosensor for paraquat based on electrochemical nanoprobes This work is dedicated to the memory of Dr. Francisco Sánchez-Baeza. Sensors and Actuators, B: Chemical. 2014;194:353-360.
- García-Febrero R., Salvador J.-P., Sánchez-Baeza F., Marco M.-P. Rapid method based on immunoassay for determination of paraquat residues in wheat, barley and potato. Food Control. 2014;41(1):193-201.
- Fernández F., Pinacho D.G., Gratacos-Cubarsi M., García-Regueiro J.-A., Castellari M., Sanchez-Baeza F. et al. Immunochemical determination of fluoroquinolone antibiotics in cattle hair: A strategy to ensure food safety. Food Chemistry. 2014;157:221-228.
- Pinacho D.G., Sánchez-Baeza F., Pividori M.-I., Marco M.-P. Electrochemical detection of fluoroquinolone antibiotics in milk using a magneto immunosensor. Sensors (Switzerland). 2014;14(9):15965-15980.
- Esteban-Fernández De Avila B., Campuzano S., Pedrero M., Salvador J.-P., Marco M.-P., Pingarron J.M. Lipoprotein(a) determination in human serum using a nitrilotriacetic acid derivative immunosensing scaffold on disposable electrodes. Analytical and Bioanalytical Chemistry. 2014;406(22):5379-5387.

Highlights

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

In collaboration with Pharmasans Labs Inc. (USA) the group developed immunoreagents against neurotransmitters of interest in neurodegenerative and neurological disorders. Specifically, the group has developed antibodies against neurotransmitters derived from the phenylalanine patways such as the catecholamines, adrenaline and noradrenaline.

Other neurotransmitters have been developed during this collaboration and are being exploited in the project TryKySeNS (CTQ2011-29163-C03-01). An ELISA has been validated for kynurenic acid, a neuroprotector involved in neurological disorders. The assay has been tested on real samples from patients suffering Alzheimer's and from healthy controls using cerebrospinal fluid and plasma provided by the 12 de Octubre Hospital in Madrid. The results are promising and Nb4D hopes to be able to design a point-of-care biosensor device.

In the area of infectious disease detection the group has continued their studies on the detction of bacteria such as Pseudomonas aeruginosa (pycocyanin, a toxin produced by the bacteria) and Staphylococcus aureus. The assays have been tested on samples of plasma and sputum from patients. The group has applied to the Spanish Patents Office to patent the immunoreagents it has developed to detect pyocyanin and has received interest from various companies and research groups.

The group is also developing immunoreagents against biomarkers of interest in cardiovascular diseases. The hope is to be able to develop a point-of-care device that can be used to determine the stage of cardiac disease that the patient is at. These studies are part of the NanoCardioCoco project (IPT2001-1337-010000) whose objective is work with enterprises to translate the research results into viable products for the benefit of society as a whole.

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Applied Molecular Chemistry Group of the IDM

Programme: Nanomedicine / Biomaterials and Advanced Therapies

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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

- Díez P., Sánchez A., Gamella M., Martínez-Ruiz P., Aznar E., De la Torre C. et al. Toward the design of smart delivery systems controlled by integrated enzyme-based biocomputing ensembles. Journal of the American Chemical Society. 2014;136(25):9116-9123.
- Mas N., Arcos D., Polo L., Aznar E., Sánchez-Salcedo S., Sancenón F. et al. Towards the development of smart 3D "gated scaffolds" for on-command delivery. Small. 2014; 10(23):4859-4864.
- Giménez C., Climent E., Aznar E., Martánez-Manez R., Sancenón F., Marcos M.D. et al. Towards chemical communication between gated nanoparticles. Angewandte Chemie - International Edition. 2014; 53(46):12629-12633.
- De la Torre C., Mondragon L., Coll C., Sancenon F., Marcos M.D., Martínez-Manez R. et al. Cathepsin-B induced controlled release from peptide-capped mesoporous silica nanoparticles. Chemistry - A European Journal. 2014; 20(47):15309-15314.
- Moragues M.E., Toscani A., Sancenón F., Martínez-Manez R., White A.J.P., Wilton-Ely J.D.E.T. A chromofluorogenic synthetic "canary" for CO detection based on a pyrenylvinyl ruthenium(II) complex. Journal of the American Chemical Society. 2014; 136(34):11930-11933.

Highlights

During 2014, we started with activities in the Intramural Projects NANOHYPERTERMIA, NEURO-MON, TBIO-GATE SPRING and NANOSENFIBRO and in the transfer project MICHORMON-PRO. We have also continued with the ECO EXOLUNG project. Within all these projects, we have prepared a collection of new gated materials for controlled release applications and as sensors. A part from continuing our current regional and National Plan projects, in 2014 we have been granted with an EXPLORA project related with the development of probes for biomolecules using gating mechanisms and also with two seed projects to establish collaborations with Hospital "La Fe" about new detection systems of prostate cancer using multiplatform analysis of urine samples and the theranostic application of nanoparticles in experimental ischemic ictus.

Also this year, we have continued with an intense scientific activity publishing over thirty-three articles in international journals of high impact factor. In these works we have demonstrated that it is possible to develop systems that chemically communicate using gated nanoparticles, or in collaboration with the group of María Vallet, that our delivery systems can be integrated in three-dimensional matrices or scaffolds.

At the international level, we have participated in the preparation of various European projects proposals. In addition, we hosted five PhD students from India, United States, Netherlands, United Kingdom and a postdoctoral from India. In addition, two of our PhD students have spent several months in Ireland and Italy.

Finally, in 2014 our group has participated in the CIBER-BBN training program being granted with three scholarships and six students have defended their PhD thesis during this year.

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Molecular Immunobiology (ASSOCIATED GROUP)

Programme: Nanomedicine

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Main lines of research

- NANOMEDICINE WITH SEVERAL DENDRIMERS AND NANOPARTICLES: Genetic therapy, nanovaccines with dendritic cells against infectious illness, cancer, pretreatment and development of microbicides against HIV,HSV-2, HCV and HBV with dendrimers per se and dendrimers in the treatment of solid tumors.
- HIV INFECTION: Research based in HIV reservoir, viral reactivation with dendrimers or nanoparticles as antilatency drugs and treatment with antiretroviral therapy. Image in collaboration with other CIBER groups.
- IMMUNOPATHOLOGY OF HIV INFECTION.
- PAEDIATRICS AND HIV INFECTION.

Most relevant scientific articles

- Perise-Barrios A.J., Jiménez J.L., D'Ominguez-Soto A., De La Mata F.J., Corbi A.L., Gómez R. et al. Carbosilane dendrimers as gene delivery agents for the treatment of HIV infection. Journal of Controlled Release. 2014;184(1):51-57.
- Vacas-Córdoba E., Climent N., De la Mata F.J., Plana M., Gómez R., Pion M. et al. Dendrimers as nonviral vectors in dendritic cell-based immunotherapies against human immunodeficiency virus: Steps toward their clinical evaluation. Nanomedicine. 2014;9(17):2683-2702.
- Sánchez-Rodríguez J., Vacas-Córdoba E., Gómez R., De la Mata F.J., Munoz-Fernández Ma. A. Nanotech-derived topical microbicides for HIV prevention: The road to clinical development. Antiviral Research. 2014;113: 33-48.
- Sepulveda-Crespo D., Lorente R., Leal M., Gómez R., De la Mata F.J., Jiménez J.L. et al. Synergistic activity profile of carbosilane dendrimer G2-STE16 in combination with other dendrimers and antiretrovirals as topical anti-HIV-1 microbicide. Nanomedicine: Nanotechnology, Biology, and Medicine. 2014;10(3):609-618.

Highlights

Along the year 2014 we took a great step in the use of nanotechnology in infectious diseases. We went from basic-clinical research to traslational research having developed a vaginal and rectal microbicide for topical application. We showed that our vaginal microbicide polianionic carbosilan dendrimers gel impeded 85% of HIV-1 infection in a humanized mouse model (BLT-mice) as a concept proof. We also showed that the combination of the polianionic carbosilan dendrimers with tenofovir or maraviroc, which work in the first steps of the HIV viral replication cycle as microbicide, stopped 100% the HIV-1 infections. This proved to be a breakthrough in our research not only in the use of dendrimers as microbicides, but also in the use of dendrimers as delivery systems, biodistribution, toxicology, etc in animal models. We also used these nanosytems as anti-latency drugs, nanovaccines and Ag presentation with dendritic cells. Finally, we established the in vitro and in vivo nanobioguided platform with the objective to test new nanosystems against other infectious diseases such as infections caused by HSV-2, HCV, Chijungunya, ebola...We got very promising results, showing how various dendrimers depending on their synthesis, nucleus, peripheral charges, generation, etc act against different virus. We have contributed to the development of new treatments against HIV-1, HSV-2 and HCV and to the search of potential cure for viral infections.

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Cellular and Respiratory Biomechanics Group (ASSOCIATED GROUP)

Programme: Nanomedicine

Lead Researcher: Navajas Navarro, Daniel

Group Members

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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

- Almendros I., Wang Y., Becker L., Lennon F.E., Zheng J., Coats B.R. et al. Intermittent hypoxia-induced changes in tumor-associated macrophages and tumor malignancy in a mouse model of sleep apnea. American Journal of Respiratory and Critical Care Medicine. 2014;189(5):593-601.
- Isetta V., Leon C., Torres M., Embid C., Roca J., Navajas D. et al. Telemedicine-based approach for obstructive sleep apnea management: Building evidence. Journal of Medical Internet Research. 2014;16(2).
- Andreu I., Luque T., Sancho A., Pelacho B., Iglesias-García O., Melo E. et al. Heterogeneous micromechanical properties of the extracellular matrix in healthy and infarcted hearts. Acta Biomaterialia. 2014;10(7):3235-3242.
- Martínez-García M.-A., Martorell-Calatayud A., Nagore E., Valero I., Selma M.J., Chiner E. et al. Association between sleep disordered breathing and aggressiveness markers of malignant cutaneous melanoma. European Respiratory Journal. 2014;43(6):1661-1668.
- Moreno-Indias I, Torres M, Montserrat JM, Sanchez-Alcoholado L, Cardona F, Tinahones FJ et al. Intermittent hypoxia alters gut microbiota diversity in a mouse model of sleep apnoea.The European respiratory journal. 2014.

Highlights

The research activity of the group has an interdisciplinary and translational character, integrating basic and clinical aspects. In 2014 the research has focused mainly on the corporate programs "Sleep Apnea-Hypopnea Syndrome" (SAHS) and "Acute Lung Injury" (ALI). In the first program we have obtained very significant achievements in the study of the relationship between cancer and SAHS. We have established that there is increased cancer mortality in patients with SAHS, that SAHS enhances human malignant melanoma and we have shown that the immune system plays an important role in cancer-related SAHS. We have also shown that telemetric tools are useful for diagnosing and home monitoring of SAHS. We have developed research contracts with companies to improve instrumentation equipment for SAHS therapy. In animal models we have determined that age induces significant changes in brain response to apneas and male fertility is greatly reduced by the intermittent hypoxia of SAHS. In ALI we have used tissue engineering tools to advance the understanding of the basic mechanisms of lung regeneration/repair. Using nano- and micro-technologies we first described local changes in rigidity of the extracellular matrix in normal and fibrotic lungs. These results will allow understanding cell-matrix interaction in lung regeneration. We have characterized the local viscoelasticity of normal and fibrotic cardiac tissue, which is relevant to understand cardiac remodeling in pulmonary hypertension. We have also studied the mechanical changes induced in pulmonary extracellular matrix by freezing/thawing and sterilization of the lung tissue. We also described for the first time that the partial pressure of oxygen enhances physiological differentiation of stem cells into lung epithelial phenotypes, being relevant for the optimization of lung regeneration.

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Tissue Engineering Research Group

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Obieta Vilallonga, Isabel

Group Members

STAFF MEMBERS: Argárate Madariaga, Nerea

ASSOCIATED MEMBERS: Álvarez Luque, Noelia | Atorrasagasti Goyalde, Garbiñe | Bilbao Alba, Leire | Braceras Izaguirre, Iñigo | Briz Izeta, Nerea | Bustero Zuazu, Izaskún | Eguizabal Luzuriaga, Ainhoa | Garagorri Ganchegi, Nerea | Garmendia Arcelus, Nerea | Goikoetxea Mendizábal, Leire | Jurado Oñate, María Jesús | Lorenzo Chocardo, Jaione | Madarieta Pardo, Iratxe | Murua Larrañaga, Olatz | Olalde Graells, Beatriz | Sáez Martínez, Virginia | Valero Congil, Jesús Manuel.

CONTRIBUTORS: Azpiroz Dorronsoro, Patxi | Gastón Caminos, Ainhoa | Vera Martín, Carolina

Main lines of research

DEVICES AND MATERIALS FOR *IN VIVO* APPLICATIONS.

- Biodegradable matrices for tissue regeneration.
- Non-degradable materials for bone implants with controlled porosity.
- Functionalization of device surfaces through humid chemistry.
- Biodegradable materials for advanced therapies (polymeric coatings and nanoparticles for supplying medicines and injectable hydrogels for cell therapy).

IN VITRO DIAGNOSTIC DEVICES AND CELL-BASED TESTS.

- Materials and technologies that allow 3D in vitro cell culture.
- Customised consumable-based polystyrene design.
- Carbon nanotubes with integrated biosensors.

BIOLOGICAL ASSESSMENT.

- CE marking, certification of standard ISO 10993.
- Characterization of the biological impact for new materials and products.
- Nano-safety: biological impact assessment for nanomaterials (cell consumption, mutagenicity, pro-inflammatory action, etc).

Most relevant scientific articles

- Alio del Barrio J.L., Chiesa M., Gallego Ferrer G., Garagorri N., Briz N., Fernández-Delgado J. et al. Biointegration of corneal macroporous membranes based on poly(ethyl acrylate) copolymers in an experimental animal model. Journal of Biomedical Materials Research - Part A. 2014.
- Braceras I., Vera C., Ayerdi-Izquierdo A., Munoz R., Lorenzo J., Álvarez N. et al. Ion implantation induced nanotopography on titanium and bone cell adhesion. Applied Surface Science. 2014;310:24-30.
- Braceras I., Pacha-Olivenza M.A., Calzado-Martin A., Multigner M., Vera C., Broncano L.L.-. et al. Decrease of Staphylococcal adhesion on surgical stainless steel after Si ion implantation. Applied Surface Science. 2014;310:36-41.
- Argarate N., Olalde B., Atorrasagasti G., Valero J., Carolina Cifuentes S., Benavente R. et al. Biodegradable Bi-layered coating on polymeric orthopaedic implants for controlled release of drugs. Materials Letters. 2014;132:193-195.

Institution: Fundación Tecnalia Research & Innovation

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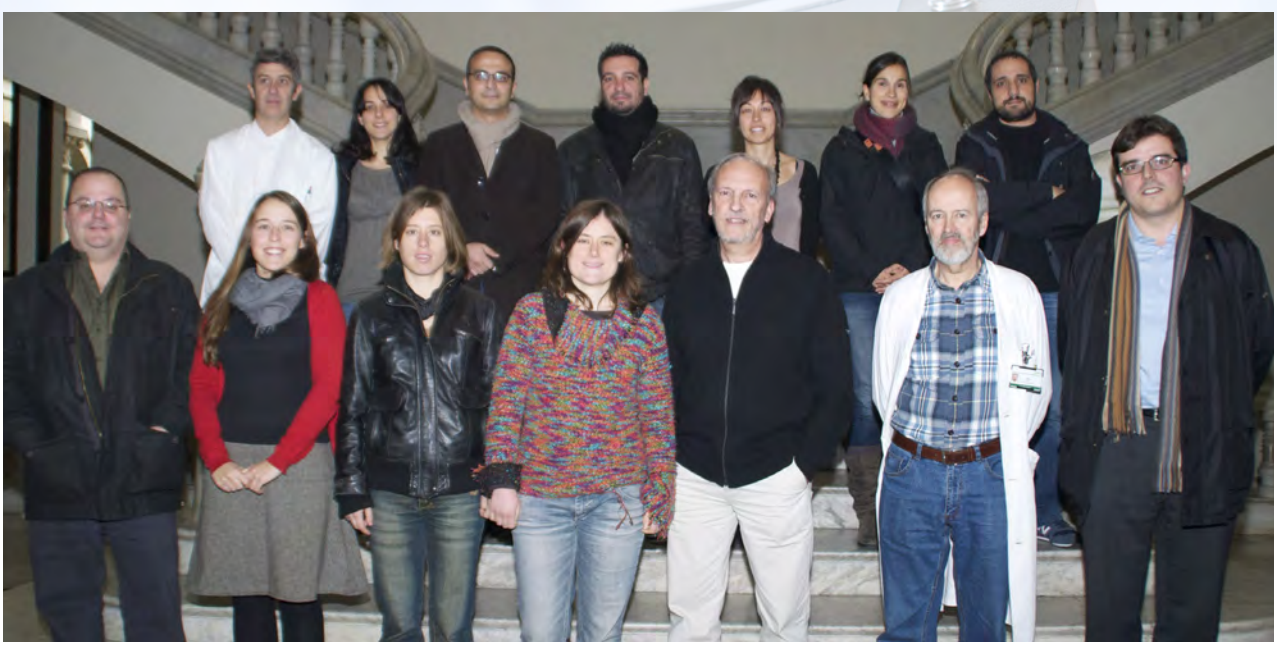
Biomedical Imaging Group

Bioengineering and Medical Imaging



Lead Researcher: Pavía Segura, Javier

Group Members

STAFF MEMBERS: Tudela Fernández, Raúl

ASSOCIATED MEMBERS: Cot Sanz, Albert | Falcón Falcón, Carlos | Gispert López, Juan Domingo | Juvells Prades, Ignacio | Pareto Onghena, Deborah | Ros Puig, Domingo | Sempau Roma, Josep | Setoain Perego, Javier | Soria Rodríguez, Guadalupe.

CONTRIBUTORS: Calvo Boixet, Anna | Gallego, Judit | Herance Camacho, Raúl | Martí Fuster, Berta | Pino Sorroche, Francisco | Roé Vellvé, Núria | Romera Martínez, Ingrid.

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

- Martí-Fuster B., Esteban O., Thielemans K., Setoain X., Santos A., Ros D. et al. Including anatomical and functional information in MC simulation of PET and SPECT brain studies. Brain-VISET: A voxel-based iterative method. IEEE Transactions on Medical Imaging. 2014;33(10):1931-1938.
- Perissinotti A., Setoain X., Aparicio J., Rubi S., Fuster B.M., Donaire A. et al. Clinical role of subtraction ictal SPECT coregistered to MR imaging and 18F-FDG PET in pediatric epilepsy. Journal of Nuclear Medicine. 2014;55(7):1099-1105.
- Riga M.S., Soria G., Tudela R., Artigas F., Celada P. The natural hallucinogen 5-MeO-DMT, component of Ayahuasca, disrupts cortical function in rats: reversal by antipsychotic drugs. International Journal of Neuropsychopharmacology. 2014.
- Ninerola-Baizan A., Rojas S., Bonastre M., Tudela R., Lomena F., Pavia J. et al. In vivo evaluation of the dopaminergic neurotransmission system using [123I]FP-CIT SPECT in 6-OHDA lesioned rats. Contrast Media and Molecular Imaging. 2014.
- Roe-Vellve N., Pino F., Falcon C., Cot A., Gispert J.D., Marin C. et al. Quantification of rat brain SPECT with 123I-ioflupane: Evaluation of different reconstruction methods and image degradation compensations using Monte Carlo simulation. Physics in Medicine and Biology. 2014;59(16):4567-4582.

Highlights

PHD THESIS

- Francisco Pino Sorroche. University of Barcelona, 21/10/2014. "Reconstrucción y cuantificación de estudios SPECT en animal pequeño".
- Foteini Popota. Pompeu Fabra University, 27/11/2014. "Comparative study of dedicated Monte Carlo simulation codes for the performance evaluation of small animal PET systems".
- Sebastià Rubí Sureda, 24/11/2014. "Aplicación de la Tomografía por Emisión de Positrones cerebral con diferentes trazadores en la valoración prequirúrgica de pacientes con epilepsia".
- Monica Giraldo Chica, 29/10/2014. "Anatomical differences of the lateral geniculate nucleus in subjects with dyslexia".

CLINICAL TRIALS

- Begining of three clinical trials for brain amyloid imaging with new 18F-radiotracers (Florbetapir and flutemetamol).

NEW RESEARCH LINE

- Quantification of PET studies with radiotracers binding beta-amyloid protein in Alzheimer disease.

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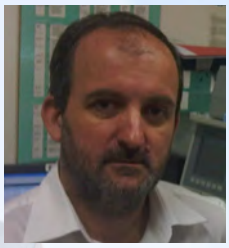

NanoBioCel: Micro and Nano Technologies, Biomaterials and Cells Research Group

Programme: Nanomedicine

Lead Researcher: Pedraz Muñoz, José Luis

Group Members

STAFF MEMBERS: Ciriza Astrain, Jesús | Losada Narvaez, Ángela

ASSOCIATED MEMBERS: Esquisabel Alegría, Amaia | Hernández Martín, Rosa María | Igartúa Olaechea, Manoli | Orive Arroyo, Gorka | Zarate Sesma, Jon.

CONTRIBUTORS: Agirre Díez, Mireia | Egusquiaguirre Martín, Susana Patricia | Gainza Luzea, Garazi | Garate Letona , Ane | Gartziandia López de Goikoetxea, Oihane | Herrán Martínez, Enara | Moreno Sastre, María | Pastor Navarro, Marta | Saenz del Burgo Martínez, Laura | Salvador Martínez, Aiala | Santos Vizcaíno, Edorta.

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.

- Pharmacocinetic 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, antineoplasics and antibiotics.

Most relevant scientific articles

- Puras G., Mashal M., Zarate J., Agirre M., Ojeda E., Grijalvo S. et al. A novel cationic niosome formulation for gene delivery to the retina. Journal of Controlled Release. 2014;174(1):27-36.
- Gainza G., Pastor M., Aguirre J.J., Villullas S., Pedraz J.L., Hernandez R.M. et al. A novel strategy for the treatment of chronic wounds based on the topical administration of rhEGF-loaded lipid nanoparticles: In vitro bioactivity and in vivo effectiveness in healing-impaired db/db mice. Journal of Controlled Release. 2014;185(1):51-61.
- Pastor M., Moreno-Sastre M., Esquisabel A., Sans E., Vinas M., Bachiller D. et al. Sodium colistimethate loaded lipid nanocarriers for the treatment of Pseudomonas aeruginosa infections associated with cystic fibrosis. International Journal of Pharmaceutics. 2014;477(1-2):485-494.
- Herran E., Requejo C., Ruiz-Ortega J.A., Aristieta A., Igartua M., Bengoetxea H. et al. Increased antiparkinson efficacy of the combined administration of VEGF- and GDNF-loaded nanospheres in a partial lesion model of Parkinson's disease. International Journal of Nanomedicine. 2014;9(1):2677-2687.
- Del Burgo L.S., Hernández R.M., Orive G., Pedraz J.L. Nanotherapeutic approaches for brain cancer management. Nanomedicine: Nanotechnology, Biology, and Medicine. 2014;10(5):905-919.

Highlights

During 2014, several relevant facts had been achieved regarding scientific results and also with respect to contracts with companies.

As a result of team work we got two patents with Praxis, a spanish pharmaceutical company: "lipid nanoparticles of tobramicine" and biodegradable biobnanoparticles to release GSE24-2 peptides:

procedure of extraction and usage. Regarding national projects: we got a "Reto de Investigación 2013" project from the Ministery of Economy and Competitiveness: nanoencasulated neurotrophic factors and gene therapy to treatment of neurodegenerative diseasesusing less invasive routes: NANOTEG.The duration of this project is from 2014 to 2018 and has a grant of 200.000 euros. We got also a "Reto de Colaboración" project with Sylentis a RNAi therapeutics company jointly with two CIBER BBN groups: NN-UMH from Elche led by Eduardo Fernandez and GQNA-CSIS led by Rammon Eritja from Barcelona. The ttle of the project is: new treatments to combat degenerative retina illnesses.

Another aspect to highlight, during 2014, is the total income the group obtained through different contracts tallied to 741.069 euros.

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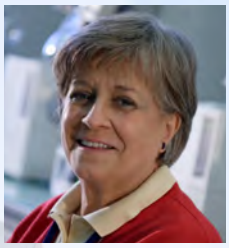
Biofunctional Nanomaterials Laborator

Programme: Nanomedicine



Lead Researcher: Penadés Ullate, Soledad

Group Members

STAFF MEMBERS: García Martín, Isabel

ASSOCIATED MEMBERS: Aranaiz Villanueva, Blanca Ester | Carril García, Mónica | Del Valle Carrandi, Lourdes | Di Giavincenzo, Paolo | Giner Casarés, Juan José | Liz Marzan, Luis M | Martín Lomas, Manuel | Michelena Elizalde, Olatz | Reichardt, Niels Christian.

Main lines of research

MICROARRAY BASED GLYCOMICS

- Solution and solid-phase synthesis of biologically important oligosaccharides.
- Development of glycan and lectin array-based tools for glycan biomarker discovery and the study of carbohydrate-protein interactions.
- Bioassays for carbohydrate processing enzymes.

GLYCONANOTECHNOLOGY

- Preparation of multivalent gold glyconanoparticles for studying biological interactions where carbohydrate are involved.
- Gold glyconanoparticles as microbicides and vaccines against pathogens (HIV, Streptococcus pneumoniae).
- Targeted biofunctional magnetic and fluorescent nanoparticles as multimodal probes for different imaging techniques (MRI, CT, PET).
- Targeted magnetic nanoparticles for diagnosis of the vulnerability of atheroma plaques and neurodegenerative diseases.

Most relevant scientific articles

- Frigell J., García I., Gómez-Vallejo V., Llop J., Penadés S. 68Ga-labeled gold glyconanoparticles for exploring blood-brain barrier permeability: Preparation, biodistribution studies, and improved brain uptake via neuropeptide conjugation. Journal of the American Chemical Society. 2014;136(1):449-457.
- Chiodo F., Marradi M., Park J., Ram A.F.J., Penadés S., Van Die I. et al. Galactofuranose-coated gold nanoparticles elicit a pro-inflammatory response in human monocyte-derived dendritic cells and are recognized by DC-SIGN. ACS Chemical Biology. 2014;9(2):383-389.
- Candiota A.P., Acosta M., Simoes R.V., Delgado-Goni T., Lope-Piedrafita S., Irure A. et al. A new ex vivo method to evaluate the performance of candidate MRI contrast agents: A proof-of-concept study. Journal of Nanobiotechnology. 2014;12(1).
- Etxebarría J., Calvo J., Reichardt N.-C. Nanostructured weathering steel for matrix-free laser desorption ionisation mass spectrometry and imaging of metabolites, drugs and complex glycans. Analyst. 2014;139(11):2873-2883.
- Murray R.A., Qiu Y., Chiodo F., Marradi M., Penadés S., Moya S.E. A quantitative study of the intracellular dynamics of fluorescently labelled glyco-gold nanoparticles via fluorescence correlation spectroscopy. Small. 2014;10(13):2602-2610.

Highlights

The year 2014 was especially important to strengthen the research of the group towards translational medicine.

The group of Niels-Christian Reichardt at CIC biomaGUNE has developed the CarboQuant platform technology for absolute glycan quantifition by mass spectrometry. The patented technology is based on the preparation and use of stable isotope labeled glycans as internal standards. Applications include clinical diagnosis and quality control for the development and production of biopharmaceuticals. A market study has been made and a business plan written to prepare for the commercialization of the technology via a spin-off company which is planned for March 2015.

Based on the CarboQuant technology two kits for quantitative glycan profiling employing MALDI-Tof MS termed mAbsolute have been developed and validated. These kits, and a quantification software are currently being tested in a pilot study for their use in biopharmaceutical quality control by Roche/Germany and MSD/The Netherlands. A dedicated kit will be employed in a first clinical diagnostics study with Leiden/The Netherlands University Medical Center.

IMMUNOSHAPE, coordinated by Niels-Christian Reichardt is a Marie Curie European Training Network which brings together 14 leading European partners in a transnational network, implementing a multidisciplinary and multisectorial research and training programme between academic and industrial partners in the fields of biomedical glycoscience and its industrial applications. IMMUNOSHAPE aims at training a new generation of scientists that will be capable to develop new lead structures for highly selective glycan based multivalent immunotherapeutics with clinical applications.

Midatech Biogune S.L., part of the Midatech Pharma group, has completed the refit of its plant in Bilbao. The aim was to adapt the installations and infrastructure in order to allow manufacture of its nano medicine products in the pre-clinical phase in sterile conditions. "Project financed by the Ministry of Economy and Competition, through the program EQUIPA 2014".

Institution: CIC biomaGUNE

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Website: http://www.cicbiomagune.es/secciones/investigacion/ficha_laboratorio.php?idioma=en&unidad=1&subgrupo=2&subseccion=unidades_investigacion

Health Technology Group

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Peris Serra, José Luis

Group Members

STAFF MEMBERS: Primo Capella, Víctor Javier | Utrera Molina, Miguel Ángel

ASSOCIATED MEMBERS: Atienza Vicente, Carlos Manuel | Belda Lois, Juan Manuel | Bermejo Bosch, Ignacio | De Rosario Martínez, Helios | Gómez Pérez, Amelia L | Gómez Sendra, Fernando | Molla Domenech, Fernando | Oltra Pastor, Alfonso | Page del Pozo, Álvaro Felipe | Prat Pastor, Jaime Miguel | Roger López, Isabel | Sánchez Lacuesta, José Javier | Villanueva García, Manuel.

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.

TECHNOLOGY CONSULTANCY.

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

BIOMECHANICAL EVALUATION OF MEDICAL DEVICES

TRAINING

TIC APPLICATIONS

Most relevant scientific articles

- Page A., De Rosario H., Mata V., Besa A. Model of soft tissue artifact propagation to joint angles in Human movement Analysis. Journal of Biomechanical Engineering. 2014;136(3).
- De Rosario H., Page T., Mata V. Point of optimal kinematic error: Improvement of the instantaneous helical pivot method for locating centers of rotation. Journal of Biomechanics. 2014;47(7):1742-1747.
- De Rosario H., Belda-Lois J.M., Fos F., Medina E., Poveda-Puente R., Kroll M. Correction of joint angles from kinect for balance exercising and assessment. Journal of Applied Biomechanics. 2014;30(2):294-299.
- Sánchez-Sánchez M.L., Belda-Lois J.-M., Mena-del Horno S., Viosca-Herrero E., Gisbert-Morant B., Igual-Camacho C. et al. Functional principal component analysis as a new methodology for the analysis of the impact of two rehabilitation protocols in functional recovery after stroke. Journal of NeuroEngineering and Rehabilitation. 2014;11(1).

Highlights

During 2014, GTS-IBV group from CIBER has participated in different activities to define and prepare a proposal, called InnoLife, for the call 2014 of the European Institute of Innovation & Technology (EIT) for a new Knowledge & Innovation Community (KIC) on Healthy Living and Active Ageing. This proposal has won the call for the new KIC on health (EIT Health).

EIT Health is a consortium of more than 144 top European companies, universities and research centres from 14 European countries, with nodes in Spain, France, United Kingdom, Belgium, Sweden and Germany. Its objective is to promote living longer and better lives: to age more independently and to reach more sustainable healthcare systems. To achieve this, new products, services and concepts will be developed in the framework of collaborative projects between companies, research centres, universities, hospitals and other stakeholders.

EIT Health will address the following societal challenges: (i) to promote healthy living (self-management of health and lifestyle interventions), (ii) to support active ageing (workplace interventions and overcoming functional loss), and (iii) to improve healthcare (improving healthcare systems and treating and managing chronic diseases).

Other relevant projects:

- ISTOPFALLS: European funded Collaborative project. To develop a home-based system that helps older people to prevent their risk of falling, by means of Kinect games and monitorisation of their daily physical activity.
- HARKEN: Research for SME Call. To develop a new sensor to capture heart rate and respiration signals from the interior of a car, using only the textile elements of the car, without devices worn by the driver.
- MAMMOCARE: Research for SME Call. Breast biopsy system guided by Positron Emission Mammography allowing real-time 3D visualization of tumour lesion and needle insertion guidance for higher sampling accuracy and efficiency.

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Centre of Regenerative Medicine in Barcelona

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Raya Chamorro, Ángel

Group Members

STAFF MEMBERS: Garreta Bahima, Elena

ASSOCIATED MEMBERS: Bedford Guaus, Sylvia | Montserrat Pulido, Nuria

CONTRIBUTORS: Cortina Duran, Carme

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

- Navarro S., Moleiro V., Molina-Estevez F.J., Lozano M.L., Chinchon R., Almarza E. et al. Generation of iPSCs from genetically corrected Brca2 hypomorphic cells: Implications in cell reprogramming and stem cell therapy. Stem Cells. 2014;32(2):436-446.
- Castano A.G., Hortiguela V., Lagunas A., Cortina C., Montserrat N., Samitier J. et al. Protein patterning on hydrogels by direct microcontact printing: Application to cardiac differentiation. RSC Advances. 2014;4(55):29120-29123.
- Gu Y., Liu G.-H., Plongthongkum N., Benner C., Yi F., Qu J. et al. Global DNA methylation and transcriptional analyses of human ESC-derived cardiomyocytes. Protein and Cell. 2014;5(1):59-68.
- Zhang K., Liu G.-H., Yi F., Montserrat N., Hishida T., Esteban C.R. et al. Direct conversion of human fibroblasts into retinal pigment epithelium-like cells by defined factors. Protein and Cell. 2014;5(1):48-58.

Highlights

The CMR[B] is a research centre focused on the investigation of the mechanisms that regulate cell differentiation and patterning during development and regeneration. In the same manner, the general activity of the center is orientated towards the research in regenerative medicine, with special emphasis in the generation of patient-derived induced pluripotent stem cells (iPSCs) for disease modelling. Our goal is to define efficient protocols for the differentiation of mesenchymal stem cells (MSCs) from human tissues (adipose and bone marrow tissues) and iPSCs towards bone, cartilage, retinal pigmented epithelial cells, hematopoietic cells and cardiac muscle cells. Our newly defined protocols include the use of soluble factors, chemically defined media, biomatrices and tissue-specific genes.

In order to accomplish our aims we have been working in collaboration with Dr. Ivon Cusco from the CIBERER-UPF, Dr. Juan Bueren from CIBERER-CIEMAT, among other collaborating studies.

Besides, we have continued collaborating with Dr. Elena Martínez (IBEC; CIBER-BBN). As result of this research, we presented a poster at the 8th CIBER-BBN Annual Conference (10-11/11/2014, Girona):

Authors: E. Garreta, A. G. Castaño, E. Martínez, A. Raya

Title: Derivation of retinal neurons from human induced pluripotent stem cells on top of hydrogel substrates with different topographies

Dr. Bedford presented a research project to the ISCIII, AES 2014 call, which was granted:

PI14/02184 Desarrollo de una plataforma de reprogramación de alto rendimiento basada en extractos de ovocito empaquetados en liposomas

Furthermore, our group, as coordinator team, presented a proposal to the ISCIII, AES 2014 call for CIBER's Integrated projects of Excellence and this proposal was selected for funding:

PIE14/0061 Molecular links between diabetes and neurodegenerative disorders

Coordinator PI: Ángel Raya

Total funding amount: 660.000€

Project duration: 01/01/2015 - 31/12/2017

Twelve groups from different CIBER (CIBERER, CIBERNED, CIBERDEM, CIBERBBN) are involved in this project.

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Small Biosystems Lab

Programme: Nanomedicine

Lead Researcher: Ritort Farran, Félix

Group Members

STAFF MEMBERS: Pastor del Campo, Isabel

ASSOCIATED MEMBERS: Huguet, Josep María | Palassini, Matteo

CONTRIBUTORS: Alemany, Anna | Bongini, Lorenzo | Camuñas Soler, Joan | Mañosas Castejón, María | Rey Serra, Blanca | 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

- Bosco A., Camunas-Soler J., Ritort F. Elastic properties and secondary structure formation of single-stranded DNA at monovalent and divalent salt conditions. Nucleic Acids Research. 2014;42(3):2064-2074.
- Liu Z., Frutos S., Bick M.J., Vila-Perello M., Debelouchina G.T., Darst S.A. et al. Structure of the branched intermediate in protein splicing. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(23):8422-8427.
- Ribezzi-Crivellari M., Ritort F. Free-energy inference from partial work measurements in small systems. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(33).
- Alemany A, Ritort F. Determination of the elastic properties of short ssDNA molecules by mechanically folding and unfolding DNA hairpins.Biopolymers. 2014;101(12):1193-9.

Highlights

Heterogeneity has become a major Trojan horse in several evolutionary diseases such as cancer and neurological disorders due to the disparate variety of underlying factors and causes: two cells grown from the same strain may often exhibit strikingly distinct behaviors. During this year we have made an important breakthrough: we have demonstrated (publication 3) that it is possible to characterize energy and entropy processes by inference (rather than by direct measurement) by imposing the validity of general physical laws in molecular systems. The result should be applicable to extract generic properties of heterogeneous molecular and cellular ensembles. Most relevant is the study of mechanical properties of cancer cell populations: mechanical phenotyping or the quantitative testing of deformability in a cell population is already used as a diagnostic tool for oral cancers. Measuring deformation characteristics may allow for the identification of different cell populations in a tumor: Invasive metastatic cancer cells that need to be motile and malleable are expected to be much softer than other cancer cells and this should be reflected by their elastic moduli. This study is carried out in the framework of the collaborative intra-CIBER project (PENTRI) led by Dr. Simo Schwartz. Our preliminary measurements of the stiffness of normal cancer cells were presented in the general CIBER conference past November and show a large heterogeneity with two characteristic sub-populations of cancer cells that we expect to identify during the current year 2015. Our long-term contribution is to be able to assist clinical groups in the identification of mechanics based biomarkers.

Other intraCIBER project concerns the stabilizing effects of anticancer drugs binding to nucleic acids. In the framework of a intra-CIBER collaboration with the group led by F. Albericio we have investigated the intercalator peptide Thiocoraline (clinical phase trial I) finding it binds DNA preferentially to CG dinucleotide motifs. These results have been recently published and continued with the study of Yondelis (Pharmamar) binding DNA, a anticancer drug for soft tissue sarcoma and ovarian cancer.

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Biomedical Engineering Research Group

Programme: Bioengineering and Medical Imaging

Lead Researcher: Roa Romero, Laura

Group Members

STAFF MEMBERS: Estudillo Valderrama, Miguel Ángel | Naranjo Hernández, David

ASSOCIATED MEMBERS: Gómez Cia, Tomás | Milán Martín, José Antonio | Palma Álvarez, Alfonso | 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.

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- **Métodos y técnicas de electromagnetismo aplicadas a nanotecnología médica:** modelado y caracterización de las interacciones de los campos electromagnéticos con tejidos biológicos a diferentes escalas, y sus aplicaciones; diseño de dispositivos inteligentes para diagnóstico/terapia a nivel micro-/nano, y sus comunicaciones.

Most relevant scientific articles

- Estudillo-Valderrama M.A., Talaminos-Barroso A., Roa L.M., Naranjo-Hernández D., Reina-Tosina J., Areste-Fosalba N. et al. A distributed approach to alarm management in chronic kidney disease. IEEE Journal of Biomedical and Health Informatics. 2014;18(6):1796-1803.
- Callejón M.A., Reina-Tosina J., Naranjo-Hernández D., Roa L.M. Galvanic coupling transmission in intrabody communication: A finite element approach. IEEE Transactions on Biomedical Engineering. 2014; 61(3):775-783.
- Calvillo-Arbizu J., Roa-Romero L.M., Milán-Martín J.A., Areste-Fosalba N., Tornero-Molina F., Macia-Heras M. et al. Methodological approach for designing a telecare system for patients on pre-dialysis and peritoneal dialysis. Nefrologia. 2014; 34(2):149-157.

Highlights

Collaboration with University Hospitals HUVM (Sevilla), HCSC (Madrid), NSCT (Tenerife) and HUDN (Gran Canaria), has led to the clinical transfer of the e-Nefro platform to the respective Units of Nephrology. E-Nefro is a research project (AES, call 2011), aimed at the research of an e-health platform for renal patients. The surveys prepared to assess the usability and accessibility of end-users have been requested to be used by different professionals belonging to other hospitals.

The data distribution service (DDS) specification has been proposed for the alarm management system of e-health platforms. The study has been applied to the case of use of the e-Nefro platform, demonstrating the potential of DDS as a communication infrastructure for the personalization and prioritization of alarms and the optimal delivery of information.

Knowledge has been disclosed about galvanic coupling intrabody communication (IBC) transmission mechanisms by using a realistic model of the human arm. This approach has provided an insight into signal transmission paths through the human body, showing them to be considerably dependent on variables such as frequency and inter-electrode distance.

Regarding multiscale modeling, a computational model of the human cardiovascular system has been proposed as a training tool for medicine students.

On-going collaboration with the Respiratory Unit at HUVR (Seville) has led to two grants (Neumosur and Health Council, Government of Andalucía).

With regard to smart devices, a national patent has been submitted on a Bioimpedance measurement system, with different companies interested on its exploitation.

Two workshops have been organized: "TAOEI Day", with AIRBUS DS to seek for common areas of interest, and "Double-Use Technologies", with the participation of AIRBUS DS and Academia General del Aire San Javier.

In the context of staff training, a PhD Thesis has been concluded and presented (David Naranjo Hernández), and several Master Thesis and Degree Thesis have been graded.

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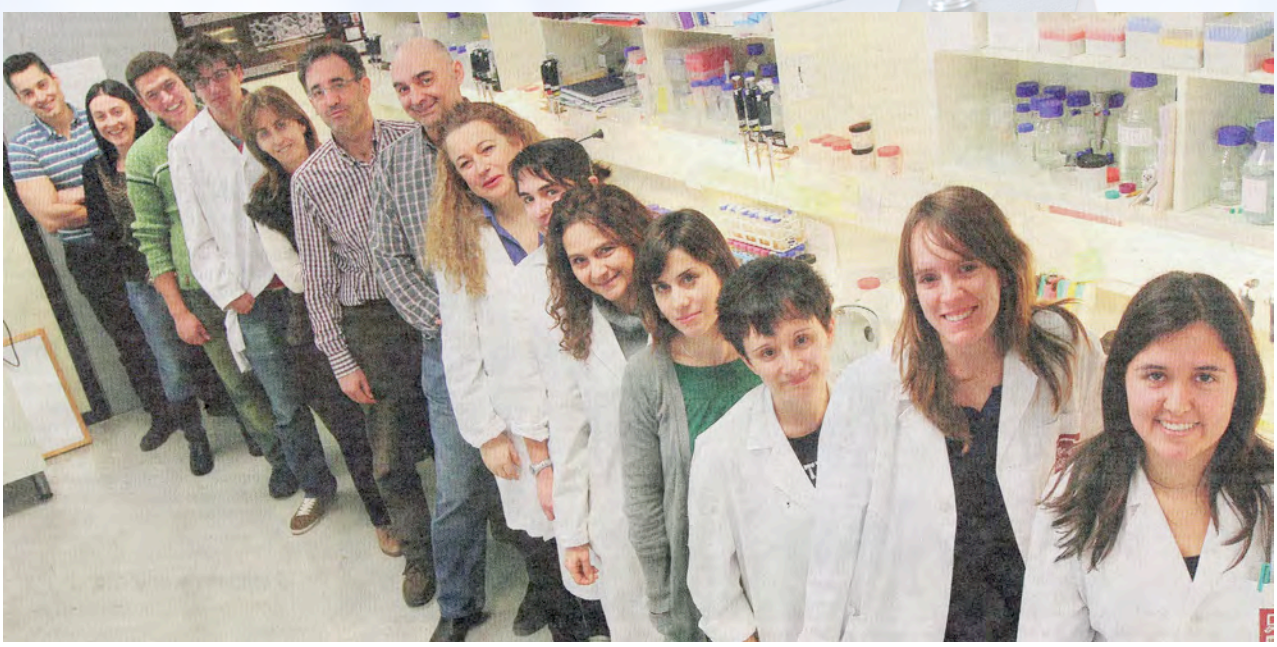
BIOFORGE

Programme: Biomaterials and Advanced Therapies



Lead Researcher: Rodríguez Cabello, José Carlos

Group Members

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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 bioactivd 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

- Tejeda-Montes E., Klymov A., Nejadnik M.R., Alonso M., Rodríguez-Cabello J., Walboomers X.F. et al. Mineralization and bone regeneration using a bioactive elastin-like recombinamer membrane. Biomaterials. 2014;35(29):8339-8347.
- González De Torre I., Quintanilla L., Pinedo-Martin G., Alonso M., Rodríguez -Cabello J.C. Nanogel formation from dilute solutions of clickable elastin-like recombinamers and its dependence on temperature: Two fractal gelation modes. ACS Applied Materials and Interfaces. 2014;6(16):14509-14515.
- Fernández-Colino A., Arias F.J., Alonso M., Rodríguez-Cabello J. Self-organized ECM-mimetic model based on an amphiphilic multiblock silk-elastin-like corecombinamer with a concomitant dual physical gelation process. Biomacromolecules. 2014;15(10):3781-3793.
- Costa R.R., Girotti A., Santos M., Arias F.J., Mano J.F., Rodríguez-Cabello J.C. Cellular uptake of multilayered capsules produced with natural and genetically engineered biomimetic macromolecules. Acta Biomaterialia. 2014;10(6):2653-2662.
- Tejeda-Montes E., Smith K.H., Rebollo E., Gómez R., Alonso M., Rodríguez-Cabello J.C. et al. Bioactive membranes for bone regeneration applications: Effect of physical and biomolecular signals on mesenchymal stem cell behavior. Acta Biomaterialia. 2014;10(1):134-141.

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Tissue Bioengineering and Cell Therapy Group

Programme: Biomaterials and Advanced Therapies / Nanomedicine

Lead Researcher: Ruiz Romero, Cristina

Group Members

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CONTRIBUTORS: Arufe Gondar, María | Fenández Pernas, Pablo | Freire Ruaño, Alicia | Hermida Gómez, Tamara | Sanjurjo Rodríguez, Clara | Vela Anero, Ángela.

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

- Rocha B., Calamia V., Casas V., Carrascal M., Blanco F.J., Ruiz-Romero C. Secretome analysis of human mesenchymal stem cells undergoing chondrogenic differentiation. Journal of Proteome Research. 2014;13(2):1045-1054.
- Burguera E.F., Vela-Anero T., Magalhaes J., Meijide-Failde R., Blanco F.J. Effect of hydrogen sulfide sources on inflammation and catabolic markers on interleukin 1β-stimulated human articular chondrocytes. Osteoarthritis and Cartilage. 2014;22(7):1026-1035.
- Cicione C, Muiños-López E, Hermida-Gómez T, Fuentes-Boquete I, Díaz-Prado S, Blanco FJ. Alternative protocols to induce chondrogenic differentiation: transforming growth factor-β superfamily.Cell and tissue banking. 2014.
- Magalhaes J., Crawford A., Hatton P.V., Blanco F.J., Roman J.S. Poly(2-ethyl-(2-pyrrolidone) methacrylate) and hyaluronic acid-based hydrogels for the engineering of a cartilage-like tissue using bovine articular chondrocytes. Journal of Bioactive and Compatible Polymers. 2014;29(6):545-559.
- Volkmer T., Magalhaes J., Sousa V., Santos L.A., Burguera E.F., Blanco F.J. et al. 2-(dimethylamino)ethyl methacrylate/(2-hydroxyethyl) methacrylate/α-tricalcium phosphate cryogels for bone repair, preparation and evaluation of the biological response of human trabecular bone-derived cells and mesenchymal stem cells. Polymers. 2014;6(10):2510-2525.

Highlights

In 2014, GBTTC-CHUAC has generated 17 peer-reviewed publications, describing: the relevance of secretome analysis for understanding possible mechanisms responsible for cartilage formation and the potential of a panel of extracellular markers described for the evaluation of tissue development in cell therapy or cartilage tissue engineering (TE) approaches; the therapeutic potential of exogenous sources of H2S in osteoarthritis (OA) through the regulation of relevant genes involved in the pathology and progression of the OA disease; the efficacy of different growth factors for the chondrogenic differentiation of mesenchymal stem cells; and the potential of hybrid hydrogels (PEPM-HA) for applications in cartilage TE.

GBTTC-CHUAC has obtained financial support from Xunta de Galicia to create the first Galician Network of Biomaterials together with other 5 groups, and obtained funding from the ISCIII for the development of strategies to identify markers of cartilage degradation (PI14/01707). The group has also started a science communication project funded by FECYT "Biomedicine with and for the Society" with the main goal of promoting public awareness of biomedical research through social media.

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Nanomedicine Group

Programme: Nanomedicine

Lead Researcher: Samitier Martí, Josep

Group Members

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CONTRIBUTORS: Bogachan Tahirbegi, Islam | Funes Luque, Miriam | Hortigüela Lázaro, Verónica | Izquierdo García, David | López Bosque, María Jesús | Pardo, Wilmer Alfonso | Parra Cabrera, César Alejandro | Sebastián Ávila, Jose L | Tahirbegi, Islam Bogachan | Zaffino, Rosa L.

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

- Tahirbegi I.B., Mir M., Schostek S., Schurr M., Samitier J. In vivo ischemia monitoring array for endoscopic surgery. Biosensors and Bioelectronics. 2014;61:124-130.
- Lagunas A., Castano A.G., Artes J.M., Vida Y., Collado D., Perez-Inestrosa E. et al. Large-scale dendrimer-based uneven nanopatterns for the study of local arginine-glycine-aspartic acid (RGD) density effects on cell adhesion. Nano Research. 2014;7(3):399-409.
- Comelles J., Caballero D., Voituriez R., Hortiguela V., Wollrab V., Godeau A.L. et al. Cells as active particles in asymmetric potentials: Motility under external gradients. Biophysical Journal. 2014;107(7):1513-1522.
- Van Heirstraeten L., Spang P., Schwind C., Drese K.S., Ritzi-Lehnert M., Nieto B. et al. Integrated DNA and RNA extraction and purification on an automated microfluidic cassette from bacterial and viral pathogens causing community-acquired lower respiratory tract infections. Lab on a Chip - Miniaturisation for Chemistry and Biology. 2014;14(9):1519-1526.
- Rigat-Brugarolas L.G., Elizalde-Torrent A., Bernabeu M., De Niz M., Martin-Jaular L., Fernández-Becerra C. et al. A functional microengineered model of the human splenon-on-a-chip. Lab on a Chip - Miniaturisation for Chemistry and Biology. 2014;14(10):1715-1724.

Highlights

- **Intrammural Projects:** The group NANOMED-IBEC started this year two intramural projects: Chondronanonet and E-Leukemia (E-leukemia was qualified as project of excellence by ANEP). The project chondronanonet has been selected to be evaluated for its transfer to the industry.
- **National Competitive Projects:** The group is involved in the preparation of two manuscripts derived from the work developed within the framework of the Oligocodes project (in colaboration with the CIBER-BBN group GQNA-CSIC).
- **European Projects:** the NANOMED-IBEC group participates in a highly innovative project of the European FET-Open program PLANTOID.
- **Transfer Projects to the industry:** NANOMED-IBEC and Genomica S.A.U. (Grupo Zeltia) company, the leading Spanish company in molecular diagnostics, created a Joint Research Unit that will provide an operational framework for close interaction on various R&D activities related to healthcare, including the development of a diagnostic device which will be clinically validated.
- **Other collaborating companies:** Nanoimmunotech, Zeu-inmunotec S.L., Enantia, Talleres Fiestas S.L., Biokit S.A., Microfluidics Chip Shop GmbH
- **Transfer of Clinical Research:** The NANOMED-IBEC group established a collaboration with the Hospital Vall d'Hebron to develop a sensor for the early diagnostics of prostate cancer (project funded through FIS ISCIII). NANOMED-IBEC is in collaboration with the Hospital Clínic de Barcelona in a project for the detection of neurodegenerative diseases.
- **Initiatives involving NANOMED-IBEC as coordinator or partner;** The NANOMED-IBEC group coordinates the relevant Spanish node of the Knowledge and Innovation Community (KIC) on healthy living and active ageing and manages the Spanish Nanomedicine Platform (Nanomed) and the Health UB campus (HUBc). Moreover, NANOMED-IBEC group participate as advisor in the European Commission's Key Enabling Technologies (KET).
- **Grants:** Elena Martínez (affiliated member to the NANOMED-IBEC group) received the prestigious Consolidator Grant from the European Research Council.

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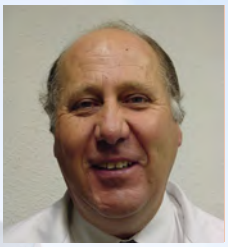
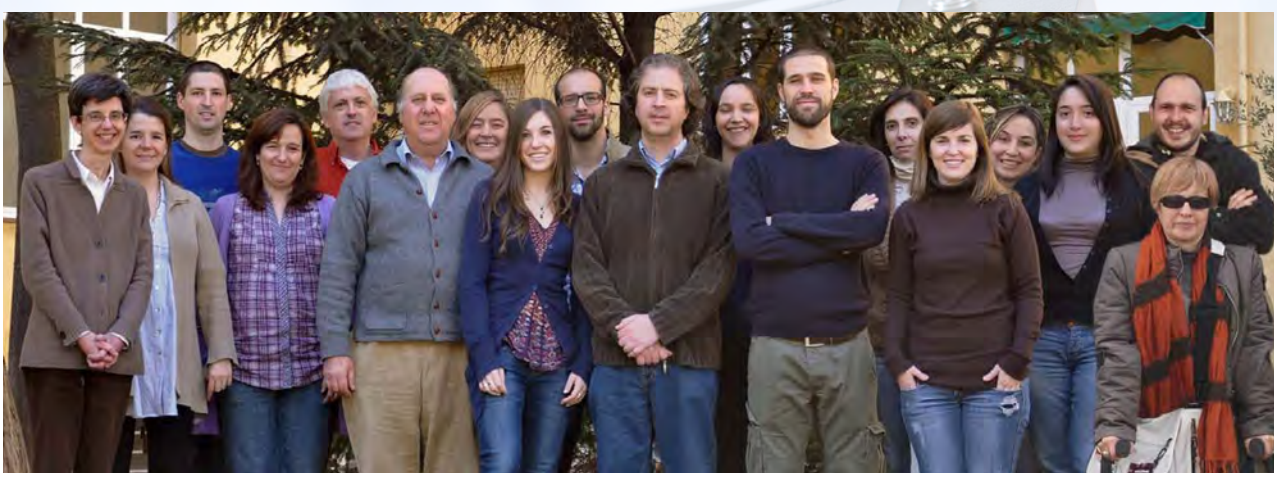
Biomaterials Group

Programme: Biomaterials and Advanced Therapies





Lead Researcher: San Román Del Barrio, Julio

Group Members

STAFF MEMBERS: Parra Cáceres, Juan

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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 mean 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 offers 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

- Dinjaski N., Fernández-Gutiérrez M., Selvam S., Parra-Ruiz F.J., Lehman S.M., San Román J. et al. PHACOS, a functionalized bacterial polyester with bactericidal activity against methicillin-resistant Staphylococcus aureus. Biomaterials. 2014;35(1):14-24.
- Zamora-Mora V., Fernández-Gutiérrez M., Román J.S., Goya G., Hernández R., Mijangos C. Magnetic core-shell chitosan nanoparticles: Rheological characterization and hyperthermia application. Carbohydrate Polymers. 2014;102(1):691-698.
- Gomez-Mascaraque L.G., Mendez J.A., Fernández-Gutiérrez M., Vazquez B., San Román J. Oxidized dextrins as alternative crosslinking agents for polysaccharides: Application to hydrogels of agarose-chitosan. Acta Biomaterialia. 2014;10(2):798-811.
- Aguilar M.R., San Román J. Smart Polymers and their Applications. Smart Polymers and their Applications. 2014;:1-568.
- Salerno A., Fernández-Gutiérrez M., San Román Del Barrio J., Pascual C.D. Macroporous and nanometre scale fibrous PLA and PLA-HA composite scaffolds fabricated by a bio safe strategy. RSC Advances. 2014;4(106):61491-61502.

Highlights

During 2014, the GBP-CSIC carried out research projects with groups of excellence participating in the CIBER-BBN network, through HOT-SCAFF and NANOVITE intramural CIBER-BBN projects, and a project in collaboration with clinicians external to CIBER-BBN funded by CIBER- ECO Foundation (Foundation for the Research of the Hospital Universitario of Getafe, Madrid). It has collaborated with companies from the biomedical sectors, by setting up of R+D contracts through the INNPACTO program (PROCUSENS and BACTDENT projects). Other specific contracts subscribed directly with companies such as LVD BIOTECH and INIBSA, have been developed and have given excellent results. In particular this success is reflected in the filling of 1 patent, setting up of procedures and even in products in the vascular, dental and ocular fields. On the other hand, the members of the groups published 18 publications in SCI journals and attended more than 10 international and national conferences presenting invited lectures.

The importance given to specialized training through the PhD programs should also be underlined, with two theses presented and defended at the Complutense University and several PhD theses in progress. Also the interchange of several PhD and Post doctoral students with foreign Universities has been carried out.

At national level the group has organized the XII Jornadas sobre Biomateriales y el Entorno Celular in Ávila, 14th February 2014, with the participation of more than 40 delegates. At international level, the group organized the UNESCO Catedra Course of University of La Havana, Cube, during the days 17 – 21 November 2014, and the International Course dedicated to Tissue Engineering Applied for the Treatment of Cardiovascular Diseases and Diabetes, in Merida Yucatán, Mexico, during 8 – 10 March 2014.

During December 2014 the group has received the first award INIBSA granted by the General Foundation of University of Salamanca for Regenerative Medicine in the Musculoskeletal Apparatus, funded by the company.

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Nanostructured Films and Particles

Programme: Nanomedicine

Lead Researcher: Santamaría Ramiro, Jesús

Group Members

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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. A 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

- Timko B.P., Arruebo M., Shankarappa S.A., McAlvin J.B., Okonkwo O.S., Mizrahi B. et al. Near-infrared-actuated devices for remotely controlled drug delivery. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(4):1349-1354.
- Sebastian V., Arruebo M., Santamaría J. Reaction engineering strategies for the production of inorganic nanomaterials. Small. 2014;10(5):835-853.
- Martin-Saavedra F.M., Cebrián V., Gomez L., Lopez D., Arruebo M., Wilson C.G. et al. Temporal and spatial patterning of transgene expression by near-infrared irradiation. Biomaterials. 2014;35(28):8134-8143.
- Urries I., Munoz C., Gómez L., Marquina C., Sebastián V., Arruebo M. et al. Magneto-plasmonic nanoparticles as theranostic platforms for magnetic resonance imaging, drug delivery and NIR hyperthermia applications. Nanoscale. 2014;6(15):9230-9240.
- Regiel-Futyra A., Kus-Liskiewicz M., Sebastián V., Irusta S., Arruebo M., Stochel G. et al. Development of noncytotoxic chitosan-gold nanocomposites as efficient antibacterial materials. ACS Applied Materials and Interfaces. 2014;7(2):1087-1099.

Highlights

MAIN PROJECTS

- HECTOR / MICROWAVE-ASSISTED MICROREACTORS: DEVELOPMENT OF A HIGHLY EFFICIENT GAS PHASE CONTACTOR WITH DIRECT CATAYST HEATING
  Jesus Santamaría. 01-mar-2011/ 28-feb-2016
- NANOVALID / DEVELOPMENT OF REFERENCE METHODS FOR HAZARD IDENTIFICATION, RISK ASSESSMENTAND LCA OF ENGINEERED NANOMATERIALS
  Jesus Santamaría. 01-nov-2011/ 31-oct-2015
- NANOHEDONISM / A photo-triggered on-demand drug delivery system for chronic pain
  Manuel Arruebo. 01-mar-2014/ 28-feb-2019

PATENTS

- MEDIO DE CALENTAMIENTO SENSIBLE A LA RADIACIÓN ELECTROMAGNÉTICA BASADO EN MATERIALES DE MOTT, Patente de invención, María Reyes Mallada Viana; José Gracia Budria; Jesús Santamaría Ramiro; Miguel Escuin Melero; Nuria Navascues García, UNIVERSIDAD DE ZARAGOZA, P201430542, 2014
- PROCESSO DE OBTENÇÃO DE NANOPARTÍCULAS POLIMÉRICAS, NANOPARTÍCULAS POLIMÉRICAS E SEU USO, Maria Aparecida de Souza, Erika Rosa Maria Kedor, Maria Inés Rocha Miritello Santoro, Jesus Santamaría Ramiro, Manuel Arruebo Gordo, Víctor Sebastián Cabeza, Laura Victoria Español Mariño; BR 10 2014 027403-0, Brasil, 03/11/2014, UNIVERSIDADE DE SÃO PAULO (Brasil)

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Biomedical Imaging Technology Group

Programme: Bioengineering and Medical Imaging

Lead Researcher: Santos Lleó, Andrés

Group Members

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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.

Most relevant scientific articles

- Fernández-de-Manuel L., Wollny G., Kybic J., Jiménez-Carretero D., Tellado J.M., Ramón E. et al. Organ-focused mutual information for nonrigid multimodal registration of liver CT and Gd-EOB-DTPA-enhanced MRI. Medical Image Analysis. 2014;18(1):22-35.
- Castro-Gonzalez C., Luengo-Oroz M.A., Duloquin L., Savy T., Rizzi B., Desnoulez S. et al. A Digital Framework to Build, Visualize and Analyze a Gene Expression Atlas with Cellular Resolution in Zebrafish Early Embryogenesis. PLoS Computational Biology. 2014;10(6).
- Arenal A., Pérez-David E., Avila P., Fernández-Portales J., Crisostomo V., Baez C. et al. Noninvasive identification of epicardial ventricular tachycardia substrate by magnetic resonance-based signal intensity mapping. Heart Rhythm. 2014;11(8):1456-1464.
- Marti-Fuster B., Esteban O., Thielemans K., Setoain X., Santos A., Ros D. et al. Including anatomical and functional information in MC simulation of PET and SPECT brain studies. Brain-VISET: A voxel-based iterative method. IEEE Transactions on Medical Imaging. 2014;33(10):1931-1938.
- Guerra P., Udias J., Herranz E., Santos-Miranda J., Herraiz J., Valdivieso M. et al. Feasibility assessment of the interactive use of a Monte Carlo algorithm in treatment planning for intraoperative electron radiation therapy. Physics in Medicine and Biology. 2014;59(23):7159-7179.

Highlights

A digital framework to build, visualize and analyze a gene expression atlas during zebrafish early embryogenesis has been published and the tools developed have been made freely available on line.

Research on image-guided liver surgery planning has produced a registration method to combined contrast-enhanced MR and CT images, combining the good capabilities to detect liver lesions of the former with the high specificity of the latter. This work has led to an international publication and is being evaluated with clinical cases.

Two new research contracts have been signed with Massachusetts Institute of Technology and Fundación madri+d para el Conocimiento. One has the aim of developing energy-based technologies to reduce central-line infections in hemodialysis patients and the other is to improve pulmonary embolism detection and prognosis using computer vision.

The work on determining the prognosis of patients suffering from pulmonary embolism has led to an international patent application, given the commercial interest expressed by several companies in the sector, and a prospective clinical study has been approached in Brigham and Women's Hospital.

A fast acquisition module for PET imaging has been designed, built and tested, producing a technology transfer to the Spanish company Sedecal that incorporates this module in its new line of high resolution PET scanners.

Finally, the group has participated in two international challenges: one for automated vessel segmentation in lung CT images, and another for cell tracking in microscopy images. Their results have been released in two journal publications.

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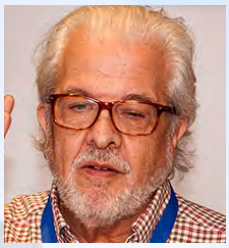
Nanomembrane Group

Programme: Nanomedicine



Lead Researcher: Sanz Carrasco, Fausto

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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., Darwish N., Saletra W.J., Pérez-García L., Sanz F., Puigmarti-Luis J. et al. Highly conductive single-molecule wires with controlled orientation by coordination of metalloporphyrins. Nano Letters. 2014;14(8):4751-4756.
- Izquierdo-Serra M., Gascon-Moya M., Hirtz J.J., Pittolo S., Poskanzer K.E., Ferrer E. et al. Two-photon neuronal and astrocytic stimulation with azobenzene-based photoswitches. Journal of the American Chemical Society. 2014;136(24):8693-8701.
- Pérez-Madrigal M.M., Giannotti M.I., Armelin E., Sanz F., Aleman C. Electronic, electric and electrochemical properties of bioactive nanomembranes made of polythiophene:thermoplastic polyurethane. Polymer Chemistry. 2014;5(4):1248-1257.
- Pittolo S., Gómez-Santacana X., Eckelt K., Rovira X., Dalton J., Goudet C. et al. An allosteric modulator to control endogenous G protein-coupled receptors with light. Nature Chemical Biology. 2014.
- Redondo-Morata L., Giannotti M.I., Sanz F. Structural impact of cations on lipid bilayer models: Nanomechanical properties by AFM-force spectroscopy. Molecular Membrane Biology. 2014;31(1):17-28.

Highlights

Aiming to demonstrate that drugs can display enhanced therapeutic effects and reduced side effects by means of remote regulation of their activity with light, we have published two studies targeting G protein-coupled receptors (GPCRs): A photochromic ligand of the adenosine receptor (http://dx.doi.org/10.1021/bc5003373) and an allosteric modulator of metabotropic glutamate receptor mGlu5 (http://dx.doi.org/10.1038/nchembio.1612). The latter displayed outstanding advantages in vitro (nanomolar potency in metabotropic glutamate receptor mGlu5, photoresponsive activity, availability of a large library of active analogue compounds, patent protection pending P8657EP00 / PCT EP13382374) and thus made a robust lead compounds that was tested in the framework of an ERC-Proof-of-concept grant (TheraLight).

We have also been pioneers in the photoisomerization of azobenzene-based neuronal ligands by illumination with infrared pulsed lasers ("two-photon switching") (http://dx.doi.org/10.1021/ja5026326). This method has the advantage of providing extreme (submicron) focusing of the activation volume and thus pushes the limits of therapeutic targeting to the subcellular scale.

During 2014 we have published the first results of the Nanoxen++ CIBER-bbn intramural project (e.g. in vivo testing with small transparent animals), demonstrating the general methodology (http://dx.doi.org/10.14440/jbm.2014.29) and the pharmacological importance of a light-regulated drug (http://dx.doi.org/10.1038/nchembio.1612).

We have moved towards higher complexity systems within the "nanomechanics of biosystems". As the understanding of membrane organization and functionality improves, it is likely that the mechanisms behind several diseases be better understood, followed by the development of new or improved treatments. We evaluate the influence of different constituent of lipid bilayers into their stability and function, a platform that can be relevant in the evaluation of various molecules of interest in nanomedicine (like potential drugs) or in diagnostics of different pathologies. We have specifically obtained interesting results on the influence of cholesterol and cerebrosides (normally present in brain tissue, but accumulated in excess in several neurodegenerative diseases) in the domains formation and the mechanical stability in model membranes. In addition, we have been working on the development and characterization of polymeric-based platforms to manipulate and enhance cellular attachment and growth. We used AFM to characterize films/membranes mechanical and electrical properties which influence the interaction with cell membranes (http://dx.doi.org/10.1021/am502150q; http://dx.doi.org/10.1039/C3PY01313H), and to characterize the surface of contact lenses of different materials (http://dx.doi.org/10.1016/j.colsurfb.2014.06.026).

Last but not least, we have published several review articles in most fields where the laboratory is active.

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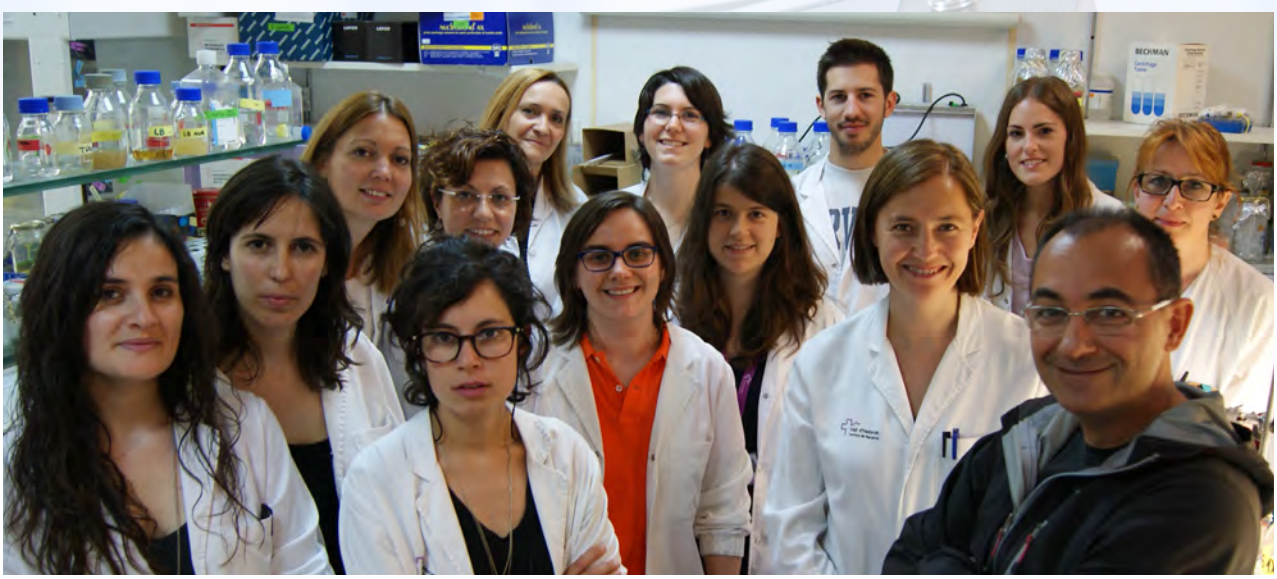
Drug Delivery and Targeting Group

Programme: Nanomedicine



Lead Researcher: Schwartz Navarro, Simó

Group Members

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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

- Alana L., Sese M., Canovas V., Punyal Y., Fernández Y., Abasolo I. et al. Prostate tumor OVerexpressed-1 (PTOV1) down-regulates HES1 and HEY1 notch targets genes and promotes prostate cancer progression. Molecular Cancer. 2014;13(1).
- Candiota A.P., Acosta M., Simoes R.V., Delgado-Goni T., Lope-Piedrafita S., Irure A. et al. A new ex vivo method to evaluate the performance of candidate MRI contrast agents: A proof-of-concept study. Journal of Nanobiotechnology. 2014;12(1).
- Mouradov D., Sloggett C., Jorissen R.N., Love C.G., Li S., Burgess A.W. et al. Colorectal cancer cell lines are representative models of the main molecular subtypes of primary cancer. Cancer Research. 2014;74(12):3238-3247.
- Mateo F, Meca-Cortés O, Celià-Terrassa T, Fernández Y, Abasolo I, Sánchez-Cid L et al. SPARC mediates metastatic cooperation between CSC and non-CSC prostate cancer cell subpopulations.Molecular cancer. 2014;13:237.
- Rodrigues P, Macaya I, Bazzocco S, Mazzolini R, Andretta E, Dopeso H et al. RHOA inactivation enhances Wnt signalling and promotes colorectal cancer.Nature communications. 2014;5:5458.

Highlights

The group on Drug Delivery and Targeting seeks two main goals; on the one hand, the identification of new disease biomarkers and therapeutic targets, with special focus on cancer, and on the other hand, the development of new drug delivery and targeting approaches for clinical applications. Among our projects are a new EuroNanoMed II project focused in nanomedicine applications involving SME's in which animal models are being used for preclinical validation of new therapies directed against tumor cells (DiamESTar), and four additional projects, two of them from Marató TV3 (Nanofabry: focused in drug delivery systems for the Fabry disease and Pentri: for active targeting against cancer stem cells), an INNPACTO (also involving industry) granted in 2013 and a RETOS project recently approved together with SMEs and focused into scale-up and preclinical validation of drug delivery systems. Additional National grants were also obtained. Several in vitro and in vivo cancer models have been generated by the group for preclinical testing of nanomedicines, including the generation of specific cancer stem cell models. Two patents from the group are in National Fases. Dr Schwartz Jr is also member of the Nanomedicine Spanish Platform (NanomedSpain), the "European Platform for Nanomedicine" and the "European Fundation for Clinical Nanomedicine" (CLINAM). Dr Schwartz has also been appointed as Scientific Advisor by the Southern Denmark University of the excellence center NANOCAN for Nanomedicine andacts as an external evaluator of the Swedish Research Council and associate editor of Nanomedicine NMB (FI:6,9). Further, Dr Schwartz's group published papers in top science journals in 2014.

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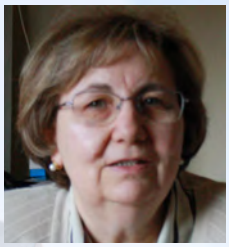
Colloidal and Interface Chemistry Group

Programme: Nanomedicine



Lead Researcher: Solans Marsà, Concepción

Group Members

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CONTRIBUTORS: Homs San Millán, María | Martínez Rodríguez, 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

- Morral-Ruiz G., Melgar-Lesmes P., Garcia M.L., Solans C., García-Celma M.J. Polyurethane and polyurea nanoparticles based on polyoxyethylene castor oil derivative surfactant suitable for endovascular applications. International Journal of Pharmaceutics. 2014;461(1-2):1-13.
- Ahmad N., Ramsch R., Llinas M., Solans C., Hashim R., Tajuddin H.A. Influence of nonionic branched-chain alkyl glycosides on a model nano-emulsion for drug delivery systems. Colloids and Surfaces B: Biointerfaces. 2014;115:267-274.
- Vilchez A., Rodriguez-Abreu C., Menner A., Bismarck A., Esquena J. Antagonistic effects between magnetite nanoparticles and a hydrophobic surfactant in highly concentrated pickering emulsions. Langmuir. 2014;30(18):5064-5074.
- Melgar-Lesmes P., Morral-Ruiz G., Solans C., García-Celma M.J. Quantifying the bioadhesive properties of surface-modified polyurethane-urea nanoparticles in the vascular network. Colloids and Surfaces B: Biointerfaces. 2014;118:280-288.
- Siriviriyanun A., Imae T., Caldero G., Solans C. Phototherapeutic functionality of biocompatible graphene oxide/dendrimer hybrids. Colloids and Surfaces B: Biointerfaces. 2014;121:469-473.

Highlights

The research activities have mainly focused to the design, characterization and functionalization of advanced multifunctional polymeric nanoparticles for the therapy of neurodegenerative diseases performed in the frame of the CIBER-BBN intramural project "*Novel nanocarriers as delivery systems across the Blood-Brain barrier*"(Nano3B). The nanoparticles, with sizes below 100 nm, have been prepared by nano-emulsion templating using low-energy methods. This technology, developed in our group, allows nanoparticle size control and high drug entrapment efficiency using biocompatible components. Moreover, it can be performed under mild processing conditions (e.g. at low temperature, 25ºC, allowing the preservation of pharmacological properties of molecules chemically unstable at high temperature), requires simple equipment and it is easily scalable. The nanoparticles have been functionalized with self-penetrating peptides and monoclonal antibodies for the specific blood-brain barrier (BBB) targeting and encapsulated with specific drugs to treat X-linked adrenoleukodystrophy (X-ALD) disease. In addition, in vitro and in vivo evaluation of the drug–loaded functionalized nanoparticles has been performed. The results have showed that the designed nanoparticles are appropriate for the intended application. The group has also performed research activities in the frame of the following projects: "*Multifunctional nanotechnology for selective detection and treatment of cancer*" (FP7-NMP-2010-LARGE-4; C-NMP/0878), "*Studies on amphiphile self-assembly processes and technologies for eco-friendly and biocompatible applications*" (CTQ2011-29336-C03) and "*Formation of Pickering emulsions by low-energy methods for the preparation of new porous nanostructured materials*" (CTQ2011- 23842). The most important outcomes of the results obtained are reflected in 21 indexed publications, as well as in the presentation of 13 (one of them invited) oral and 18 poster presentations in national and international conferences. Two PhD thesis and 1 Master thesis have been presented.

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Research Group in Intelligent Biomaterials

Programme: Biomaterials and Advanced Therapies

Lead Researcher: Vallet Regí, María

Group Members

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CONTRIBUTORS: Guisasola Cal, Eduardo | Martínez Carmona, Marina | Martínez Villacorta, Ángel

Main lines of research

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

Most relevant scientific articles

- Arcos D., Boccaccini A.R., Bohner M., Diez-Perez A., Epple M., Gomez-Barrena E. et al. The relevance of biomaterials to the prevention and treatment of osteoporosis. Acta Biomaterialia. 2014;10(5):1793-1805.
- Simmchen J., Baeza A., Ruiz-Molina D., Vallet-Regi M. Improving catalase-based propelled motor endurance by enzyme encapsulation. Nanoscale. 2014;6(15):8907-8913.
- Mas N., Arcos D., Polo L., Aznar E., Sanchez-Salcedo S., Sancenon F. et al. Towards the development of smart 3D "gated scaffolds" for on-command delivery. Small. 2014;10(23):4859-4864.
- Linares J., Matesanz M.C., Vila M., Feito M.J., Goncalves G., Vallet-Regi M. et al. Endocytic mechanisms of graphene oxide nanosheets in osteoblasts, hepatocytes and macrophages. ACS Applied Materials and Interfaces. 2014;6(16):13697-13706.
- A. Baeza, E. Guisasola, A. Torres-Pardo, J.M. González-Calbet, G.J. Melen, M. Ramirez, M. Vallet-Regí. Hybrid enzyme-polymeric capsules/mesoporous silica nanodevice for in situ cytotoxic agent generation. Adv. Funct. Mater. 24 (29), 4625-4633 (2014).

Highlights

The most important achievements during 2014 include the design, optimization and implantation of 3D scaffolds based on bioceramics for bone tissue regeneration and the development of nanotechnological strategies to design smart drug delivery systems for antitumor therapy and infection treatment. During 2014, GIBI group has developed diverse research lines in the frame of different national research projects including MAT2012-35556, MAT2013-43299-R and CSO2010-11384-E. 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). GIBI group has also published18 original research articles, 2 patents, 4 book chapters, 1 complete book entitled "Bioceramics with Clinical Applications" edited by María Vallet-Regí (John Wiley & Sons Limited, United Kingdom) and a total of 19 invited conferences in international research forums. Furthermore, the Thesis entitled "A new nanocomposite bioceramic for bone tissue regeneration" has been also disserted. In addition, 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, Research Institute of Hospital 12 de Octubre (I+12). Finally, the group has received the award IDEA2 (2014) with the Nanoimpant proyect.

http://mvisionconsortium.mit.edu/2014-idea%C2%B2-madrid-awardees-announced.

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Molecular Nanoscience & Organic Materials Group

Programme: Nanomedicine

Lead Researcher: Veciana Miró, Jaume

Group Members

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ASSOCIATED MEMBERS: Ferreas Ribas, Lourdes | Mas Torrent, Marta | Mugnani, Verónica | Ratera Bastardas, Inmaculada | Rovira Angulo, Concepción | Ventosa Rull, Leonor | Vidal Gancedo, José

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Main lines of research

NANOMOL makes a valuable contribution to the advancement of knowdedge 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
- Large area electronics
- Molecular magnetism
- Supercritical fluids processing
- Nanomedicine & Biomaterials

Most relevant scientific articles

- Sánchez G., Curiel D., Tatkiewcz W., Ratera I., Tarraga A., Veciana J. et al. Highly sensitive and selective detection of the pyrophosphate anion biomarker under physiological conditions. Chemical Science. 2014;5(6):2328-2335.
- Cespedes M.V., Unzueta U., Tatkiewicz W., Sanchez-Chardi A., Conchillo-Sole O., Alamo P. et al. In vivo architectonic stability of fully de novo designed protein-only nanoparticles. ACS Nano. 2014;8(5):4166-4176.
- Mentink Vigier F., Shimon D., Mugnaini V., Veciana J., Feintuch A., Pons M. et al. The 13C solid DNP mechanisms with perchlorotriphenylmethyl radicals-the role of 35,37Cl. Physical Chemistry Chemical Physics. 2014;16(36):19218-19228.
- Santana H., Avila C.L., Cabrera I., Paez R., Falcon V., Pessoa A. et al. How does growth hormone releasing hexapeptide self-assemble in nanotubes?. Soft Matter. 2014;10(46):9260-9269.
- Hankel R.F., Rojas P.E., Cano-Sarabia M., Sala S., Veciana J., Braeuer A. et al. Surfactant-free CO2-based microemulsion-like systems. Chemical Communications. 2014;50(60):8215-8218.

Highlights

- 2-D and 3-D microscale engineering of protein-based nanoparticles for cell guidance and the study of the supramolecular organization of such nanoparticles (bacterial inclusion bodies).
- Surface-confined electroactive molecules for multistate charge storage information and for modifying of the surface properties.
- Study of bistability phenomena of molecule-based dyads with potential applications as memories and sensors.
- Modified mesoporous silica nanoparticles as a reusable, selective chromogenic sensor for mercury(II) recognition.
- New bilayer conducting materials as temperature and pressure sensors.
- Silk/molecular conductor composites useful for humidity sensing, electrical current driven actuators, and the study of complex moisture diffusion processes.
- Synthesis and structural characterization of radical dendrimers based on a cyclotriphosphazene core with TEMPO Radicals for their use as MRI agents.
- Novel organic field effect transistors stable in air and water as potential platforms for developing (bio) sensors.
- Patterned surfaces with different electroactive molecules for controlling the interaction and release of analytes locally on the surface.
- New radicals for Dynamic Nuclear Polarization (DNP) applications.
- Development of self-assembled monolayers (SAMs) on gold of a multidentate receptor for highly sensitive and selective detection of hydrogen pyrophosphate anion biomarker under physiological conditions.
- New nanomedicine candidate for the treatment of complex wounds, based on nanovesicles loaded with an Epidermal Growth Factor, was licensed to the biotechnological company HeberBiotech for the treatment of diabetic foot ulcers.
- DELOS-susp has been successfully used for the preparation of alpha-galactosidase loaded nanoliposomes with enhanced enzymatic activity for Fabry`s desease. This result shows the potential of this technological platform, based on the use of compressed fluids, for the safe, energy- and resource-efficient manufacturing of colloidal nanotherapeutics.

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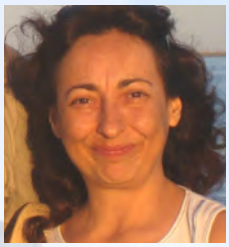

Research Group in Bone Physiopathology and Biomaterials

Programme: Biomaterials and Advanced Therapies / Nanomedicine

Lead Researcher: Vilaboa Díaz, Nuria

Group Members

STAFF MEMBERS: Bensiamar Hadia, Fátima Zohra | Boré Medina, Alba | Martín Saavedra, Francisco Manuel

ASSOCIATED MEMBERS: García Cimbrelo, Eduardo | Gil Garay, Enrique | González Carrasco, José Luis | Martín Hervás, Carmen | Saldaña Quero, Laura | Vallés Pérez, Gema

CONTRIBUTORS: Crespo García, Lara

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

- Martín-Saavedra F.M., Cebrián V., Gómez L., López D., Arruebo M., Wilson C.G. et al. Temporal and spatial patterning of transgene expression by near-infrared irradiation. Biomaterials. 2014;35(28):8134-8143.
- Frutos E., Alvarez D., Fernández L., Gónzalez-Carrasco J.L. Effects of bath composition and processing conditions on the microstructure and mechanical properties of coatings developed on 316 LVM by hot dipping in melted AlSi alloys. Journal of Alloys and Compounds. 2014;617:646-653.
- Saldana L., Crespo L., Bensiamar F., Arruebo M., Vilaboa N. Mechanical forces regulate stem cell response to surface topography. Journal of Biomedical Materials Research - Part A. 2014;102(1):128-140.
- Calzado-Martin A., Crespo L., Saldana L., Bore A., Gómez-Barrena E., Vilaboa N. Human bone-lineage cell responses to anisotropic Ti6Al4V surfaces are dependent on their maturation state. Journal of Biomedical Materials Research - Part A. 2014;102(9):3154-3166.
- Braceras I., Pacha-Olivenza M.A., Calzado-Martin A., Multigner M., Vera C., Broncano L.L.-. et al. Decrease of Staphylococcal adhesion on surgical stainless steel after Si ion implantation. Applied Surface Science. 2014;310:36-41.

Highlights

The group of Bone Physiopathology and Biomaterials has performed a thorough characterization of several modifications of polymers and 316 LVM steel and Ti64 alloys, including analyses of thermolectrical and mechanical behaviour as well as biocompatibility tests. The group has progressed in the development of gene switches for the spatial and temporal regulation of the expression of therapeutic transgenes, which have been adapted to control osteogenic and angiogenic proteins in tissue engineering applications. Furthermore, the ability of focused ultrasounds and near-infrared irradiation to activate these switches has been demonstrated. Moreover, the group has studied the influence of mechanical stimulation on human cells cultured on biomedical alloys. The clinical scientists of the group have continued their participation in clinical trials for therapeutical 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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Nanobiotechnology

Programme: Nanomedicine / Biomaterials and Advanced Therapies

Lead Researcher: Villaverde Corrales, Antoni

Group Members

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ASSOCIATED MEMBERS: Cubarsi Morera, Rafael | Ferrer Miralles, Neus | Pesarrodona Roches, Mireia | Vázquez Gómez, Esther | Vázquez Lima, Felicitas

CONTRIBUTORS: Cano Garrido, Olivia | Saccardo, Paolo | Zhikun, Xu

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, of interest in protein replacement therapies, gene therapy and regenerative medicine. In particular, we are interested in developing novel 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

- Céspedes M.V., Unzueta U., Tatkiewicz W., Sánchez-Chardi A., Conchillo-Sole O., Alamo P. et al. In vivo architectonic stability of fully de novo designed protein-only nanoparticles. ACS Nano. 2014;8(5):4166-4176.
- Seras-Franzoso J., Tsimbouri P.M., Burgess K.V., Unzueta U., García-Fruitos E., Vazquez E. et al. Topographically targeted osteogenesis of mesenchymal stem cells stimulated by inclusion bodies attached to polycaprolactone surfaces. Nanomedicine. 2014;9(2):207-220.
- Unzueta U., Saccardo P., Domingo-Espin J., Cedano J., Conchillo-Sole O., García-Fruitos E. et al. Sheltering DNA in self-organizing, protein-only nano-shells as artificial viruses for gene delivery. Nanomedicine: Nanotechnology, Biology, and Medicine. 2014;10(3):535-541.
- Seras-Franzoso J., Peebo K., Garcia-Fruitos E., Vázquez E., Rinas U., Villaverde A. Improving protein delivery of fibroblast growth factor-2 from bacterial inclusion bodies used as cell culture substrates. Acta Biomaterialia. 2014;10(3):1354-1359.
- Pesarrodona M., Ferrer-Miralles N., Unzueta U., Gener P., Tatkiewicz W., Abasolo I. et al. Intracellular targeting of CD44+ cells with self-assembling, protein only nanoparticles. International Journal of Pharmaceutics. 2014;473(1-2):286-295.

Highlights

In close collaboration with Profs Ramón Mangues and Simó Schwartz, the group has developed functional protein nanoparticles for targeted therapy in colorectal and breast cancers, which are stable in vivo and that escape renal clearance. These features dramatically increase the circulation time thereof and its bioavailability, and it allows the accumulation of these vehicles and their cargos in target tissues, with a very effective biodistribution .The group also designs and produces diverse functional nanostructured materials , mainly based on proteins, for various therapeutic and regenerative medicine purposes. This is achieved in collaboration with other CIBER groups and with external groups.These activities are carried out through the following projects:

- Personalized nanomedicine for triple negative breast cancer stem cells. TV32013-133930. E. Vazquez. 2013-16.
- Vehicle and cargo engineering in non- viral gene therapy of metastatic colorectal cancer. PI12/00327. E. Vazquez. 2013-16.
- Optimization period of dry cow by protein nanoparticles. RTA2012-00028-C02-02. E. García. 2013-16.
- Functionalized nanoliposomes for the development of therapies for intracellular-based diseases. Application to Fabry disease and homozygous familial hypercholesterolemia. (Lipocell). JL. Corchero. 2014-15. Developing therapies for the treatment of rare congenital metabolic diseases (TERARMET). JL. Corchero. 2014-16.
- Genotoxic nanoparticles targeting colorectal cancer stem cells. TV32013-132031. A. Villaverde. 2014-16.
- ENGINEERING OF PROTEIN NANOPARTICLES FOR Targeted DELIVERY of THERAPEUTIC PROTEINS AND NUCLEIC ACIDS. BIO2013-41019-P. A. Villaverde. 2014-16.

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7. ANNEXE

PUBLICATIONS 2014 1ST QUARTILE

CIBER-BBN Groups	Publications 2014 1st quartile	Impact factor	doi	pubmed
AGUILO LLOBET, JORDI	Del Campo F.J., Abad L., Illa X., Prats-Alfonso E., Borrise X., Cirera J.M. et al. Determination of heterogeneous electron transfer rate constants at interdigitated nanoband electrodes fabricated by an optical mix-and-match process. Sensors and Actuators, B: Chemical. 2014;194:86-95.	3,84	10.1016/j.snb.2013.12.016	
AGUILO LLOBET, JORDI	Guimera A., Illa X., Traver E., Herrero C., Maldonado M.J., Villa R. New trends in quantitative assessment of the corneal barrier function. Sensors (Switzerland). 2014;14(5):8718-8727.	2,048	10.3390/s140508718	
AGUILO LLOBET, JORDI	Illa X., Vila S., Yeste J., Peralta C., Gracia-Sancho J., Villa R. A novel modular bioreactor to in Vitro study the hepatic sinusoid. PLoS ONE. 2014;9(11).	3,534	10.1371/journal.pone.0111864	
ALBERICIO PALOMERA, FERNANDO	Spengler J., Albericio F. Synthesis of all the diastereomers of 2-amino-3-hydroxy-4,5- dimethylhexanoic acid. European Journal of Organic Chemistry. 2014;2014(1):44-47.	3,154	10.1002/ejoc.201301257	
ALBERICIO PALOMERA, FERNANDO	Just-Baringo X., Albericio F., Alvarez M. Thiopeptide antibiotics: Retrospective and recent advances. Marine Drugs. 2014;12(1):317-351.	3,512	10.3390/md12010317	24445304
ALBERICIO PALOMERA, FERNANDO	Custodio L., Soares F., Pereira H., Barreira L., Vizetto-Duarte C., Rodrigues M.J. et al. Fatty acid composition and biological activities of Isochrysis galbana T-ISO, Tetraselmis sp. and Scenedesmus sp.: Possible application in the pharmaceutical and functional food industries. Journal of Applied Phycology. 2014;26(1):151-161.	2,492	10.1007/s10811-013-0098-0	
ALBERICIO PALOMERA, FERNANDO	Cruz L.J., Rueda F., Simon L., Cordobilla B., Albericio F., Domingo J.C. Liposomes containing NY-ESO-1/tetanus toxoid and adjuvant peptides targeted to human dendritic cells via the Fc receptor for cancer vaccines. Nanomedicine. 2014;9(4):435-449.	5,824	10.2217/nnm.13.66	24910875
ALBERICIO PALOMERA, FERNANDO	Postma T.M., Albericio F. Disulfide formation strategies in peptide synthesis. European Journal of Organic Chemistry. 2014;2014(17):3519-3530.	3,154	10.1002/ejoc.201402149	
ALBERICIO PALOMERA, FERNANDO	Just-Baringo X., Albericio F., Alvarez M. Chiral thiazoline and thiazole building blocks for the synthesis of peptide-derived natural products. Current Topics in Medicinal Chemistry. 2014;14(10):1244-1256.	3,453	10.2174/1568026614666140423105730	
ALBERICIO PALOMERA, FERNANDO	Ruiz-Rodriguez J., Miguel M., Preciado S., Acosta G.A., Adan J., Bidon-Chanal A. et al. Polythiazole linkers as functional rigid connectors: A new RGD cyclopeptide with enhanced integrin selectivity. Chemical Science. 2014;5(10):3929-3935.	8,601	10.1039/c4sc00572d	
ALBERICIO PALOMERA, FERNANDO	Seelbach R.J., Fransen P., Peroglio M., Pulido D., Lopez-Chicon P., Duttenhoefer F. et al. Multivalent dendrimers presenting spatially controlled clusters of binding epitopes in thermoresponsive hyaluronan hydrogels. Acta Biomaterialia. 2014;10(10):4340-4350.	5,684	10.1016/j.actbio.2014.06.028	
ALBERICIO PALOMERA, FERNANDO	Guerrero A.R., Hassan N., Escobar C.A., Albericio F., Kogan M.J., Araya E. Gold nanoparticles for photothermally controlled drug release. Nanomedicine. 2014;9(13):2023-2039.	5,824	10.2217/nnm.14.126	

ALBERICIO PALOMERA, FERNANDO	Fernandez-Llamazares A.I., Adan J., Mitjans F., Spengler J., Albericio F. Tackling lipophilicity of peptide drugs: Replacement of the backbone n -methyl group of Cilengitide by N -oligoethylene glycol (N -OEG) chains. Bioconjugate Chemistry. 2014;25(1):11-17.	4,821	10.1021/bc4003844	24328341
ALBERICIO PALOMERA, FERNANDO	Gongora-Benitez M., Tulla-Puche J., Albericio F. Multifaceted roles of disulfide bonds. peptides as therapeutics. Chemical Reviews. 2014;114(2):901-926.	45,661	10.1021/cr400031z	24446748
ALBERICIO PALOMERA, FERNANDO	Parra A., Martin-Fonseca S., Rivas F., Reyes-Zurita F.J., Medina-O'Donnell M., Martinez A. et al. Semi-synthesis of acylated triterpenes from olive-oil industry wastes for the development of anticancer and anti-HIV agents. European Journal of Medicinal Chemistry. 2014;74:278-301.	3,432	10.1016/j.ejmech.2013.12.049	24480359
ALBERICIO PALOMERA, FERNANDO	Pulido D., Albericio F., Royo M. Controlling multivalency and multimodality: Up to pentamodal dendritic platforms based on diethylenetriaminepentaacetic acid cores. Organic Letters. 2014;16(5):1318-1321.	6,324	10.1021/ol500022n	24527761
ALBERICIO PALOMERA, FERNANDO	Postma T.M., Albericio F. Cysteine pseudoprolines for thiol protection and peptide macrocyclization enhancement in fmoc-based solid-phase peptide synthesis. Organic Letters. 2014;16(6):1772-1775.	6,324	10.1021/ol5004725	24617568
ALBERICIO PALOMERA, FERNANDO	Postma T.M., Albericio F. Immobilized N-chlorosuccinimide as a friendly peptide disulfide-forming reagent. ACS Combinatorial Science. 2014;16(4):160-163.	3,401	10.1021/co500003p	
ALBERICIO PALOMERA, FERNANDO	Fransen P., Pulido D., Sevrin C., Grandfils C., Albericio F., Royo M. High control, fast growth OEG-based dendron synthesis via a sequential two-step process of copper-free diazo transfer and click chemistry. Macromolecules. 2014;47(8):2585-2591.	5,927	10.1021/ma500166e	
ALBERICIO PALOMERA, FERNANDO	Siano A., Humpola M.V., De Oliveira E., Albericio F., Simonetta A.C., Lajmanovich R. et al. Antimicrobial peptides from skin secretions of hypsiboas pulchellus (anura: Hylidae). Journal of Natural Products. 2014;77(4):831-841.	3,947	10.1021/np4009317	24717080
ALBERICIO PALOMERA, FERNANDO	Just-Baringo X., Bruno P., Pitart C., Vila J., Albericio F., Alvarez M. Dissecting the structure of thiopeptides: Assessment of thiazoline and tail moieties of baringolin and antibacterial activity optimization. Journal of Medicinal Chemistry. 2014;57(10):4185-4195.	5,48	10.1021/jm500062g	24738558
ALBERICIO PALOMERA, FERNANDO	Just-Baringo X., Albericio F., Alvarez M. Thiopeptide engineering: A multidisciplinary effort towards future drugs. Angewandte Chemie - International Edition. 2014;53(26):6602-6616.	11,336	10.1002/anie.201307288	
ALBERICIO PALOMERA, FERNANDO	Agrigento P., Albericio F., Chamoin S., Dacquignies I., Koc H., Eberle M. Facile and mild synthesis of linear and cyclic peptides via thioesters. Organic Letters. 2014;16(15):3922-3925.	6,324	10.1021/ol501669n	25032897
ALBERICIO PALOMERA, FERNANDO	Parra A., Martin-Fonseca S., Rivas F., Reyes-Zurita F.J., Medina-O'Donnell M., Rufino-Palomares E.E. et al. Solid-phase library synthesis of bi-functional derivatives of oleanolic and maslinic acids and their cytotoxicity on three cancer cell lines. ACS Combinatorial Science. 2014;16(8):428-447.	3,401	10.1021/co500051z	
ALBERICIO PALOMERA, FERNANDO	Pérez-Perarnau A, Preciado S, Palmeri CM, Moncunill-Massaguer C, Iglesias-Serret D, González-Gironès DM et al. A trifluorinated thiazoline scaffold leading to pro-apoptotic agents targeting prohibitins.Angewandte Chemie (International ed. in English). 2014;53(38).	11,336	10.1002/anie.201405758	25196378

ALBERICIO PALOMERA, FERNANDO	Paradis-Bas M., Albert-Soriano M., Tulla-Puche J., Albericio F. Linear versus branched poly-lysine/arginine as polarity enhancer tags. Organic and Biomolecular Chemistry. 2014;12(37):7194-7196.	3,487	10.1039/c4ob01354a	
ALBERICIO PALOMERA, FERNANDO	Paradís-Bas M, Albert-Soriano M, Tulla-Puche J, Albericio F. Linear versus branched poly-lysine/arginine as polarity enhancer tags.Organic & biomolecular chemistry. 2014;12(37).	3,487	10.1039/c4ob01354a	25162452
ALBERICIO PALOMERA, FERNANDO	Lorente A., Albericio F., Alvarez M. Selective formation of a z -trisubstituted double bond using a 1-(tert -butyl) tetrazolyl sulfone. Journal of Organic Chemistry. 2014;79(21):10648-10654.	4,638	10.1021/jo501988e	
ALBERICIO PALOMERA, FERNANDO	Lorente A, Albericio F, Álvarez M. Selective formation of a Z-trisubstituted double bond using a 1-(tert-butyl) tetrazolyl sulfone.The Journal of organic chemistry. 2014;79(21).	4,638	10.1021/jo501988e	25280270
ALBERICIO PALOMERA, FERNANDO	Cherkupally P., Ramesh S., De La Torre B.G., Govender T., Kruger H.G., Albericio F. Immobilized coupling reagents: Synthesis of amides/peptides. ACS Combinatorial Science. 2014;16(11):579-601.	3,401	10.1021/co500126y	
ALBERICIO PALOMERA, FERNANDO	Paradis-Bas M., Tulla-Puche J., Albericio F. 2-methoxy-4-methylsulfinylbenzyl: A backbone amide safety-catch protecting group for the synthesis and purification of difficult peptide sequences. Chemistry - A European Journal. 2014;20(46):15031-15039.	5,696	10.1002/chem.201403668	
ALBERICIO PALOMERA, FERNANDO	Cherkupally P, Ramesh S, de la Torre BG, Govender T, Kruger HG, Albericio F. Immobilized coupling reagents: synthesis of amides/peptides.ACS combinatorial science. 2014;16(11).	3,401	10.1021/co500126y	25330282
ALBERICIO PALOMERA, FERNANDO	Jad Y.E., Khattab S.N., De La Torre B.G., Govender T., Kruger H.G., El-Faham A. et al. Oxyma-B, an excellent racemization suppressor for peptide synthesis. Organic and Biomolecular Chemistry. 2014;12(42):8379-8385.	3,487	10.1039/c4ob01612b	
ALBERICIO PALOMERA, FERNANDO	Torres-Garcia C., Pulido D., Albericio F., Royo M., Nicolas E. Triazene as a powerful tool for solid-phase derivatization of phenylalanine containing peptides: Zygosporamide analogues as a proof of concept. Journal of Organic Chemistry. 2014;79(23):11409-11415.	4,638	10.1021/jo501830w	
ALBERICIO PALOMERA, FERNANDO	Novoa E.M., Camacho N., Tor A., Wilkinson B., Moss S., Marin-Garcia P. et al. Analogs of natural aminoacyl-tRNA synthetase inhibitors clear malaria in vivo. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(51):E5508-E5517.	9,809	10.1073/pnas.1405994111	
ALBERICIO PALOMERA, FERNANDO / DEL POZO GUERRERO, FRANCISCO	Perez-Rodriguez R., Rodriguez C., Costa U., Caceres C., Tormos J.M., Medina J. et al. Anticipatory assistance-as-needed control algorithm for a multijoint upper limb robotic orthosis in physical neurorehabilitation. Expert Systems with Applications. 2014;41(8):3922-3934.	1,965	10.1016/j.eswa.2013.11.047	
ARUS CARALTO, CARLES	Julia-Sape M., Majos C., Camins A., Samitier A., Baquero M., Serrallonga M. et al. Multicentre evaluation of the INTERPRET decision support system 2.0 for brain tumour classification. NMR in Biomedicine. 2014;27(9):1009-1018.	3,559	10.1002/nbm.3144	
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