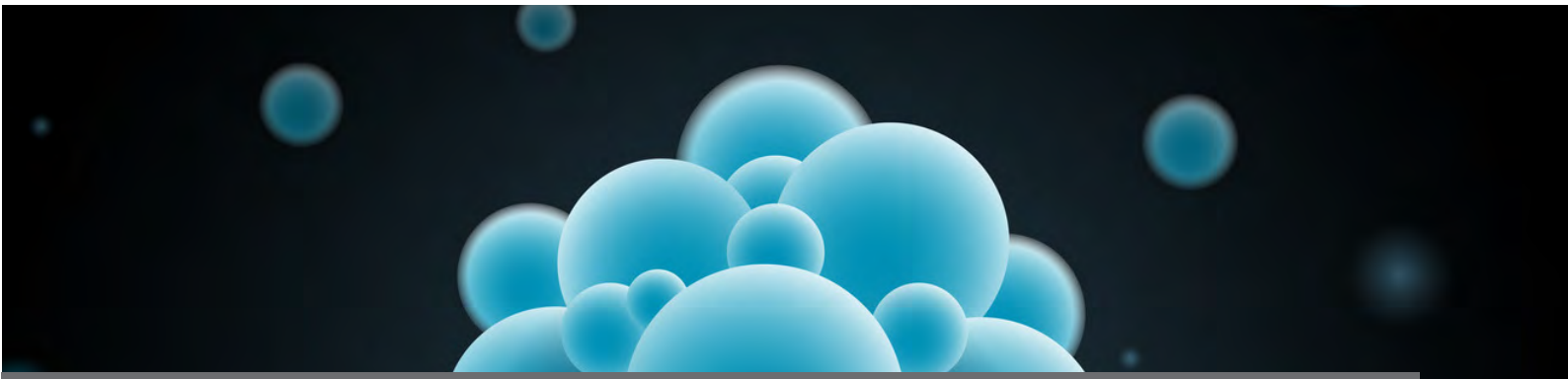
Annual Report 2013

ciber-bbn

Centro de Investigación Biomédica en Red
Bioingeniería, Biomateriales y Nanomedicina

INDEX

1
Organization



Introduction: CIBER-BBN in 2013

Letter from the Scientific Director

When reviewing the main actions and results from 2013 in CIBER-BBN, there seems to be a clearly positive evolution, and while still far from representing the translational levels we would like, these actions and results do show the consolidation of a trend in the right direction. The milestones which I consider deserve being mentioned explicitly in this report are described below.

Like every year, the annual evaluation of the groups in the centre for fiscal year 2012 has been done. Despite the evident effects of the economic difficulties existing during the fiscal year, we can still continue to ponder several indicators that are still on the rise in virtually all the evaluated aspects. This is most certainly the result of the system's inertia and of the researchers' commitment, which at present has allowed us to absorb the negative effects of a serious recession. I am afraid, though, that if the situation is not reversed soon, our centres' potential will be seriously affected, and the aforementioned inertia will become a hindrance more than a salvation.

As a result of evaluations from previous years and of the particular situations of each group, there is one group that left CIBER-BBN on December, 31, 2013, and several groups were asked to submit an action plan to reorient their activity and involvement in CIBER-BBN. In addition, a new associated clinical group has been incorporated, bringing such "explicit" associated clinical groups up to 3. We hope that the next call for proposals within the framework of the AES (Acción Estratégica en Salud) includes the possible participation of new groups, making CIBER-BBN healthily dynamic.

As for the more day-to-day activity, two forums with companies have been held: one in bone therapies and the other in biomedical monitoring systems, in addition to three others that are more clinically oriented, one in ophthalmology in collaboration with the OFTARED Network, another one with the Cell Therapy Network TERCEL, and a third clinical forum in cardiology with the Cardiovascular Research Network RIC. Conferences were also held for disseminating the CIBER's capabilities in some health research institutes, such as the IMIBIC of Cordoba and the IBIS of Seville.

As a continuation of some of these clinical forums held in previous years, joint projects between the CIBERES and SEPAR, started up at the beginning of 2013 as the result of the "mini-call for proposals" jointly launched at the end of 2012. Four of the eleven projects that were submitted were funded, and I believe that it can be considered a success given what it means for promoting clinical-technological interaction. The same occurred at the end of the year with the call for proposal opened with the ECO Foundation (Foundation for Excellence and Quality in Oncology). In this case, eight applications were submitted, and given the top-level and across-the-board quality of all the proposals according to the panel of judges, six have been funded, again for the purpose of "sowing seeds" in clinical-technological projects and collaborations which in the near future may be reported as a success.

As regards training aspects, in addition to the usual initiation programmes in research and mobility, the effort we made together with the UNED and ENS to design a course specialising in nanomedicine must be highlighted. Unfortunately, this effort was not compensated with a strong enough demand, and the course had to be cancelled.

With respect to the platform programme, an application has been submitted for recognizing the platform as a Singular Scientific and Technical Infrastructure (ICTS). Said application is pending resolution as of the date of writing this report.

To round off this series of actions, CIBER-BBN has participated as a member entity in events organized by the European Nanomedicine Platform and, through programme managers, in a number of conferences and seminars disclosing the capabilities of our centre. Furthermore, like in previous years, CIBER-BBN was represented together with other CIBERs in events organized in Madrid and Barcelona in the framework of Science Week.

In addition to this annual reflection/summary, 2013 saw us immersed in developing a new strategic plan for the 2014-2017 period, which was approved by the Board of Trustees in December. It allowed us to think about the centre, its objectives, and the mechanisms for leading us towards them. The reflection was made from inside and outside, such that we do not only place importance on how we see ourselves, which can always contain some sort of bias, but we analyzed how we are seen by external agents that we have been collaborating with to achieve our objectives.

With respect to the Scientific Advisory Board (SAB), a mechanism for renewing half the members every two years was established, assuring continuity of knowledge while at the same time periodically renewing members. Therefore, Professor Ruth Duncan, Professor Rogério Gaspar, Professor Jean Louis Coatrieux and Professor Roger Kamm left their positions on the SAB, and we would like to thank them and acknowledge them for their help, advise, questions, and support for CIBER-BBN. New people have joined the CIBER-BBN SAB, and Professor Leif Sörnmo, Professor Matthias Epple, Professor Patrick Boisseau and Professor Wolfgang Parak are now part of the SAB. We would also like to thank them for serving in this capacity.

At the end of 2013 a decision that had already been made months before, i.e., concentrating the administrative offices of the different CIBERs in Madrid, was instituted. This decision means that the CIBER-BBN is now legally a part of a major centre, CIBER without any other name, but retains all the scientific and organisational independence of our programmes just like up until now. Grouping the administrative part in a single office in Madrid means that the staff from the Zaragoza office had to choose between moving to Madrid or, where staff circumstances did not allow, abandoning the CIBER-BBN as of December 31. This marked the life of the office throughout this year, and I would like to personally thank all the people from the office for having remained committed and professional until leaving the centre. In addition, the new administrative operating guidelines that entered into force on January 1, 2014 were initiated in the last few months in 2013 in specific conferences.

The annual conference was held in Malaga in November, and taking into account that the second biannual period for the 2010-2013 4-year period strategic plan (13 projects in Bioengineering, 10 in Biomaterials and 21 in Nanomedicine) just ended, time was allocated to go over the achievements earned in different intramural projects, and then time was allocated to design and define projects that could be submitted in the next intramural call for proposal. Said next call will be the one in the first 2-year period of the 2014-2017 strategic plan. This Plan keeps the intramural programme as the backbone of CIBER-BBN's collaborative activity, but with some changes. These latter projects were evaluated by the ANEP, and they necessarily required including a clinical partner, such that the translation to clinical practice may be better oriented as

from the design of the project. The resources for carrying out these projects will be assigned to the groups according to evaluation results, and they must meet one of the four 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.

In the call for intramural proposal, the transfer project sub-programme, which is conceived to go that extra mile takes so much in order to transfer scientifically matured developments to the industrial or business sector deserves special mention. To advance in that line, this sub-programme directly supports those initiatives supported by a company such that direct funding is assigned, 50% co-funded by the company and the other 50% by CIBER-BBN. Four projects are finally funded in this programme for the 2014-2015 period.

Finally, there were two presentations in the conferences on two very popular topics and very interesting challenges to be resolved in coming years: "Polymer conjugates as nanosized medicines", given by Professor Mª Jesús Vicent, from the Príncipe Felipe Research Centre, and "A Description of the Human Brain Project", given by Professor Vicente Martín, from the Universidad Politécnica de Madrid.

Certificates of recognition were also given to researchers who obtained grants from the "Starter" program, co-sponsored by Caja de Ingenieros, during the year. This modest "initiation" aid allows us to be a bit more generous in numbers with our programme to seduce the 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 calls for proposal.

In summary, year 2013 was a new step, where the results of the continued effort made by the centre since it was created are becoming realities, while at the same time an enormous effort has been made to rethink the scientific strategy (with its strategic plan) and administrative strategy (with the unification of offices) so that the path that is taken can be reinforced in the coming years and be better protected against unfavourable situations, like the one we are in now.

Pablo Laguna
CIBER-BBN Scientific Director

Who we are

Directory of Groups and Consortium Institutions

In 2013, CIBER-BBN was formed by 47 research groups, 45 of which were full member groups and 2 of which were associated groups:

IP	INSTITUCIÓN	CCAA
Jordi Aguiló	Universidad Autónoma de Barcelona	Catalonia
Fernando Albericio	Inst. de Investigación Biomédica de Barcelona – IRB Barcelona	Catalonia
Carles Arús	Universidad Autónoma de Barcelona	Catalonia
José Becerra	Universidad de Málaga	Andalusia
Juan Manuel Bellón	Universidad de Alcalá	Madrid
Jerónimo Blanco	CSIC	Catalonia
Margarita Calonge	Universidad de Valladolid	Castile and Leon
Bernardo Celda	Universidad de Valencia	Comm. of Valencia
Alberto de Leiva	Inst. de Investigación Hospital de Santa Cruz y San Pablo	Catalonia
Francisco del Pozo	Universidad Politécnica de Madrid	Madrid
Manuel Doblaré	Universidad de Zaragoza	Aragón
Elisabeth Engel	Instituto de Bioingeniería de Cataluña	Catalonia
Ramón Eritja	CSIC	Catalonia
Eduardo Fernández	Universidad Miguel Hernández de Elche	Comm. of Valencia
Alejandro Frangi	Universitat Pompeu Fabra	Catalonia
Rafael Gómez	Universidad de Alcalá	Madrid
Mª Luisa González	Universidad de Extremadura	Extremadura
Juan Carlos Izpisúa	Centro de Medicina Regenerativa de Barcelona	Catalonia
Raimon Jané	Instituto de Bioingeniería de Cataluña	Catalonia
Pablo Laguna	Universidad de Zaragoza	Aragón
Laura Lechuga	CSIC	Catalonia
Ramón Mangues	Instituto de Investigación Hospital de Santa Cruz y San Pablo	Catalonia
M. Pilar Marco	CSIC	Catalonia
Ramón Martínez	Universidad Politécnica de Valencia	Comm. of Valencia

Manuel Monleón	Universidad Politécnica de Valencia	Comm. of Valencia
Isabel Obieta	Fundación TECNALIA	Basque Country
Javier Pavía	Universidad de Barcelona	Catalonia
José Luis Pedraz	Universidad del País Vasco	Basque Country
Soledad Penadés	CIC biomaGUNE	Basque Country
José Luis Peris	Instituto de Biomecánica de Valencia	Comm. of Valencia
Félix Ritort	Universidad de Barcelona	Catalonia
Laura Roa	Universidad de Sevilla	Andalusia
José C. Rodríguez	Universidad de Valladolid	Castile and Leon
Cristina Ruiz	Servicio Gallego de Salud - Hsp. Juan Canalejo	Galicia
Josep Samitier	Instituto de Bioingeniería de Cataluña	Catalonia
Julio San Román	CSIC	Madrid
Jesús Santamaría	Universidad de Zaragoza	Aragón
Andrés Santos	Universidad Politécnica de Madrid	Madrid
Fausto Sanz	Universidad de Barcelona	Catalonia
Simó Schwartz	Inst. Catalán de Salud - Hospital Vall d'Hebron	Catalonia
Concepción Solans	CSIC	Catalonia
María Vallet-Regí	Universidad Complutense de Madrid	Madrid
Jaume Veciana	CSIC	Catalonia
Nuria Vilaboa	Servicio Madrileño de Salud / Hospital La Paz	Madrid
Antonio Villaverde	Universidad Autónoma de Barcelona	Catalonia
Mª Ángeles Muñoz Fernández(*)	Servicio Madrileño de Salud - Hospital General Universitario Gregorio Marañón	Madrid
Daniel Navajas(*)	Universidad de Barcelona	Catalonia

Research groups forming CIBER-BBN. (*) Associated groups

Organizational Structure of Ciber and its Technical Office

Like other CIBERs, CIBER in Bioengineering, Biomaterials and Nanomedicine is legally classified as a consortium among the different participating institutions. The basic and functional units of CIBER-BBN are the research groups. In addition, CIBER-BBN also has governing bodies and operating bodies, as established in the Articles of Association.

According to the Articles of Association, CIBER-BBN has governing and steering bodies (Board of Trustees, Permanent Commission and Scientific Director), supporting and advisory bodies (External Scientific Advisory Committee and Steering Committee) and administrative management bodies (Managing Director).

The Board of Trustees is the maximum decision-making body in the consortium, and consists of three representatives from the ISCIII (Instituto de Salud Carlos III) and one institucional representative from each of the consortium institutions. It is chaired by the Director of ISCIII and meets on a six-month basis.

Board of Trustees Members and Representatives

BOARD OF TRUSTEES 2013		
INSTITUTION	**REPRESENTATIVE**	**POSITION**
Centro de Medicina Regenerativa de Barcelona	Margarita Sala Azón	Managing Director, CMRB
CIC biomaGUNE	Manuel Martín Lomas	Scientific Director of CIC biomaGUNE
Consejo Superior de Investigaciones Científicas	Dolores González Pacanowska	Coordinator of the Biology and Biomedicine Commission of the State Agency of the CSIC
Instituto Catalán de Salud - Hospital Universitario Vall d´Hebron	Joan X. Comella Carnicé	Vall d´Hebron University Hospital Research Foundation Director
Fund. Tecnalia Research & Innovation	Jesús Valero	Health Technologies Unit Director
Inst. de Bioenginyeria de Catalunya	Josep Samitier	IBEC Director
Institut de Recerca de L'Hospital de la Santa Creu i Sant Pau	Jaume Kulisevsky	Santa Creu and Sant Pau Hospital Research Institute Director
Universidad de Zaragoza	Luis M. García Vinuesa	Vice-Chancellor of Scientific Policy
Inst. de Biomecánica de Valencia	Pedro Manuel Vera Luna	IBV Director
Instituto de Salud Carlos III	Antonio Andreu Périz	ISCIII Director
Instituto de Salud Carlos III	Margarita Blázquez	General Deputy Director of Research Networks and Centres
Instituto de Salud Carlos III	Pedro Cortegoso Fdez.	General Secretary
Inst. for Research in Biomedicine – IRB Barcelona	Margarida Corominas Bosch	Manager and Legal Representative
Servicio Gallego de Salud	Javier Paz Esquete	G.S. of Research, Learning and Innovation, SERGAS General Management
Servicio Madrileño de Salud	Patricia Flores	Madrid Health Service Deputy Healthcare Counselor
Universidad de Alcalá	Jorge Pérez Serrano	"Biomedicine" C.A.I. Director
Universidad Autónoma de Barcelona	Ferrán Sancho Pifarre	Chancellor of the Universidad Autónoma de Barcelona
Universidad Complutense de Madrid	José F. Tirado Fernández	Vice-Chancellor of Research
Universidad de Barcelona	Xavier Meneses Martínez	Research Support Director
Universidad de Extremadura	Manuel A. González Lena	Vice-Chancellor of Research, Transfer and Innovation
Universidad de Málaga	María Valpuesta Fernández	Vice-Chancellor of Research and Transfer
Universidad de Sevilla	Manuel García León	Vice-Chancellor of Research
Universidad de Valencia	Ana Mª. Cortés Herreros	OTRI Director
Universidad de Valladolid	Jose M. López Rodríguez	Vice-Chancellor of Research and Scientific Policy
Universidad Miguel Hernández de Elche	Fernando Borrás Rocher	Vice-Chancellor of Research and Innovation
Universidad País Vasco	Fernando Plazaola Muguruza	Vice-Chancellor of Research
Universidad Politécnica de Madrid	Roberto Prieto López	Vice-Chancellor of Research of the UPM
Universidad Politécnica de Valencia	José Capilla Romá	Vice-Chancellor of Research, Development and Innovation
Universidad Pompeu Fabra	Francesc Posas	Vice-Chancellor of Scientific Policy

The **Permanent Commission** is formed by the Vice-president of the Board of Trustees (General Deputy Director of Cooperative Research Networks and Centres), the Scientific Director, four committee members representing the consortium institutions, and the General Manager, acting as the Secretary. The Permanent Commission sometimes meets to make those decisions which, given their nature, cannot wait to be approved by the Board of Trustees. The Permanent Commission members in 2013 were:

- Instituto de Salud Carlos III.
- Centro de Medicina Regenerativa de Barcelona.
- Instituto de Bioingeniería de Cataluña.
- Universidad de Valencia.
- Universidad de Valladolid.

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 Committee Members

STEERING COMMITTEE 2013	
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	Begoña Pérez Magallón

The members that are part of the 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 2013		
Programme	**Name**	**Institution**
Bioengineering and Biomedical Imaging	Prof. Jean Louis Coatrieux	Université de Rennes 1
	Prof. Nilo Saranummi	VTT Technical Research Centre of Finland
Biomaterials and Tissue Engineering	Begoña Castro	Histocell
	Prof. Roger D. Kamm	Massachusetts Institute of Technology
	Prof. C. James Kirkpatrick	Institute of Pathology, Johannes Gutenberg University, Mainz
Nanomedicine	Prof. Ruth Duncan	University of Cardiff
	Prof. Mario Adolfo Barbosa	Instituto de Engenharia Biomédica, Laboratório de Biomateriais, Universidade do Porto
	Prof. Rogerio Gaspar	Facultad de Farmacia, Universidad de Lisboa
Horizontal Programmes	Dr. Joan Bigorra	Director de Innovación del Hospital Clinic de Barcelona
	Dr. Pilar Calvo	Responsable de Desarrollo Farmacéutico de PHARMAMAR

A Medical Advisory Board was created in 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 aspects relating to interactions between their scientific programme and clinical practice. The members of this Medical Advistory Committee are:

Medical Advistory Committee Members

MEDICAL ADVISTORY BOARD 2013		
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
Pneumology	Emilia Barrot Cortés	Hospital Virgen del Rocío, Sevilla
Pharmacology and Regulatory Affairs	Joan Bigorra Llosas	Hospital Clínic, Barcelona

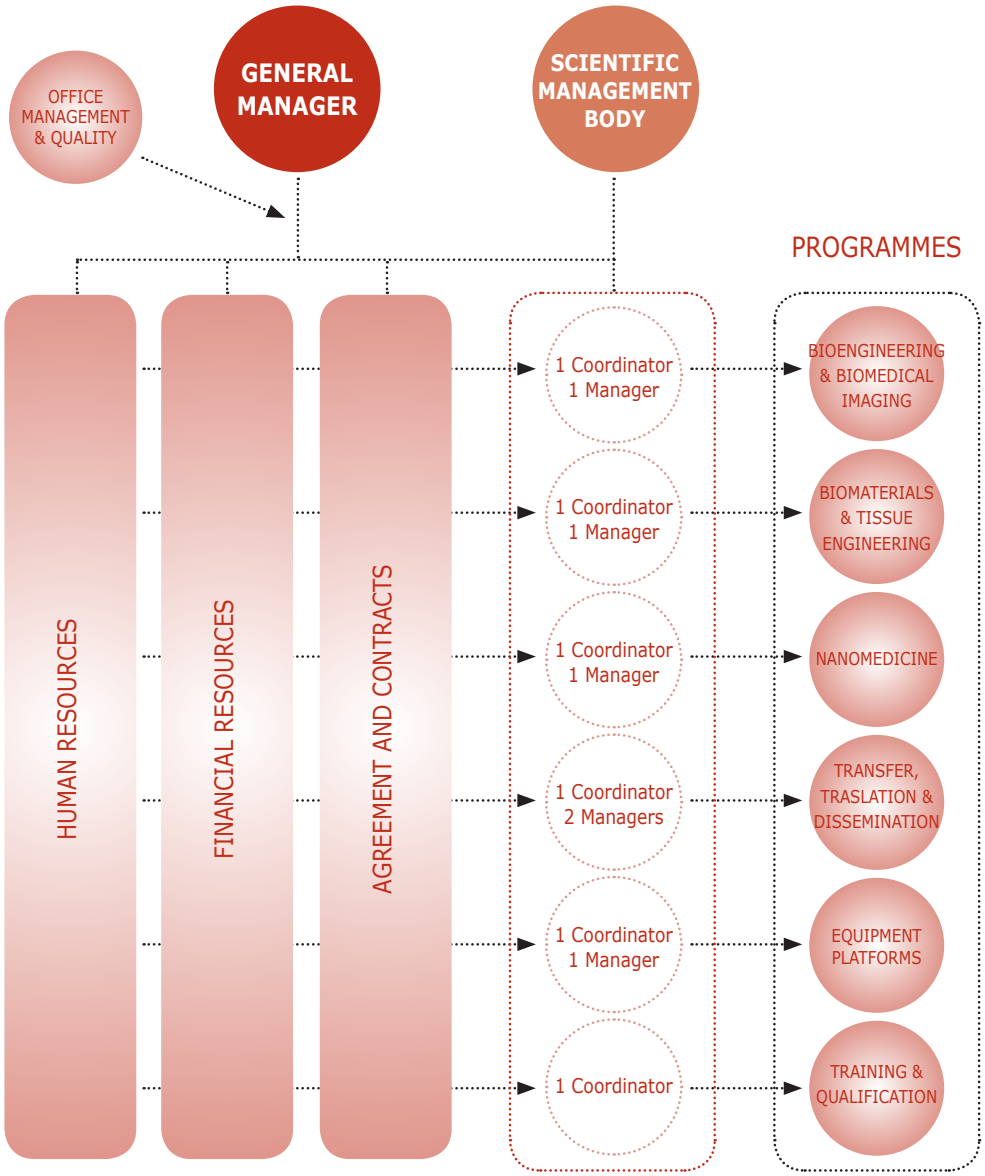
As advisory bodies of CIBER-BBN, the Scientific Advisory Board (SAB) and the Medical Advistory Board held a joint meeting with the centre's Steering Committee on November 22 in Malaga at the 7th Annual CIBER-BBN Conference. The centre's activity in 2013, the annual scientific evaluation results, and the new strategic plan drawn up by CIBER-BBN over the year were discussed during the work session. In that session, the comments received at the meeting held between both Committees the previous year were taken into account. As regards the composition of the SAB, 4 members were renewed and will be part of said Board starting 2014.

As regards the Administrative bodies, the Managing Director is in charge of managing human, financial and material resources. From the scientific point of view, the organisational structure is based on the member research groups and the Research Programmes in which they are grouped.

In 2013, CIBER-BBN had 47 research groups, 45 of which were full member groups and 2 of which were associated groups, described in the preceding section of this Report.

The research staff hired in CIBER-BBN is distributed among the 45 full member research groups. The administration and management team comprises staff from the technical office in Zaragoza and programme managers distributed into some research groups.

CIBER-BBN functional structure

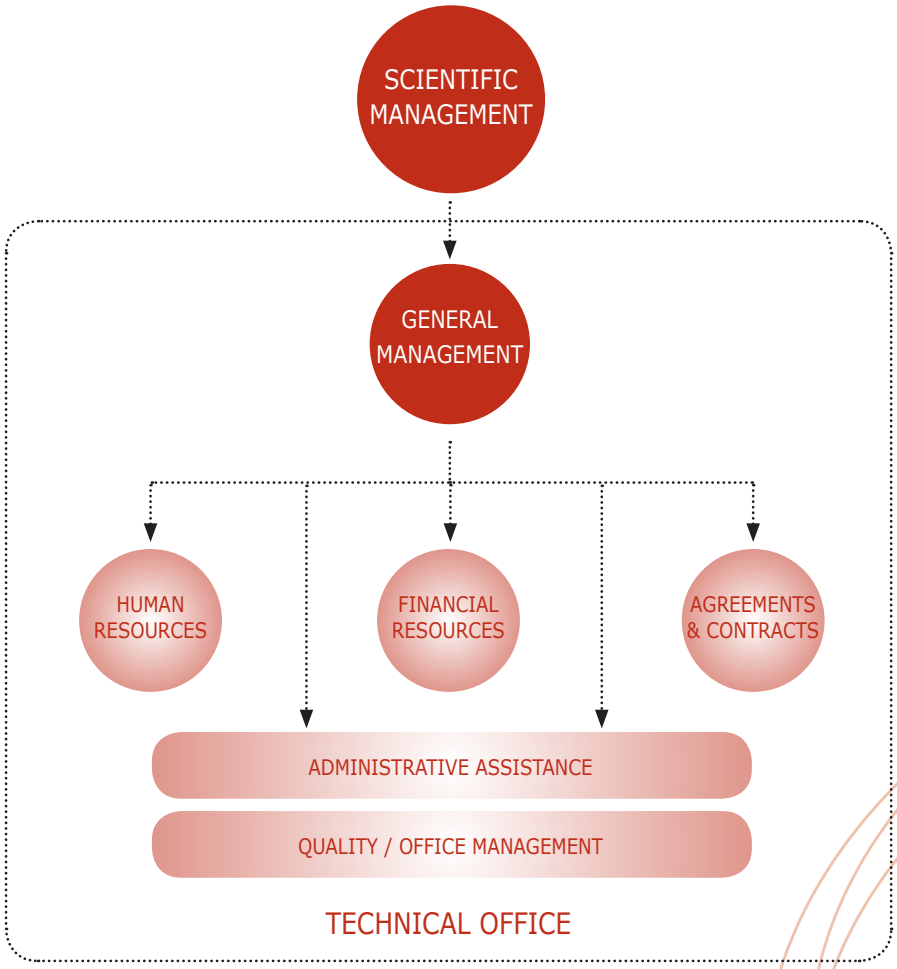


The Managing Director, **Ms. Begoña Pérez Magallón** was in charge of the managerial structure of CIBER-BBN.

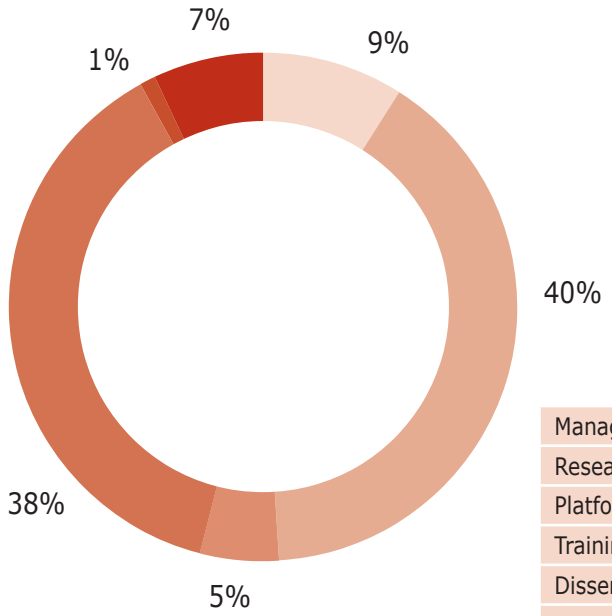
The areas forming the CIBER-BBN management office depend directly on the Managing Direction. These areas are under the responsibility of:

- Human Resources Area: **César García Gallego.**
- Financial Resources Area: **Raquel Campo Usieto.**
- Agreements and Contracts Area: **Margarita Casado Martínez.**
- Communication Area: **Inés Ortega Villanueva.**
- Office Manager: **Aránzazu Trigo Sánchez.**
- Quality and External Funding Manager: **Inés Villa Martínez.**
- Administrative Support: **Elena Andrés Portero.**

Organizational Chart



2013 Budget



Management	420.622 €
Research Programmes	1.917.796 €
Platforms	224.483 €
Training	1.847.064 €
Dissemination	56.956 €
Transfer and Translation	337.109 €
Total	4.804.030 €

		ENTRY	BUDGET
CIBER-BBN PROGRAMMES	MANAGEMENT	Management	420.622 €
	BIOENGINEERING PROGRAM	Intramural Bioengineering Projects	458.860 €
	BIOMATERIALS PROGRAM	Intramural Biomaterials Projects	682.720 €
	NANOMEDICINE PROGRAM	Intramural Nanomedicine Projects	776.215 €
	PLATFORMS	Platforms	224.483 €
	TRAINING	Training Grants	216.779 €
		Mobility	18.097 €
		Qualification	1.612.188 €
	TRANSFER, TRASLATION & DISSEMINATION	Dissemination	56.956 €
		Technology Transfer	237.109 €
		Translational Research Collaborations	100.000 €
		TOTAL	4.804.030 €

CIBER-BBN Staff

In 2013 staff hiring by the CIBER-BBN member research groups with regard to group and equipment platform staff has remained stable concerning the number of hires. This year CIBER-BBN had an average of 129 hires, a figure that indicates the slight adjustment occurring mostly due to the hiring limitations laid out by Budget Law of 2013.

Consolidation of the **Qualification Sub-programme**, within the CIBER-BBN Training Programme continued in 2013. Its purpose is to boost the transverse research methodologies in various groups within the foremost CIBER-BBN lines established in the 2010-2013 Master Plan.

This was done by providing human resources to the groups to promote the creation of these methodologies, procuring that they complement activities that the groups are currently developing in order to foment collaboration possibilities and increase competitiveness of the consortium. There is one person per group that belongs to this line of work.

Contract Type

		Nr.	%
CONTRACTS	Indefinite	73	58.9%
	Temporary	51	41.1%
TOTAL		124	100%

Number of hires according to contract type

Hired staff profiles are essentially the most specialized (PhD's and Bachelors of Science), according to the excellence required of the human resources in a competitive organisation such as CIBER-BBN. These profiles form over 88% of the total CIBER-BBN staff.

Professional Categories

CATEGORY	STAFF	PERCENTAGE
PhDs with Experience	44	35,5%
PhDs without Experience	23	18,5%
Bachelor's of Science	43	34,7%
Diploma Graduate	1	0,8%
Level II Vocational Training Technician	9	7,3%
Level I Vocational Training Technician	4	3,2%
TOTAL	124	100%

Number of hires according to professional category

The average age of hired staff is around 34 years, and is generally higher the more specialized the profiles are.

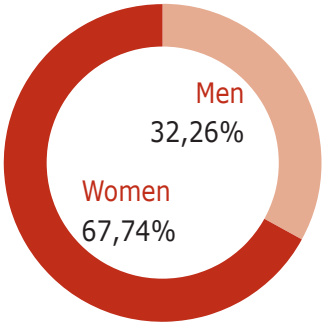
Average staff age

CATEGORY	AVERAGE AGE
Intern	24
Diploma Graduate	33
Phd WITH EX	40
Phd WITHOUT	35
Bachelor's of Science	33
Voc. Train. Lev. I	38

Concerning the distribution by gender and studies, the following is observed:

Distribution by staff gender and studies

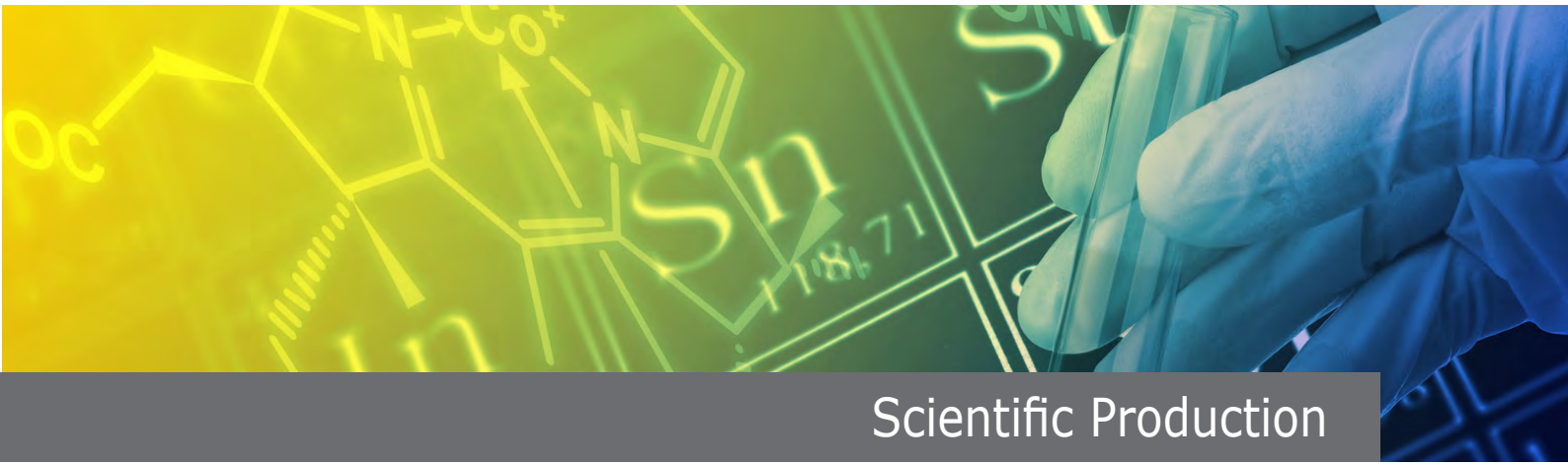
CATEGORY	MEN	WOMEN
PhDs with Experience	16	28
PhDs without Experience	6	17
Bachelor's of Science	16	27
Diploma Graduate	0	1
L. II Vocational Training Tech.	1	8
L. I Vocational Training Tech.	1	3
TOTAL	**40**	**84**



There is a majority of women on staff hired by CIBER-BBN, especially in the most qualified categories.

In addition to the people hired by CIBER-BBN in research groups, in 2013 there were **318 researchers assigned** to the entity but linked job-wise to other institutions, and there were a total of **415 collaborators**.

The number of researchers and administration and management staff of CIBER-BBN, including those that are assigned and collaborators, amounted to 857 people in 2013.



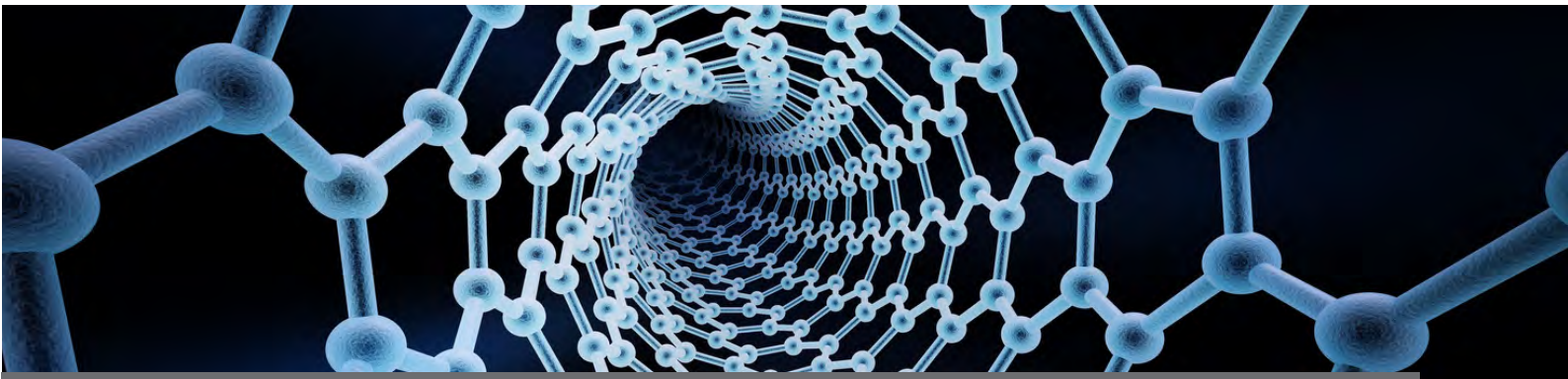
Scientific Production

The final scientific production data of CIBER-BBN in 2013 may sustain a minor modification with respect to those shown below:

Indicators	Year 2013
A Publications	
1. JCR Publications	630
1.1. Publications in the first quartile	422
1.2. Publications in the first decile	182
1.3. Publications in journals with IF > 15	14
1.4. Publications in the second quartile	153
1.5. Publications in the third quartile	29
1.6. Publications in the fourth quartile	20
2. Collaborative Publications	
2.1. IntraCIBER	114
2.1.1. Two groups	89
2.1.2. Three groups	13
2.1.3. Four groups or more	14
2.2. InterCIBER	25
2.3. On a state level	451
2.4. On an international level	267
2.5. Publications in collaboration with hospitals	117
3. Affiliated Publications	
3.1. Publications affiliated with CIBER-BBN	491
3.1. Publications not affiliated with CIBER-BBN	137
B Projects	
1. Requested and non-granted European projects	31
2. Granted European projects	91
3. International projects (NIH, NSF, etc)	14
4. Granted national projects	223
5. Granted Autonomous Community projects	110
6. Projects of private institutions	33
7. Cooperative projects	
7.1.IntraCIBER	48
7.1.1. Two groups	39
7.1.2. Three groups	6
7.1.3. Four groups or more	5

C Patents	
1. Total international patents	42
Original applications	8
Applications for extensions	28
Granted and Registered	6
2. Total national patents	23
Filed	14
Registered	9
3. Collaborative patents	
With other CIBER-BBN groups	22
With hospitals	8
D Transfer	
1. Enterprises created (Spin offs)	0
2. Contracts with enterprises	225
E Translation	
1. Healthcare Translation	
1.1. National or international clinical guidelines	6
1.2. New services included in the service portfolio	42
2. Clinical trials	156
3. Projects approved by the AETS	3
4. Social dissemination and disclosure activities	228
F Funds	
1. Public funds obtained	21.588.552
2. Private funds obtained	6.091.735
Total funds obtained	27.680.287
3. Funds obtained for intramural projects	1.433.732
G Training of Human Resources	
1. Staff in pre-doctoral training	213
2. Directed dissertations	86
3. Training mobility	244
4. Organized courses, seminars and conferences	137
H Internationalisation	
1. Conferences invited to participate in international forums	339
2. Editorial committee of international journals	139
3. Scientific committee of scientific associations	112
4. Foreign staff recruiting	21
5. Characteristic staff training abroad	67
6. Confirmable collaborations with foreign groups	214
7. Funding programme evaluation	54
7.1.FP7	11
7.2. Others	39
8. Marketing and technological bidding activities	66

2 Scientific programmes



P1. Bioengineering

Coordinator and assigned groups

Coordinator: Jordi Aguiló. *Biomonitoring Group of the National Microelectronic Centre (GBIO-CNM)*

The **assigned groups** to this programme in 2013 are:

BIOENGINEERING GROUPS	
PI	**NAME OF THE GROUP**
Laura Roa	Biomedical Engineering Research Group, Universidad de Sevilla (GIB-US)
Pablo Laguna	Communications Technologies Group of the Engineering Research Institute, Universidad de Zaragoza (GTC-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)
Alejandro Frangi	Centre for Computational Imaging, Universidad Pompeu Fabra (CISTIB)
Bernardo Celda	Research group of Biomedical and Biophysical Applications of the NMR, Universidad de Valencia (GABBRMN-UVEG)
Javier Pavía Segura	Biomedical Imaging Group, Universidad de Barcelona (GIB-UB)
Andrés Santos Lleó	Biomedical Imaging Technology Research Group, Universidad Politécnica de Madrid (BIT-UPM)
Raimón Jané Campos	Biomedical Systems and Signals Research Group, Universidad Politécnica de Cataluña (SISBIO-UPC-IBEC)
Eduardo Fernández Jover	Neuroprosthesis and Neuroengineering Research Group, Universidad Miguel Hernández de Elche (NN-UMH)

Strategic lines of research of the programme

a) Multimodal Diagnostics:

Imaging diagnosis is increasingly complemented by another diagnosis technique based on different biophysical elements such as the combined use of different imaging techniques.

The objective of this line therefore relates to the combined analysis of all this information, promoting improvements in diagnosis systems, creating tools to aid in clinical decision making and enhancing the pre- and intraoperatory planning systems, as well as simulation and control tools in virtual surgery.

The strategic line of multimodal diagnostics of CIBER-BBN covers methods and technologies that allow detecting biological and pathological events, and facilitate understanding the relationships between the elements making up the complex organic systems. Multimodal diagnostics integrates knowledge customised in various scales and originated from different sources. Multimodal diagnostics must therefore be understood in a multiscale sense (from cellular level to organs or the body as a whole) and in a multimode sense (in reference to the basic information from medical imaging, biophysical signals, functional models, etc).

CIBER-BBN conducts its research activity with dual perspective. On one hand, CIBER-BBN deems it strategic to carry out a mid- and long-term basic research with expected results for the purpose of expanding the frontiers of knowledge in the multimodal diagnostics field and obtaining greater understanding of how such methodologies may be effective in improving diagnosis and in tracking specific pathologies. On the other hand, and without losing sight of the translational vocation of CIBER-BBN, this strategic line also gives priority to applied research which is more closely linked to clinical application and to the market of medical devices. Said applied research is expected to generate transferable results in short term.

This line is in turn complemented with others such as the line relating to Biosensors and Molecular Diagnosis and Implant Design in which similar or complementary techniques are used.

b) Intelligent devices and systems:

This implantation will involve a greater degree of autonomy for the patients and will translate into lightening the work load of healthcare personnel. Additionally, the research results from this line will offer a more thorough and continuous control of the patients since the evolution of their health condition can be tracked and different variables can be monitored simultaneously.

The growing complexity of diagnostic works requires researching for and developing new devices for capturing data at very different functional integration levels, i.e., from molecular to systemic level. Current clinical progression is mainly determined by the availability of new devices that allow unfurling preventive diagnostic strategies, early detection of pathologies or disease progression monitoring in long-term processes. Likewise, therapies suitable for those levels of action require new devices that are capable of operating in an intelligent manner according to the condition and needs at that time in the least invasive manner possible.

Micro-nano technologies have opened up vast possibilities for the development of intelligent sensing devices for in vitro and in vivo diagnosis and monitoring, the development of molecular sensors and biomarkers or the study of the communication between cells and their environment, as well as the development of associated devices and instrumentation for remote micro-nanoagent manipulation in theranostics.

The electronic instrumentation, the biosensors and the new materials create a con-

ducive environment for designing devices; as many diagnostic or therapeutic objectives as needed can be established. Problems concerning the measurement of biomedical variables at any integration level highlight the need of specific instrumentation with respect to the variables to be measured and the functionality and operating conditions required.

The development of new biomedical imaging and signal analysis techniques for the early diagnosis of prevalent pathologies or for molecular studies requires new medical imaging and signal devices and systems. This need further requires prior developments for animal models that allow essential experimentation with said technologies.

In addition, in a better and more informed society that seeks higher healthcare quality and has ever-increasing access to technology, it is logical to think of a research that aims to introduce more portable and efficient medical devices that that offer greater degree of autonomy with respect to the clinical specialist and incorporate a certain degree of intelligence. In summary, the development of "personal assistants", along with sensor network technologies for intelligent health environments and lab-on-a-chip, form the paradigm of care identified today as a point of care. Research in remote monitoring systems are, among many examples, some challenges of this strategic line. The implantation of these devices will involve a greater degree of autonomy for the patients and will translate into lightening the work load of healthcare personnel, significantly increasing patients' quality of life.

Additionally, the research results from this line will offer a more thorough and continuous control of the patients since the evolution of their health condition can be tracked and different variables can be monitored simultaneously.

Intramural projects of the programme

A total of 13 intramural projects are carried out in the Bioengineering Programme in 2012-2013:

PROGLIO	**Optimizing diagnosis, prognosis and therapy response in human glioma. Preclinical and translational studies.** Coordinating PI: Carles Arús / Participating PIs: J. Blanco, A. Villaverde, R. Mangues, S. Penadés, S. Schwartz, A. Santos.
RETINA	**Development of new therapies for degenerative retinal diseases.** Coordinating PI: Eduardo Fernández / Participating PIs: J. Aguiló, M. Calonge, J. L. Pedraz, P. Botella (external group, CSIC)
INDI-MÚSICA	**Indexes obtained from computational models and multiscale multimodal biomedical signals for the diagnosis of cardiac pathologies.** Coordinating PI: Pablo Laguna / Participating PIs: R. Jané, M. Doblaré, A. Frangi, J. Sanz (external group, Polytechnical Univ. of Valencia)
MICHOR-MON	**Advanced micro-chamber for organotypic cell culture monitoring.** Coordinating PI: Bernardo Celda / Participating PIs: J. Aguiló, R. Martínez, F. Pozo, S. Penadés, L. Roa.
PERSONA	**Personalized Decision Support System for Enhanced Control in Healthcare Platforms.** Coordinating PI: Francisco del Pozo / Participating PIs: A. Leiva, L. Roa.

THEMIS	**Image guided therapies for minimally invasive surgeries.** Coordinating PI: Francisco del Pozo. / Participating PIs: M. Doblaré, JL. Peris, Fco. M. Sánchez Margallo (external group, Jesús Usón Minimally Invasive Surgery Centre).
GLAUCO II – E-SENTINEL	**Non-invasive monitoring of intraocular pressure through a micro-nanotechnology based sensor contact lens.** Coordinating PI: Jordi Aguiló. / Participating PIs: M. Calonge.
MUDIRES	**Multimodal diagnosis by interpretation of multiscale signals in the respiratory system.** Coordinating PI: Raimon Jané. / Participating PIs: P. Laguna, D. Navajas.
ES3	**Towards a body area network for measuring stress levels.** Coordinating PI: Jordi Aguiló. / Participating PIs: P. Laguna, external clinical groups.
TAP-VAL	**Telemedical artificial pancreas: clinical validation.** Coordinating PI: Alberto de Leiva. / Participating PIs: F. del Pozo, external clinical groups.
TROPNA	**Disposable multiplexed microsensor for direct detection of BNP and troponin by impedance measurements.** Coordinating PI: Jordi Aguiló. / Participating PIs: F. Albericio, M. Doblaré, P. Marco, external clinical groups.
ULTRASEN-4BIO	**Characterization and validation of novel ultrasensitive piezoresistive all-organic sensors for multimodal biomedical signals.** Coordinating PI: Raimon Jané. / Participating PIs: J. Veciana, M. Doblaré, external clinical groups.
MIND-T	**Multimodal imaging tools for neurological diseases.** Coordinating PI: Javier Pavía. / Participating PIs: A. Frangi, A. Santos, external clinical groups.

P2. Biomaterials

Coordinator and assigned groups

Coordinator: José Becerra Ratia. *Bioengineering and Tissue Regeneration Laboratory of the Universidad de Málaga (LABRET-UMA)*

The groups involved in this programme in 2013 were:

BIOMATERIALS 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)
José Luis Peris Serra	Health Technology Group, Instituto de Biomecánica de Valencia (GTS-IBV)
Daniel Navajas Navarro	Respiratory and Cellular Biomechanics Group, Universidad de Barcelona (GBRC-UB)
Manuel Monleón Pradas	Biomaterials Center, Universidad Politécnica de Valencia (CBM-UPV)
Isabel Obieta Vilallonga	Tissue Engineering Research Group of the Health Unit, Fundación Tecnalia (TECNALIA)

Jerónimo Blanco Fernández	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 Cabello	GIR BIOFORGE, Universidad de Valladolid (BIOFORGE-UVA)
Mª Luisa González Martín	Research Group on Microbial Adhesion, Universidad de Extremadura (AM-UEX)
Juan C. Izpisúa Belmonte	Regenerative Medicine Center of Barcelona (CMRB)

Strategic lines of research of the programme

a) Regenerative medicine: Tissue engineering and Cell therapy:

Research in regenerative medicine has been identified by CIBER BBN as one of its strategic lines due to how important it is as a potent therapeutic alternative for degenerative diseases caused by specific cell death or malfunction, affecting a large number of people. Currently there are no effective treatments. These diseases include very common diseases such as diabetes, Parkinson's,

Alzheimer's, leukemia and heart diseases, and as regards trauma the group also seeks to approach topics such as wound regeneration, ocular regeneration and bone and cartilage regeneration.

Regenerative medicine could be defined as an up and coming area that seeks to maintain, improve or restore cell, tissue and body function, by means of applying methods primarily related to tissue engineering and cell therapy.

This discipline is considered the only area having the capacity to radically change the way some diseases will be handled in the future. However, this therapeutic modality is in the very early stages of development, and enormous efforts must be made to obtain real and consolidated progress. In this sense, tissue engineering is the most advanced and promising therapeutic option in this area. It has received a very positive influence from important technological advances such as the development of new cell culture techniques and the design of resorbable biopolymers.

The purpose of regeneration is based on being able to control and guide cell response in the desired direction. Accordingly, any strategy chosen for that purpose through tissue engineering, cell therapy or use of smart biomaterials, will require not only knowing but also controlling mechanisms of cellular communication with the environment. Cells read the messages they receive through biophysical and biochemical signals or stimuli of the environment triggering a series of intracellular signals modifying cell behaviour in response to said signals.

Now cells will write their own messages in extracellular space either through extracellular matrix biosynthesis and/or by remodelling the one already existing. This means a two-way communication of the extracellular matrix and the microenvironment of the cell. True regeneration engineering would require knowing and controlling all this traffic of information, signals and stimuli which is what controls cell behaviour.

However, if all the elements participating in the regeneration process are analyzed, it can be seen that there are a number of such elements and they are all relevant: a) interstitial nutrients, electrolyte and molecules; b) cell transport and cellular mobility; c) the design of the synthetic biomaterial participating in the process (degradation, mechanical properties, etc.); d) the metabolic microenvironment; e)

cell-material interactions which will be the basis of the surface properties of the material and of the adhesion of biological entities such as proteins, f) the biophysical microenvironment and biophysical and biochemical stimuli (the extracellular matrix and chemical and physical stimuli play a key role in this process); g) cell adhesion, proliferation and differentiation; h) the study of angiogenesis as a fundamental aspect in in vivo regeneration of any tissue; and finally i) the immune and inflammatory reaction. Controlling the inflammatory reaction is key for assuring both healing and regeneration.

Associated with this knowledge map to be generated, mathematical modelling of the different elements and of the process as a whole is also of maximum interest. The mathematical models can also have analytical or numerical approaches according to what is being modelled.

In this context, within its strategic line in regenerative medicine CIBER BBN has defined two priority lines of research, a line of basic research and another line of applied research. The line relating to cell biophysics and epigenetics will be the aspect in basic research where knowledge about basic cell processes is expected to be generated and mid- and long-term results are expected to be obtained. As regards the aspect of applied research, the line on specific applications of tissue engineering and implants has been considered for obtaining short-term results that are oriented on specific clinical problems and therefore more closely linked to the market and the end user.

Since this is a multidisciplinary area there will be synergies and collaborations with the other strategic lines of the CIBER BBN, which will be reflected in the proposed research projects.

b) Endoprotheses and implants:

The global objective of this line is to move forward in a new generation of patient-specific implants, taking specific patient needs into account during the design stage, with greater implant integration and a drop in risks of infection and osteolysis. It also seeks to have greater control over their behaviour and over the progress after implantation.

Customized implants with better integration and control properties will allow obtaining higher success rates, reducing the need for re-intervention. This aims to reduce health costs and increase the patient's quality of life.

The type of products and implants to be obtained are:

- Implants for Orthopaedic Surgery and Trauma (COT) (joint prostheses, osteosynthesis, external fixing, fixing systems for rachis, etc.), surgical instruments.
- Bone replacements (*scaffolds*).
- Dental implants.
- Ophthalmological implants.
- Cardiovascular implants: improved coronary stents.
- Neural implants.
- Soft tissue implants.
- Auditory implants (hearing aids, cochlear and ossicular implants).
- Single-use products: abdominal mesh, diagnosis material, probes, catheters, sutures,... with antibiotic and/or antithrombotic properties.
- Active implants.

Priority lines of action covering both basic and applied research aspects have been determined in the implant area. This dual perspective of CIBER-BBN's research activity establishes that mid- and long-term results will be obtained in basic research. In turn, objectives that are more akin to clinical application and to the market will be handled within the priority lines of applied research. The line of implants has a distinguished transverse character and is end product-oriented. Therefore, most priority lines will be lines of applied research.

Intramural projects of the programme

A total of ten intramural projects were conducted in the Biomaterials Programme in 2012-2013:

BIOSCAFF-EYE

Bio-engineered cell in ocular surface reconstruction for corneal blindness: from basic research to clinical trials.

Coordinating PI: Margarita Calonge / Participating PIs: J. A. Planell, J. Samitier, J. C. Rodríguez Cabello, I. Obieta, J. L. Pedraz.

ES-CELL-THERAPY

New therapeutic strategy as a vehicle for localized release in the treatment of brain tumours.

Coordinating PI: Jerónimo Blanco / Participating PIs: C. Arús, J. Becerra, JA. Planell, external clinical groups.

BIOPROTERIAL

Biological activity of matrix protein at the cell-material interface.

Coordinating PI: Manuel Monleón / Participating PIs: M. L. González, J. A. Planell, N. Vilaboa, JC Rodríguez Cabello, F. Albericio.

ABDOMESH

Development and validation of a new prosthetic implant concept for the repair of abdominal wall defects.

Coordinating PI: Juan Manuel Bellón / Participating PIs: J. Aguiló, M. Doblaré, J. L. Peris, E. Hurtos (external group, ASCAMM), Grober (external group, enterprise).

BIOGELANGIO

Extracellular matrices for angiogenic activation and anti-inflammatory activity in regenerative medicine.

Coordinating PI: Julio San Román / Participating PIs: M. Monleón, J. C. Rodríguez, J. M. Bellón, N. Vilaboa, M. L. González.

NACRE

New approaches for cartilage regeneration.

Coordinating PI: Cristina Ruiz / Participating PIs: J. San Román, J. A. Planell, M. Doblaré, M. Monleón, I. Obieta, J. Becerra, J. L. Peris, B. Celda.

SCAFFTIDE 3D

Three-dimensional scaffolds and functionalized implants for regenerative medicine.

Coordinating PI: María Vallet Regí / Participating PIs: J. A. Planell, J. C. Rodríguez, JM. Bellón.

MICROREN

Microfluidic devices to support renal tissue to complement haemodiafiltration and to administer regenerative therapies.

Coordinating PI: Manuel Doblaré / Participating PIs: J. Aguiló, JL. Pedraz, J. Santamaría, external clinical groups.

REWOUND

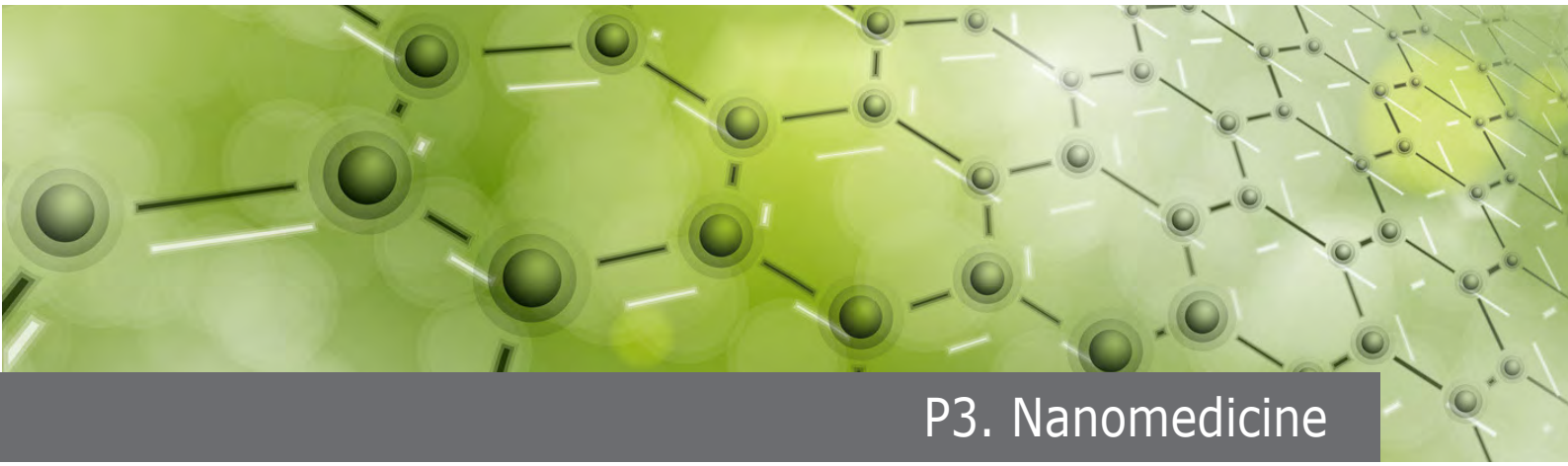
Elastin-type recombinant polymers with applications in wound healing.

Coordinating PI: JA. Planell / Participating PIs: JM. Bellón, J. Blanco, M. Doblaré, JC. Rodríguez, A. Raya (IBEC, external group).

TELTIS

Titanium-based tissue (bone tissue) engineering product for orthopaedic surgery.

Coordinating PI: J. Becerra / Participating PIs: J. Blanco, M. Doblaré, ML. González, I. Obieta, JL. Peris, JA. Planell, N. Vilaboa, Á. Raya (IBEC, external group), external clinical groups.



P3. Nanomedicine

Coordinator and assigned groups

Coordinator: María Pilar Marco. *Nanobiotechnology Group for Diagnostics of the Advanced Chemistry Institute of Catalonia of the CSIC (AMRG-IQAC)*

The groups belonging to the programme in 2013 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 Ramírez	Dendrimer Group for Biomedical Applications, Universidad de Alcalá (GDAB-UAH)
José Luis Pedraz Muñoz	Micro and Nano technologies, Biomaterials and Cells Research Group (NANOBIOCEL)
Ramón Mangues Bafalluy	Oncogenesis and Antitumor Group of the Research Institute, Hospital de la Santa Cruz y San Pablo (GOA-HSCSP)
Mª Ángeles Muñoz Fernández	Molecular immunobiology laboratory, Hospital General Universitario Gregorio Marañón (LIBM-HGUGM)
Concepción Solans Marsà	Colloidal and Interfacial Chemistry Group of the Advanced Chemistry Institute of Cataluña, CSIC (QCI-CSIC)
Ramón Martínez Máñez	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

a) Molecular diagnosis and biosensors:

This line covers new diagnosis approaches and strategies based on the latest advancements in micro(nano)technology and biotechnology. The knowledge obtained in these areas and the possibility of combining both sciences foretell the emergence of a new generation of tools for more precise, flexible and effective diagnoses. It also has enormous potential for detecting a wider range of more robust and sensitive biomarkers. The physical properties of materials, nanostructured surfaces and nanoparticles are the basis for constructing biofunctional hybrid materials as the result of the combination of organic (biomolecules) and inorganic elements, which can be described as a clear advancement in biosensors based on novel nanobiotechnological approaches.

This line gives priority to projects aimed at solving clinical problems where the application of systems based on biosensors and specific biomarker detectors provides a feasible solution and a clear advantage in diagnosis. Priority will preferably be given to the development of technologies in the context of relevant clinical needs.

This includes both the use of biomarkers for tracking the progression of a certain disease, and the recognition of targets for specific therapies. Techniques based on spectroscopic NMR, specific antibodies, etc., will be a preferred object in this line, as will be the use of highly specific and even multiplexed nanobiosensors. The use of these techniques will allow diagnoses with a stronger biological basis and more reliable results, which translates into greater precision in diagnosing different pathologies.

The general objective of this strategic line is to provide new diagnosis tools to improve and protect public health based on novel micro(nano)biotechnological approaches. In the long-term, research in this line seeks to overcome challenges that current diagnosis methods have not been able to overcome and to provide alternative in those areas where current technology limitations compromise the health of individuals and the quality of life of the society as a whole.

b) Therapeutic nanoconjugates and drug delivery systems:

This line will concentrate on the development of new pharmacological therapies based on the intelligent design of guided nanoconjugates. It contemplates both the development of pharmacological delivery systems optimized to traverse the blood-brain barrier and the delivery especially of enzymes, proteins or gene inhibition strategies by means of siRNA. Priority will be given to obtaining therapeutic nanoconjugates in prevalent clinical areas and in rare diseases.

The pharmacological reformulation of drugs already existing in clinical practice will not be a priority, nor will technological development not associated with a relevant clinical need. The line must assure that toxicological and therapeutic activity data is obtained in all the newly designed nanoconjugates. The basic objective is to obtain suitable proofs of concept.

The development of therapeutic nanoconjugates and of localized and controlled delivery systems for these nanoconjugates will 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 may entail a potential risk for the patient.

The groups is focusing on applied research with a translational research approach aimed at the therapeutic application of delivery systems for drugs and nanoparticles that have therapeutic activity, or as diagnosis agents, or agents for internalizing/distributing drugs. This approach also aims to apply active molecules or nanoconjugates in scaffolds or other mechanisms for specific applications in tissue engineering and implants.

In addition, the group is investigating the development of therapeutically active molecules, the development of nanoconjugates, compression of active devices and their internalization in tissue and integration in the organism.

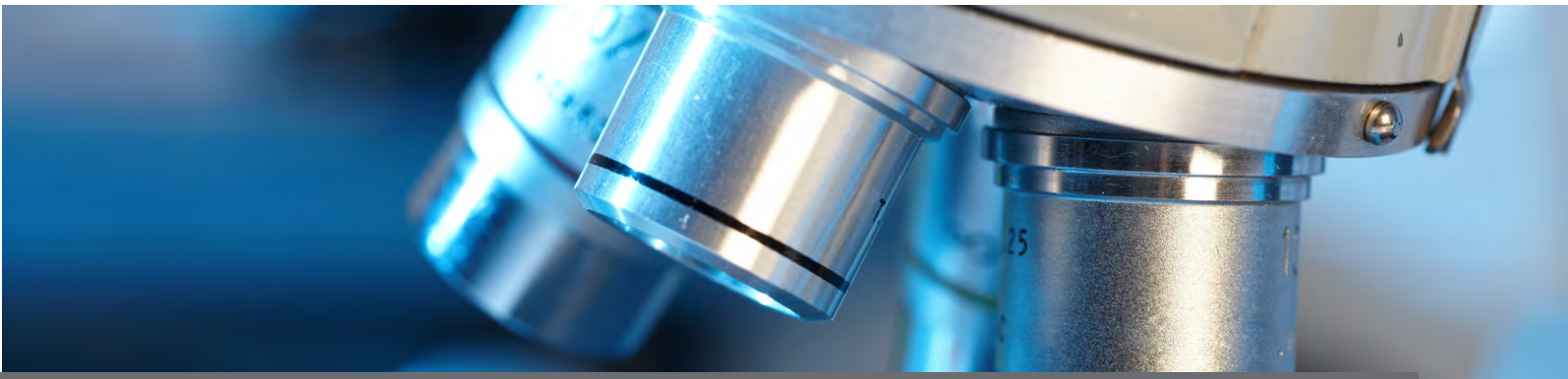
Intramural projects of the programme

A total of 21 intramural projects have been conducted in the Nanomedicine Programme in 2012-2013:

NANOXEN	**Use of non-invasive techniques for controlling nervous functions in animal models.** Coordinating PI: Fausto Sanz / Participating PIs: R. Eritja, JC. Izpisúa, external clinical groups.
NAINBO	**Nano-engineering inclusion bodies as new biomaterials for cell proliferation.** Coordinating PI: Jaume Veciana. / Participating PIs: A. Villaverde, N. Vilaboa.
NANOCOMETS	**Development of nanoparticles as vehicles for the treatment of metastatic colorectal cancer.** Coordinating PI: Ramón Mangues / Participating PIs: J. Pavía, A. Villaverde, R. Martínez, F. Albericio, S. Schwartz.
NANOSTEMNESS	**Targeted thearpy to improve the treatment of advanced breast cancer.** Coordinating PI: Simó Schwartz. / Participating PIs: J. Veciana, A. Villaverde, external groups.

OLIGOCODES	**Development of a universal multiplexed diagnostic platform based on encoded oligonucleotide nanoparticles and DNA sensor devices.** Coordinating PI: Pilar Marco. / Participating PIs: F. Albericio, R. Eritja, J. Samitier, I. Obieta, external clinical groups.
GLYCO-HIV	**Nanoparticles as new tools to fight HIV transmission.** Coordinating PI: Soledad Penadés. / Participating PIs: F. Albericio, external groups.
NANOMEDIAG	**Nanobioanalytical platforms to improve medical diagnosis of infections caused by pathogenic microorganisms.** Coordinating PI: Josep Samitier. / Participating PIs: P. Marco, M. L. González.
NANOHYPER-THERMIA	**Development of new nanoparticles and protocols for enhanced hyperthermia.** Coordinating PI: Francisco del Pozo. / Participating PIs: E. Fernández, S. Penadés, J. Santamaría, N. Vilaboa, R. Martínez. F. Palacio (external group, CSIC).
CELL-NANO-THYROID	**New orthotopic/ectopic nude mice model of human thyroid undifferentiated/anaplastic carcinoma: useful tool for new cell therapies, drug testing and validation in humans.** Coordinating PI: Alberto de Leiva. / Participating PIs: S. Schwartz, J. L. Pedraz, R. Mangues, J. Blanco.
NANORETINA	**Nanoscaffolds for relocating a detached retina.** Coordinating PI: Francisco del Pozo. / Participating PIs: J. Aguiló, J. Veciana, external clinical groups.
BIOGATES	**New nanoparticles with molecular gates for diagnosis and drug delivery.** Coordinating PI: Ramón Martínez. / Participating PIs: R. Eritja, P. Marco, S. Penadés, JL. Peris, S. Schwartz, M. Vallet.
LIVERPOC	**Advanced diagnostic tool for the early identification of renal failure.** Coordinating PI: Laura Lechuga. / Participating PIs: P. Marco, M. Doblaré, external clinical group.
METALOTRIGGER	**Development and biological evaluation of multifunctional carriers sensitive to metalloproteinase for combined therapy for advanced colorectal cancer.** Coordinating PI: Simó Schwartz. / Participating PIs: F. Albericio.
NADD	**Nucleic acid derivatives as potential drugs.** Coordinating PI: Ramón Eritja. / Participating PIs: R. Gómez, C. Solans, MA. Muñoz, JL Pedraz, F. Albericio.
NANOBICIDE	**New nano approaches for microbicidal HIV drugs.** Coordinating PI: Rafael Gómez. / Participating PIs: R. Gómez, C. Solans, MA. Muñoz, E. Fernández.
NANOFABRY	**Development of nanomedicines for enzyme replacement therapies in Fabry's disease.** Coordinating PI: Simó Schwartz. / Participating PIs: F. Albericio, F. Sanz, J. Veciana, A. Villaverde, R. Mangues.
NANOPHOR	**Development of electrophoretic and photonic techniques for identifying and monitoring pathogenic microbes.** Coordinating PI: F. del Pozo. / Participating PIs: J. Aguiló, L. Roa, external groups.

NANOPROVIR	**Customisation of the nano-architecture and function in protein-only artificial viruses.** Coordinating PI: Antoni Villaverde. / Participating PIs: R. Mangues, J. Veciana, S. Schwartz, R. Eritja.
NANO-TRANS-BRAIN	**Nanocarriers for anti-apoptotic drug transport through the blood-brain barrier.** Coordinating PI: Contxita Solans. / Participating PIs: R. Eritja, F. Sanz,R. Gómez, external clinical group.
PEPSIN	**Nanocarriers for anti-apoptotic drug transport through the blood-brain barrier.** Coordinating PI: Félix Ritort. / Participating PIs: R. Eritja, F. Albericio, C. Solans, S. Schwartz.
PHOTOTHERAPY	**Resolving the mechanisms of action of anticancer peptides: cell assays and characterization.** Coordinating PI: Jesús Santamaría. / Participating PIs: N. Vilaboa.

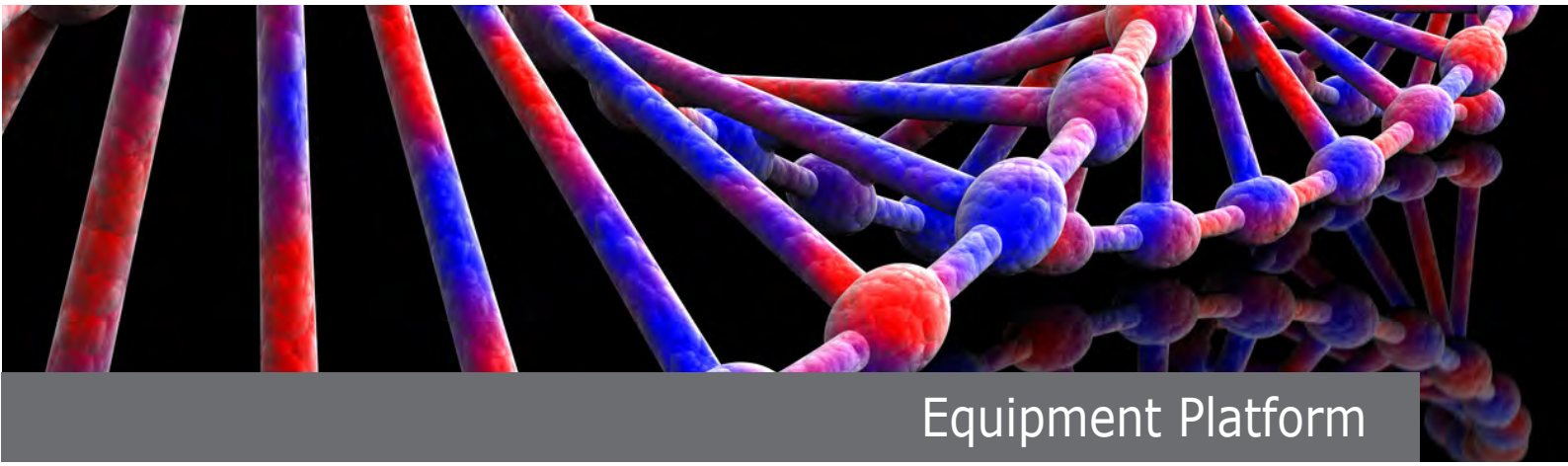


Priority Areas of Research

The following table describes the relationship between priority areas of research with the six strategic lines:

			PRIORITY AREAS							
			Basic Research				Applied Research			
		STRATEGIC LINE	Integral modelling of biological systems	Intelligent sensing	Cell biophysics and epigenetics	Development of new active molecules and nanoconjugates	Software utility integration platform	Micro- and nano- devices for *in vitro* and *in vivo* diagnosis and monitoring	Specific tissue engineering and implant applications	Nanoparticles and drug delivery
PROGRAMME	Bioengineering	Multimodal diagnosis	■	■	■		■	■		■
		Smart devices and systems		■	■		■	■	■	
	Biomaterials & Tissue Engineering	Technologies for advanced therapies in regenerative medicine	■		■	■		■	■	■
		Implants and endoprotheses	■				■	■	■	■
	Nanomedicine	Therapeutic nanoconjugates				■			■	■
		Biosensors		■	■	■		■	■	

3
Horizontal Programmes



Equipment Platform

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.

HIGH-PERFORMANCE COMPUTING PLATFORM

Units

High-performance computing, massive storage and software unit for biomedical applications.

General Objective

To provide support technical 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, recording data and images or model simulation, finite elements simulation, 3D modelling.

PLATFORM OF PRODUCTION OF BIOMOLECULES

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 its 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 projects relating to the strategic lines of Devices, Implants, Regenerative Medicine, and especially Nanoconjugates and Biosensors. 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

PLATFORM OF PRODUCTION OF BIOMATERIALS AND NANOPARTICLES

Units

- Biodeposition and biodetection
- Rapid prototyping
- Molecular biomaterial processing and nanostructuring
- Nanolithography / E-beam
- Micro/naoelectronics
- Nanoparticle synthesis
- Drug formulation (new incorporation)

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 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 Bioengineering Programme, specifically in the lines of Implants and Regenerative Medicine, and in the line of Nanomedicine, especially in Nanoconjugates. It provides services for:

- Functionalizing devices and biosensors by means of solution dispensing.
- 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.

- Stamping dies repeatedly from 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 calorimetry and characterization
- 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 optical imaging and NMR 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 phagocitic 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 quantification, in vivo and in time real, the therapeutic factors used, as well as analysing treatment-induced tissue regeneration
- Validating new therapeutic targets using optical imaging and NMR technologies
- Viewing, following up on and quantifying cellular and genetic activities relating to pathologies in a living organism in time real.

Collaboration with other platforms

- Equipments in Instituto Universitario de Nanociencia de Aragón (INA) ...
- Minimally Invasive Surgery Centre Jesús Usón
- Image Unit in CIC biomaGUNE

In 2013, the units were internally evaluated intended for giving an economic incentive to units with the highest scores. The new internal evaluation protocol was consolidated and started up in 2013.

One year later, the search for external funding was a priority in 2013 from both public and private sources. The Programme was presented in international organisms and partnering events, and in national enterprises, private research foundations and public research organisms. Promotional material was distributed at different visits to companies, research centres and industrial associations. This material was also distributed through participation in the Spanish Technology Platform MATERPLAT and the Spanish Biotechnology Platform, the European BioRegions Council (CEBR) and the recently created European project, IN2LifeSciences (IN2LS), which promotes new relations between small- and mid-sized enterprises, on one hand, and research organisms on the other. Participation in international infrastructures such as Eurobioimaging was also promoted.

The following events were attended:

- II Horizon Conference 2020 II Horizon Health Forum 2020 (Madrid).
- H2020 Conference Framework Programme Nov, Madrid.
- BioEurope Spring, March, Barcelona

- Nanomedicine Platform Conference. March
- CDTI H200 course, in El Escorial, October

The process for becoming an ICTS (Singular Scientific and Technical Infrastructure) became considerably dynamic. Contact with a complementary institution, the Jesús Usón Centre for Minimally Invasive Surgery (CCMIJU) was consolidated to create alliances that allow more competitive candidates to strengthen the ICTS application, under a single institution. Recognition of the programme as ICTS was requested by MINECO in 2013.

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

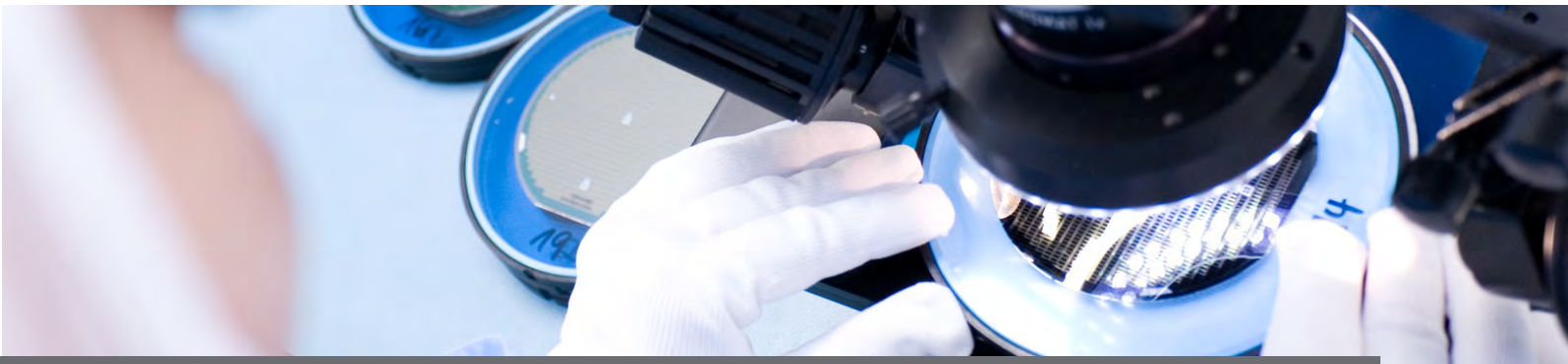
Collaborations initiated with companies were tracked. Some examples are the PHYTECH project, in which two Spanish enterprises and one unit (Surface and Calorimetry Characterization) are involved in the framework of the INNPACTO Programme, and the European project BERENICE (nanoformulation of benznidazol and triazol to fight Chagas disease), involving 2 units (molecular biomaterial processing and nanostructuring unit and the drug formulation unit), among others.

The new strategic action launched in 2011 to improve equipment platforms to develop collaboration projects with enterprises and with the participation of one or more units of the Programme continued in 2013.

In an attempt to promote collaborations with companies, making our services more appealing, the line for supporting certification according to the ISO 9001 standard of the units that are interested continued. The certification process for two units (Protein Production Platform and In vivo Experiments Unit) continued in 2013.

Participation in some European initiatives was maintained. Some examples are:

- ETP Nanofutures. http://www.nanofutures.eu
- European Institute for Biomedical Imaging Research (EIBIR). http://www.eibir.org
- Council of European Bioregions (CEBR). http://www.cebr.net
- Project SM BIOPOWER. http://www.smbiopower.eu/



Industrial Transfer and Translational Research

Patents and transfer results

In 2013, the patent entitled *Device and method for encapsulating microfluidic systems* (P201231532) was licensed to the Spanish enterprise EBERS Medical Technology SL.

A notary's record was requested for the IT application called *FOCUSDET computer programme for locating the epileptogenic source in pharmacoresistant epilepsy.*

Four patents Spanish, nine international PCT patents and one international application in national phases were filed.

Spanish patent applications:

- *Hidrogeles de fibrina con nano partículas plasmónicas* (Fibrin hydrogels with plasmon nanoparticles). P201330894 (14/06/2013).
- *Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa* (Haptens and conjugates derived from pyocyanin, antibodies thereof and immunochemical method for detecting infections caused by pseudomonas aeruginosa). P201330312 (05/03/2013).
- *Método de activación química superficial de un soporte sólido en base silicio mediante anclaje covalente directo de al menos una biomolécula de ácidos nucleicos* (Method for chemical surface activation of a solid silicon-based support by means of direct covalent anchoring of at least one biomolecule of nucleic acids). P201331587 (30/10/2013).
- *Sensor Inteligente de bioimpedancia para aplicaciones biomédicas* (Smart bioimpedance sensor for biomedical applications). P201301062 (04/11/2013).

International PCT patent applications, corresponding to first patent applications (Spanish or European) that completed their year of priority:

- *Rgd biomimetic peptide with affinity domain for type-i collagen and the uses thereof as osteogenic factor.* PCT/ES2013/000007, filing date: 01/04/2013.
- *Amphiphilic copolymers carrying alpha-tocopherol.* PCT/ES2013/070287, filing date: 05/07/2013.
- *Cell culture device and method associated with said device.* PCT/ES2013/000141, filing date: 06/12/2013.

- *Functionalized liposomes useful for the delivery of bioactive compounds.* PCT/EP2013/063646, filing date: 06/28/2013.
- *Release of substances into senescent cells.* PCT/ES2013/070581, filing date: 08/06/2013.
- *Antibodies for the detection and quantification of anticoagulant agents.* PCT/ES2013/070816, filing date: 11/26/2013.
- *Cell culture chamber on biomaterials.* PCT/ES2013/070819, filing date: 11/26/2013.
- *Modified polyarlyetherketone polymer (PAEK) and method for obtaining it.* PCT/ES2013/070928, filing date: 12/26/2013,
- *1,4,5-trisubstituted 1,2,3-triazole mimetic of RGD and/or OGP10-14, process to obtain it and uses thereof.* PCT/ES2013/070927, filing date: 12/26/2013.

International Applications in National / Regional Phases:

- *Methods and reagents for efficient and targeted delivery of therapeutic molecules to CXCR4 cells.*
- *Applications filed in 7 countries/regions: Europe (EP12704711.6; 13/08/2013), USA (13/979560; 12/07/2013), Japan (2013-548853; 12/07/2013,), China (201280011605.X; 12/07/2013), Australia (2012206533; 9/07/2013), Israel (227442; 11/07/2013) and India (2225/KOLNP/2013; 10/07/2013)*

Other Transfer and Translation Activities

CIBER-BBN-Industry Forums and Clinical Forums

Two CIBER-BBN-Industry Forums have been organized to promote collaboration between research groups and industry. The forums facilitate identification of affinities and common interests by means of describing the working subjects and technologies that the participants use in the morning of the forum conference, as well as during bilateral conversations taking place in the afternoon.

Two CIBER-Industry Forums were held in 2013:

- "Bone Therapies" (Madrid, 05/30/2013), organized in collaboration with FENIN. 21 companies 14 CIBER-BBN groups, 4 external research groups and institutions such as CDTI, OEPM and MSSSI participated. 108 bilateral interviews were held.
- "Biomedical Monitoring Systems" (Madrid, 10/3/2013), organized with the collaboration of FENIN. 36 companies (2 international), 15 groups CIBER-BBN, 12 external research centres (including the Fraunhofer Institute) and institutions such as MSSSI participated in this international forum. 140 bilateral interviews were held.

Furthermore, research services offered by our equipment platforms were presented in these forums.

Like the preceding year, meetings or forums aimed at bringing CIBER-BBN investigators to the clinical environment have been organized in 2013 as well. These forums were:

- "CIBER BBN – OFTARED Clinical Forum in Ophthalmology" (Instituto de Salud Carlos III, Madrid, 06/27/2013), organized together with OFTARED (Thematic Network of Collaborative Research in Ophthalmology). Around 65 people including clinics, companies, investigators and scientific managers participated.
- "CIBER BBN – RIC Clinical Forum in Cardiology" (Vall d'Hebron Hospital, Barcelona, 12/16/2013) in collaboration with RIC (Thematic Network of Cardiovascular Research). Around 115 people including clinics, investigators and scientific managers attended.

Outlook on technology and Technology Surveillance

A non-disclosure agreements was signed in February with the company B-ABLE to study the viability of creating a spin-off based on the patent co-owned by CIBER-BBN "Release of substances into senescent cells (P201231370)", for which confidential information was provided B-ABLE, who informed that it was interested in the technology up to the creation of a spin off.

Two non-disclosure agreements were signed with companies (for the sake of simplicity, the majority co-owner signs on behalf of CIBER):

- NDA signed with Aseptika (UK) for its interest in the patent Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa, (Haptens and conjugates derived from pyocyanin, antibodies thereof and immunochemical method for detecting infections caused by pseudomonas aeruginosa) P201330312.
- NDA signed with Ophtimalia (France) for its interest in the intramural project, Glauco.

Non-confidential information was sent to 34 companies.

A process was conducted in 2013 to give priority and value to 20 CIBER-BBN technologies (patents and intramural projects) considering their transfer potential. This process consisted of three phases: first, analysing the 20 technologies and selecting five with the highest potential for a more in-depth evaluation, then selecting the technology (the patent "Functionalized liposomes useful for bioactive compound delivery" with the highest transfer potential. A development plan has been prepared for this patent to make sure it meets significant high-value milestones allowing it to be licensed to an industrial partner.

Aspects such as the non-covered need for the product/technology, market potential, current and future competition, technological novelty, intellectual property, regulatory environment, project viability and capacity to carry it out.

Technological Offer and Conferences

Informative material in the form of brochures, posters, flyers for patents and projects, etc., containing the latest information concerning our technological offer and all the units of services grouped as a single infrastructure has been designed.

CIBER BBN has participated in the following forums and took the opportunity to disseminate its technological offer and to foster relationships that can result in future collaborations:

- Eurobioimaging Stakeholder Meeting, Vienna, January 21-23, 2013.
- 2nd Informative Conference for the Promotion and Funding of Programmes for Innovation in Biomedicine in the European Union up to the year 2020. Instituto de Salud Carlos III, Madrid, February 6, 2013.
- BioEurope Spring, Barcelona, March 11-13, 2013.
- 6th Annual Conference of the Technological Platforms of Biomedical Research: Innovative Medicinal Products, Nanomedicine, Health technology and Biotechnological Markets, Madrid, March 21-23, 2013.
- Kick off meeting of IN2 Life Sciences, Amsterdam, April 12, 2013.
- The European CLINAM & ETPN Summit, Basel, Switzerland, June 23-26, 2013.
- Medical Imaging Conference, Hannover, Germany, September 2013.
- General Assembly and Annual Event of the European Technological Platform of Nanomedicine (ETPN), Grenoble, France, October 1-2, 2013.
- 5th Euro Bioimaging Stakeholder Meeting, Heidelberg, Germany, November 25-26, 2013.
- TERCEL – CIBER BBN Technical Meeting, Madrid, December 13, 2013.

This updated offer is available in technology supply and demand websites such as Innoget, EEN (European Entreprise Network), SEINNOVA and CIBER-BBN's website. The technological offer is periodically updated.

Contacts with companies and potential shareholders

The company PRAXIS, has shown interest in the liposome patent entitled "Functionalized liposomes useful for bioactive compound delivery". P201231020 (06/19/2012)" and this results in the presentation of a project to the CIBER-BBN transfer programme (call for proposal of the year 2013) in which commitment to invest in the project totalling 200,000 euros will be obtained for years 2014 and 2015 in the event of a grant (pending resolution).

In the year 2012, a **technology transfer contract** was signed for transferring technology developed in the BIOSCAFF-EYE intramural project to the company FERRER International. Said project was under development with positive results throughout 2013. Three CIBER-BBN research groups participate in the project which objective is to develop a new drug based on advanced therapies for ocular surface reconstruction. By means of this contract, the company makes a long-term investment to find the pre-clinical and clinical studies of potential drugs arising from the research.

A **licensing contract was signed** with the company EBERS MEDICAL TECHNOLOGY S.L, for the patent entitled "Device and method for encapsulating microfluidic systems" (application P201231532).

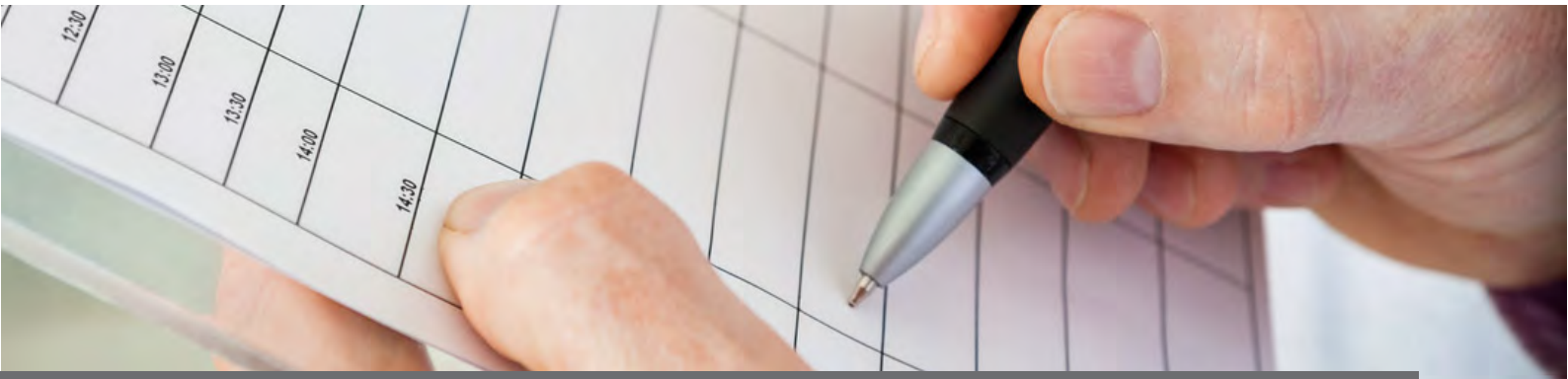
CIBER-BBN is currently in different degree of contact with many enterprises and entities which are fairly interested either in directly transferring its technologies or carrying out collaborative projects that will lead to results that can be transferred to the industry.

More than 500 copies of Service Platforms dossier have been distributed. Information concerning CIBER-BBN offer has also been disseminated through newsletters and websites of industrial associations such as ASEBIO and FENIN.

Collaborative projects with clinical entities

A joint initiative between CIBER-BBN and the ECO Foundation (Foundation for Excellence and Quality in Oncology) was launched to provide assistance in carrying out collaborative projects between the CIBER-BBN research groups and the clinical members of ECO. Eight proposals for collaboration were received and six translational research projects in oncology were funded. The projects presented were assessed by independent specialists with proven scientific background.

Likewise, a similar initiative with the Biomedical Research Foundation of Cordoba/ Maimonides Institute of Biomedical Research of Cordoba (FIBICO-IMIBIC) is currently under preparation to create new translational projects in different areas of interest for the Reina Sofía Hospital of Cordoba. These projects are expected to start in year 2014.



Training

The CIBER-BBN training program seeks to increase the research capabilities of the staff recruited into the groups by means of improving the professional competence of the research and technical staff as a factor of change, transforming attitudes, knowledge and skills depending on the needs that arise while performing their research activity.

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

Grant for research initiation training

The purpose of these "Starter" grant is to cover the transitional period from the end of studies until the resolution of the call for proposals for public pre-doctoral grants or other professional itineraries which allow recruiting a recent graduate into the work force.

In this seventh year of life of the grant for research initiation training, two calls for proposals were made in January and September. The number of grants increased with respect to the previous year.

The number of applications is high in each of the calls for proposals due to the interest these grants raise in the research groups. Fifteen grants were awarded to the candidates with the best academic transcripts and to those proposals which were best suited to the priority lines of research for CIBER-BBN.

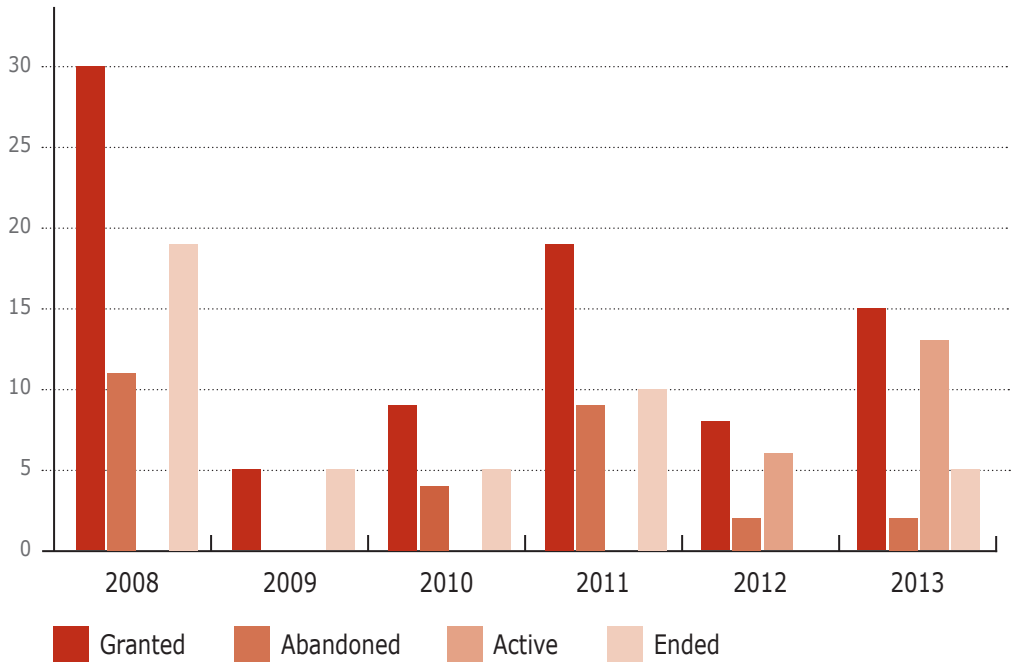
	GRANTED	ABANDONED	ACTIVE	ENDED
2008	30	11	0	19
2009	5	0	0	5
2010	9	4	0	5
2011	19	9	0	10
2012	8	2	6	0
2013	15	2	13	5

Grants for training for 2008-2013

Most of the grants are still active and the percentage of grants being declined is still relatively low.

In addition, the trend observed over recent years, except in year 2009, persists. One third in 2008 up to about half in 2010 and 2011 of the staff awarded with grants abandon said grants before the contract ends. In most cases, this is due to the staff being offered pre-doctoral grants or a contract as research staff.

Starter Grants for 2008-2013



Grants for mobility

The purpose of this training program is to motivate short stays with other research groups for training purposes among CIBER-BBN staff.

In 2013, there were two calls for proposals (January and September) and a total of twenty grants for mobility were offered for staff of CIBER-BBN groups in external groups from Spain, USA, Germany, the United Kingdom, Canada, France and Switzerland.

Disclosure and support continued for the grant for mobility for research staff between CIBER-BBN groups, proposals for which are called permanently throughout the year, and there have only been one such stay under this type of intra-CIBER action. The group of José Becerra benefited from this grant with stays in the group of Elisabeth Engel.

Other training actions

In the first half of 2013, CIBER-BBN designed a course in Nanomedicine in collaboration with the UNED and the Escuela Nacional de Sanidad but said course was finally abandones.

In 2013, continuous training management for CIBER-BBN staff through the Tripartita Foundation for the employment training continued.

This training represents a lower financial cost for CIBER-BBN since the costs of the training actions are deducted through social security bonuses. The CIBER-BBN, like any other company, has a training credit so that its employees can access the training offered under this modality.

Some examples of the courses held in 2013 for CIBER-BBN staff are:

TRAINING ACTIVITIES	TRAINER
Projects Management and PMI Certifications	Univ. Miguel Hernández of Elche
Animal and Human Cell Culture	Vértice Training
Audits of Public Companies, Entities and Agencies	Fundación FIASEP
Competency-based Management	AIBE Training

Courses held for staff 2013

In addition to the actions included in the training plan, the different groups of the consortium carry out extensive training activity for the research staff, with an average of 50 thesis year and more than 100 people in pre-doctoral training.

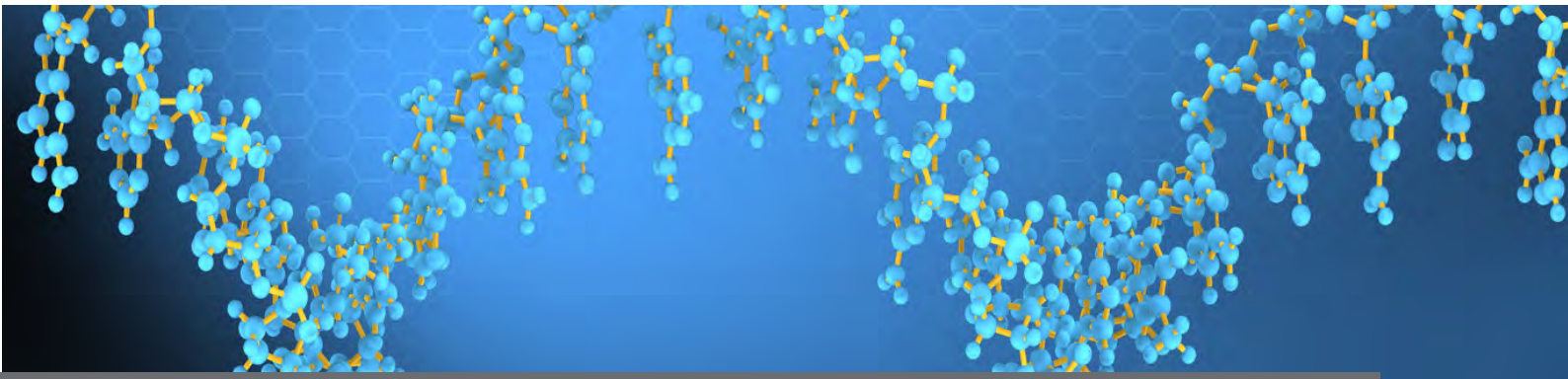
Qualification

Qualification Sub-programme

The Qualification Sub-programme implantation and management within the training programme of CIBER-BBN continued in 2013 in order to enhance the research methodologies in line with several groups in the priority lines for the CIBER-BBN established in the Master Plan 2010-2013.

It is carried out 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 developed by the groups for fomenting the possibilities of collaboration and increasing the competitiveness of the consortium. There is one researcher per group who belongs to this line of work.

The process comprises the identification of senior researcher profiles, which are already well-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 work areas of CIBER-BBN, and set the basis to form long- and mid-term competitive groups.



Dissemination

7th Annual CIBER-BBN Conferences:

The 7th Annual CIBER-BBN Conference was held on November 21 and 22, 2013 in Malaga.

The main objective of the conference was once again to favor 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.

Over 160 people attended the conference, essentially members of the CIBER-BBN groups, but also from other research institutions and centres.

The day before the conference, a prior meeting with the PIs of the consortium was held at the same location. They discussed some of the ongoing actions of the CIBER-BBN, evaluation results, evaluation parameters for future years, budget aspects, strategic plan content, etc.

Like on previous occasions, the inaugural session of the Conference included the presence of ISCIII representatives (Lisardo Boscá, as the General Subdirectorate for the Evaluation and Promotion of Research). Mr. José Ángel Narváez Bueno, Vice-Chancellor of University Coordination of the Universidad de Málaga, was also present in the inaugural act. Both accompanied Pablo Laguna, CIBER-BBN Scientific Director, in inaugurating the event.

Each of the two days of the conference, there was a plenary session conducted by important investigators from their fields. These two plenary sessions were:

- *Polymer conjugates as nanosized medicines.* Mª Jesús Vicent, Príncipe Felipe Research Centre.
- *A Description of the Human Brain Project.* Vicente Martín, Polytechnical University of Madrid.

The CIBER-BBN intramural projects were described in parallel sessions (Bioengineering, Biomaterials and Nanomedicine) moderated by the coordinators of the different programmes.

CIBER-BBN Newsletter

Five issues of the CIBER-BBN NEWSLETTER were published in 2013, and they were sent to consortium investigators. The purpose of this dissemination tool is to improve internal knowledge of the Centre (groups, services, etc.) as well as to inform enterprises and external institutions about the Centre's activity.

Web page

The web page has been constantly updated to reflect consortium activity and news on a timely basis. http://www.ciber-bbn.es

Other disseminating activities

Ten press releases were disseminated in 2013 from CIBER-BBN both in collaboration with other institutions and independently. Although the data is not complete as there is no company for following the press, around 200 appearances in the press have been registered, most of them in specialized media such as Noticias Médicas, Médico Interactivo, Madri+d, etc.

Events and other activities

a) Presence of CIBER-BBN in international scientific technological forums:

In 2013, CIBER-BBN attended a considerable number of internationally relevant scientific forums and meetings. Some of the more representative ones are shown below:

- Eurobioimaging Stakeholder Meeting, Vienna, January 21-23, 2013.
- BioEurope Spring, Barcelona, March 11-13, 2013.
- Kick off meeting of IN2 Life Sciences, Amsterdam, April 12, 2013.
- The European CLINAM & ETPN Summit, Basel, Switzerland, June 23-26, 2013.
- Medical Imaging Conference, Hannover, Germany, September 2013.
- General Assembly and Annual Event of the European Technological Platform of Nanomedicine (ETPN), Grenoble, France, October 1-2, 2013.
- 5th Euro Bioimaging Stakeholder Meeting, Heidelberg, Germany, November 25-26, 2013.

b) Other activities:

The Communication Department coordinated other disclosure and dissemination activities, such as the participation of all CIBER consortiums in Science Week for the fourth year in a row in Madrid and for the third time in the Science Week of Catalonia.

Representatives of all the CIBERs participated in Madrid in the activity *MICROPOLIX Scientific: 9 mini CIBER workshops*, intended for students in the last few years of their undergraduate studies and designed for the purpose of brining science closer to younger people and calling scientific vocations. Each CIBER held an interactive mini-workshop giving examples and explaining the research conducted in their centre. Specifically, CIBER-BBN focused its description on regenerative medicine and the design and generation of artificial tissues.

In turn, a round table was organized in CEK in Barcelona in which investigators from all CIBERs explained how to transfer their biomedical knowledge from the laboratory to clinical practice. CIBER-BBN's intervention was entitled "Systems for helping clinical decisions in the diagnosis of human brain tumors".

4
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-β-Gal). Therefore, it is useful for senescence studies, prevention and treatment of senescent-associated diseases. Besides others where β-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

International Patent Application PCT/EP2013/063646

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 phar-

maceutical 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 histo-chemical 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 mechani-

cal 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.

- **SYSTEM FOR CONTROLLED DELIVERY OF PROTEINS AND THERAPEUTIC USE**

  Spanish Patent Application P201031933

  International Patent Application PCT/IB2011/055928

The invention refers to a system for transportation and controlled delivery of proteins.

The first aspect of this invention refers to a complex to be used as carrier and controlled delivery systems. Particularly for proteins and targeted to endothelial cell lysosomes. A second aspect of the invention is the manufacturing process of these complexes in a simple way avoiding the use of both, organic solvent and extreme conditions, which could damage the protein structure. The third aspect is the use of these complexes to prepare drug in order to treat diseases, particularly, those due to enzyme disorders.

This system protects the protein structure against denaturalization in the blood flow and increases the protein efficacy through a controlled delivery in the specific cellular compartment.

- **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 P201330312

  International Patent Application PCT/ES2014/070161

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

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

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.

5 Research groups

PROGRAMME:
Bioengineering and Medical Imaging

Biomonitoring Group

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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, multimicro 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
- 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

- Altuna, A ; Bellistri, E ; Cid, E ; Aivar, P ; Gal, B (Gal, Beatriz)[2,3] ; Berganzo, J ; Gabriel, G ; Guimera, A ; Villa, R; Fernández, LJ; de la Prida, LM. SU-8 based microprobes for simultaneous neural depth recording and drug delivery in the brainLAB CHIP. 2013;13(7):1422-1430.
- Prats-Alfonso E, Abad L, Casañ-Pastor N, Gonzalo-Ruiz J, Baldrich E. Iridium oxide pH sensor for biomedical applications. Case urea-urease in real urine samples.Biosens Bioelectron. 2013 Jan 15;39(1):163-9.
- Altuna A, Bellistri E, Cid E, Aivar P, Gal B, Berganzo J, Gabriel G, Guimerà A, Villa R, Fernández LJ, Menendez de la Prida L. SU-8 based microprobes for simultaneous neural depth recording and drug delivery in the brain.Lab on a chip. 2013;13(7): 1422-1430.
- Viñas JL, Ventayol M, Brüne B, Jung M, Sola A, Pi F et al.. miRNA let-7e modulates the Wnt pathway and early nephrogenic markers in mouse embryonic stem cell differentiation.PLoS One. 2013;8(4):e60937.
- Guimerà A, Illa X, Traver E, Plata-Cordero M, Yeste J, Herrero C et al.. Flexible probe for in vivo quantification of corneal epithelium permeability through non-invasive tetrapolar impedance measurements.Biomed Microdevices. 2013 Oct;15(5):849-58.

Highlights

AT MOLECULAR LEVEL:

- Advances in simulation, design and manufacture of microelectrodes to measure cardiac and ophthalmologic biomarkers.
- Processes for the use of Graphene as a neural interface are optimized. (project requested at H2020 FET-Flagships).

AT TISSUE LEVEL:

- Two clinical trials to validate a Microsystem allowing quantifying corneal permeability in a non-invasive way have been launched.

AT ORGAN LEVEL:

- The group reported that miRNA let-7-e causes the differentiation of embryonic stem cells to renal lineage through modulation of GSK 3 Beta and production of beta catenin. (The work has been awarded with the "Ten best abstracts" award in the "50 th International Congress of the European Renal Association, Dialysis and Transplantation").
- The team with the Hospital Vall d'Hebron has patented a method that predicts the evolution of lupus nephritis, based on the quantification of gene expression level in urine neurofilina1 gene.
- A Microsystem with Microfluidics has been developed to simulate structures hepatic (liver on chip) as well as for monitoring in vitro blood-brain barrier (BBB on chip).

SYSTEM-LEVEL:

- Seven pilot observational multicentric studies in collaboration with two other universities and four hospitals have been launched to measure the stress level and to develop ad-hoc electronic instrumentation.
- As a result of a project in collaboration with CIBERES, a device for oxygen therapy is under development with the company BVentura SL.
- A "zero power" device for monitoring the abdominal pressure is under development whilst a "ultra-low-power" technology is used for other parameters. The group is also working in "energy harvesting" devices to validate their inclusion in biomedical systems.

The Group has launched four new patents, defended a PhD thesis and initiated seven other PhD lines.

PROGRAMME:
Nanomedicine

Nanoparticle and Peptide Chemical Group

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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 nanomedicines for the advanced colorectal cancer treatment. Study of the ouse 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 cartilague 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 cytoplasm 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

- Xavier Just-Baringo, Paolo Bruno, Lars K. Ottesen, Librada M. Cañedo, Fernando Albericio, Mercedes Alvarez. Total Synthesis and Stereochemical Assignment of BaringolinAngew. Chem. Int Ed. . 2013;52(30):7818 –7821.
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- Pelay-Gimeno Marta; García-Ramos Yesica; Jesús Martín María; Spengler Jan; Molina-Guijarro José Manuel; Munt Simon; Francesch Andrés M; Cuevas Carmen; Tulla-Puche Judit; Albericio Fernando. The first total synthesis of the cyclodepsipeptide pipecolidepsin ANature Communications. 2013;4(2352):2352.
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- Ana I. Fernández-Llamazares, Jesús García, Vanessa Soto-Cerrato, Ricardo Pérez-Tomás, Jan Spengler, Fernando Albericio. N-Triethylene glycol (N-TEG) as a surrogate for the N-methyl group: application to Sansalvamide A peptide analogsChemComm. 2013;49(57):6430-6432.

Highlights

- In 2013, the Peptide and Nanoparticles Chemical Group has published a total of 41 publications in international journals, some of them are high impact factor publications (Nature Communications, Angewandte Chemie, Chemical Reviews, ACS Nano, Nanomedicine, among others). Some of these publications described the synthesis of diverse marine-derived drugs with potent antitumoral properties. These scientific advances were also reported in diverse media (La Vanguardia, TV3, La Voz de Galicia , Ara). In addition the Teaching Commission of the Higher Council of the University of Buenos Aires (UBA), in Argentina, has granted the title of doctor "honoris causa" to Fernando Albericio, IP of the group, in recognition of his research and teaching activities over the course of his broad professional career.
- During this year, financial resources have been provided by various national and international agencies, that include four national grants, one EC project, a regional valorization project and a private foundation project. The group has four collaborative projects with pharmaceutical and biotech companies founded by competitive grants (POLYSFERA, NANOCARDIOCOCO, HUMANFARMA and MARINMAB, INNPACTO-MINECO). The group also applied and granted other national collaborative project (INNPACTO-MINECO, MarinMab) that was initiated in 2013. A project from the group focused on the development of personalized nanomedicine for breast cancer, has been awarded financial support from the funds raised by the La Marató de TV3 2012 call, which was dedicated to cancer research. The project will be developed in collaboration with other two CIBER BBN groups, the Nanobiotechnology research group of the Institute of Biotechnology and Biomedicine of the Autonomous University of Barcelona (UAB) and the CIBBIM - Nanomedicine from the Vall d' Hebron Research Institute (VHIR).
- Collaborations have been established and continued at the national (IBEC, IRB, CNIC, Hospital Vall d'Hebró, CIB-CSIC, Universitat Autònoma de Barcelona, Universitat de Barcelona, Universidad de Santiago de Compostela) and international levels (Chile, Argentina, Brasill, Potugal, Netherlands, Belgium, South Africa and Denmark) as well as several collaborative projects being carried out with companies form the pharmaceutical and biotechnology sectors.

PROGRAMME:
Bioengineering and Medical Imaging

Research Group in Biomedical Applications of Nuclear Magnetic Resonance (GABRMN-UAB)

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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

- Ortega-Martorell S, Ruiz H, Vellido A, Olier I, Romero E, Julià-Sapé M et al.. A Novel Semi-Supervised Methodology for Extracting Tumor Type-Specific MRS Sources in Human Brain Data.PLoS One. 2013;8(12):e83773.
- Delgado-Goñi T, Campo S, Martín-Sitjar J, Cabañas ME, San Segundo B, Arús C. Assessment of a 1H high-resolution magic angle spinning NMR spectroscopy procedure for free sugars quantification in intact plant tissue.Planta. 2013 Aug;238(2):397-413.
- Ortuño JE, Ledesma-Carbayo MJ, Simões RV, Candiota AP, Arús C, Santos A. DCE@urLAB: a dynamic contrast-enhanced MRI pharmacokinetic analysis tool for preclinical data. BMC Bioinformatics. 2013 Nov 4;14:316.
- Albert Vilamala, Paulo J.G. Lisboa, Sandra Ortega-Martorell, Alfredo Vellido. Discriminant Convex Non-negative Matrix Factorization for the classification of human brain tumoursPattern Recognition Letters. 2013;34(14):1734-1747.

Highlights

The members of the GABRMN/CIBER-BBN group have participated in the publication of 6 journal papers, one in coordination with the group of Prof. Andrés Santos which was a higly accessed paper in BMC Bioinformatics. Another publication is in coordination with CIBEREHD, and two more with clinical personnel whereas two others are the result of international collaborations. The mean impact factor has been 3.16 , 83% belong to quartile 1 and 66% to decile 2.

With respect to projects, it is worth highlighting the launch of the Marie Curie Initial Training Network TRANSACT, in which Prof. Carles Arús participates as a partner, and in which the CIBER-BBN has special visibility as Associated partner to the network. In terms of funding, the project will bring 234,381.62 Euros in four years mainly to fund one Early Stage Researcher, hired in July 2013, Mr. Victor Mocioiu. Participation in this project has also impacted the internationalisation of the CIBER-BBN group, with participation in several project-related international workshops.

Dr. Carles Aguilera and Dr. Albert Oriol have participated in a total of 18 clinical trials during 2013.

Four PhD theses have been awarded within the group. Dr. Sandra Ortega pursues her postdoctoral training at the Liverpool John Moores University, at Prof. Paulo Lisboa's group. Prof. Carles Arús belongs to the editorial committee of the Magnetic Resonance Materials in Physics, Biology and Medicine journal and Dr. Alfredo Vellido was organiser of the 21st European Symposium On Artificial Neural Networks, Computational Intelligence and Machine Learning Bruges (Belgium). The ESMRMB society awarded Prof. Carles Arús the Certificate of MR Excellence in Basic Science.

The Servei de Ressonància Magnètica of the Universitat Autònoma de Barcelona is part of the joint UAB-CIBER-BBN platform. The services provided by the platform include the maintenance of the INTERPRET and eTUMOUR multicentre databases, which have allowed technology transfer with contacts Siemens and Samsung.

PROGRAMME:
Biomaterials and Tissue Engineering

Tissue Bioengineering and Regeneration Laboratory

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Main lines of research

- Tissue engineering for bone and cartilage regeneration
- Mesenchymal stem cell differentiation towards chondro-osteogenic lineages by means of 2D and 3D cultures.
- Chemical synthesis and materials processing, materials characterization and acellular essays in vitro to study the structure-properties-function relationships of the materials in biological systems
- Development and biological 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

- Leal-Egaña A; Díaz-Cuenca A; Boccaccini AR. Tuning of cell-biomaterial anchorage for tissue regenerationADV MATER. 2013;25(29):4049–4057.
- Bagó JR, Aguilar E, Alieva M, Soler-Botija C, Vila OF, Claros S et al.. In vivo bioluminescence imaging of cell differentiation in biomaterials: a platform for scaffold development.Tissue Eng Part A. 2013 Mar;19(5-6):593-603.
- Terriza A, Díaz-Cuenca A, Yubero F, Barranco A, González-Elipe AR, Caballero JLG, Vilches J, Salido M. Light induced hydrophilicity and osteoblast adhesion promotion on amorphous TiO2J BIOMED MATER RES A. 2013;101A:1026 - 1035.
- Arrabal PM, Visser R, Santos-Ruíz L, Becerra J, Cifuentes M. Osteogenic molecules for clinical applications: improving the BMP-collagen systemBiological Research. 2013;46(4):421-9.
- Ramiro-Gutiérrez ML, Will J, Boccaccini AR; Díaz-Cuenca A. Reticulated bioactive scaffolds with improved textural properties for bone tissue engineering: Nanostructured surfaces and porosityJ BIOMED MATER RES A. 2013;0(0):1-11.

Highlights

During 2013, the group has published a total of 13 papers, 8 in Q1, 2 of them in D1. Papers belong to basic and preclinical research, but 3 are clinical orthopaedic papers. Three of them are international collaborations and one is a intraciber collaboration. Several members of the group have been authors of several articles in international books. On the other hand, the group is involved in two clinical trials promoted by an international private company. Also, we have register one international patent concerning a small molecule design to bind cells to the scaffolds of collagen type I, improving skeletal tissue engineering. The patent is currently under negotiation with companies.

Regarding to the research projects, we got several new competitive projects from public national and regional agencies. We maintain partnerships within the intramural projects NACRE, particularly intense with the groups led by J Blanco, JA Planell, JL Peris and M Monleón. In the context of the intramural projects our group is leading, TELTIS. We have got funding from the Plan Nacional in the call of 2012. In this project collaborates as associated three Ciber groups (Tecnalia, IBV, and J. Blanco) and the Instituto Tecnológico de Canarias.

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

Finally, several members within our group are promoters and teacher of Masters, have collaborated in the organization in Malaga of the Annual Meeting of the Ciber-bbn, are speakers at international forums, members of international scientific associations, etc. The IP has been interviewed in several media (radio, journals and TV) related with the projects of the group.

PROGRAMME:
Biomaterials and Tissue Engineering

Translational Research Group in Biomaterials and Tissue Engineering

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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 cryopre-

served 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, Sotomayor S, Rodríguez M, Bayon Y, Bellón JM. Behaviour of a new composite mesh for the repair of full-thickness abdominal wall defects in a rabbit model.PLoS One. 2013;8(11):e80647.
- M. Fernández-Gutierrez, E. Olivares, G. Pascual, J.M. Bellón, J. San Román. Low-density polypropylene meshes coated with resorbable and biocompatible hydrophilic polymers as controlled release agents of antibioticsACTA BIOMATER. 2013;9(4):6006-6018.
- García-Pumarino R, Pascual G, Rodríguez M, Pérez-Köhler B, Bellón JM. Do collagen meshes offer any benefits over precludeVR ePTFE implants in contaminated surgical fields? A comparative in vitro and in vivo studyJ Biomed Mat Res B. 2013;:1-10.
- Hernández-Gascón B, Peña E, Grasa J, Pascual G, Bellón JM, Calvo B. Mechanical response of the herniated human abdomen to the placement of different prostheses.J Biomech Eng. 2013 May;135(5):51004.
- Slove S, Lannoy M, Behmoaras J, Pezet M, Sloboda N, Lacolley P et al.. Potassium channel openers increase aortic elastic fiber formation and reverse the genetically determined elastin deficit in the BN rat.Hypertension. 2013 Oct;62(4):794-801.

Highlights

The second 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 intramural project ABDOMESH, has been carried out successfully during 2013. One contract of transfer, related to prosthetic infection, has been signed with the company Covidien and another one was signed with LifeCell to study the behavior of different collagen biological prostheses. Scientific production of this research line has been very consistent during 2013, with a total of ten publications (two of which included in the 1st quartile of the JCR and 4 in the 2nd) including two book chapters. Also, concerning this line of research several communications have been presented at the 15th American Hernia Repair Congress held in Orlando (USA) and TERMIS-EU Conference held in Istanbul (Turkey).

Related to our line of research in repair of skin defects, one paper has been published in Histology and Histopathology about improving healing in ischemic wounds by an angiogenesis promoter in combination with autologous stem/progenitor cells. During this year one important contract of transfer, with the company Novartis, has been signed in the area of pharmacological healing.

With respect to the vascular repair line of research, during 2013, the most important paper has been published in Hypertension journal (1st decile of JCR) in collaboration with Inserm, U698, Hôpital Bichat (Paris). A National Research Project, about venous insufficiency, funded by the Instituto de Salud Carlos III, has been awarded in 2013. Several communications have been presented at the XXIX LIAC Meeting on Vascular Research, held in Alghero (Italy), Elastin, Elastic Fibers & Microfibrils. Gordon Research Conference, Biddeford, (USA) and at the V International Congress of Histology and Tissue Engineering/ XVII SEHIT Congress of Logroño (Spain).

PROGRAMME:
Biomaterials and Tissue Engineering

Cell Therapy Research Group

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Main lines of research

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

- Bagó JR, Alieva M, Soler C, Rubio N, Blanco J. Endothelial differentiation of adipose tissue-derived mesenchymal stromal cells in glioma tumors: implications for cell-based therapy. Mol Ther. 2013 Sep;21(9):1758-66.
- Bagó JR, Aguilar E, Alieva M, Soler-Botija C, Vila OF, Claros S et al.. In vivo bioluminescence imaging of cell differentiation in biomaterials: a platform for scaffold development. Tissue Eng Part A. 2013 Mar;19(5-6):593-603.
- Bagó JR, Soler-Botija C, Casaní L, Aguilar E, Alieva M, Rubio N et al.. Bioluminescence imaging of cardiomyogenic and vascular differentiation of cardiac and subcutaneous adipose tissue-derived progenitor cells in fibrin patches in a myocardium infarct model.Int J Cardiol. 2013 Nov 15;169(4):288-95.
- Stresing V, Baltziskueta E, Rubio N, Blanco J, Arriba MC, Valls J et al.. Peroxiredoxin 2 specifically regulates the oxidative and metabolic stress response of human metastatic breast cancer cells in lungs.Oncogene. 2013 Feb 7;32(6):724-35.
- Camacho L, Meca-Cortés O, Abad JL, García S, Rubio N, Díaz A et al.. Acid ceramidase as a therapeutic target in metastatic prostate cancer.J Lipid Res. 2013 May;54(5):1207-20.

Highlights

The Cell Therapy group has focused its research activity during recent years in two interrelated aspects of cell therapy: Regenerative Medicine and Tumor Therapy, as well as in the understanding of the interactions between tumor and therapeutic stem cells.

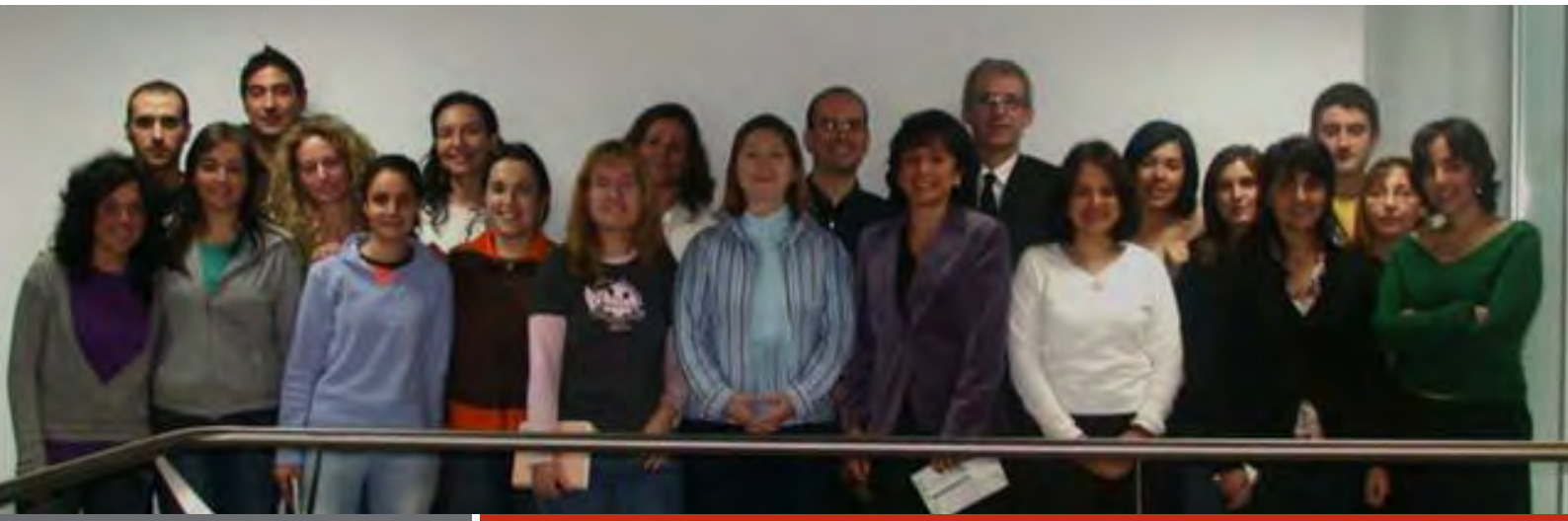
Research highlights during year 2013 have been: The validation and subsequent application of the Biomaterial Analysis Platform, resulting in publications in Tissue Engineering, International Journal of Cardiology and J. Biomed. Mater. Res. (regenerative medicine field); and the demonstration that differentiation of therapy-delivering mesenchymal stem cells to the endothelial lineage and their association with the tumor stem cell niche are required for effective tumor cell killing (tumor therapy). The group has also participated in several collaborative projects requiring bioluminescence imaging to noninvasively evaluate tumor growth, with results published in Oncogene and Journal of Lipid Research, among other journals.

In 2013, Olaia Fernandez successfully defended her Doctoral Thesis.

During year 2013 the team was supported by grants from 3 different national projects (MINECO), an "autonomic project" and a "research internationalization project", the latter directed towards the development of photo-dynamic nanoparticles for tumor therapy. In addition, the group signed several contracts for use of bioluminescence imaging technology.

In the same year, the team initiated its activities as member of TerCel, the Thematic Network for Cooperative Research in Cell Therapy (ISCiii), focusing its effort on the analysis of safety and bio-distribution of the cell types studied by the consortium.

The group has generated publications in collaboration with othe research teams: "Biomateriales para Terapia Regenerativa" (IBEC); "Laboratorio de Bioingeniería y Regeneracion Tisular" (UMA-Bionand); "Laboratorio de Patogénesis de la Metástasis" (IDIBELL), "Insuficiencia Cardíaca y y Regeneracion Cardíaca" (Hospital Germans Trias i Pujol) and "Unidad de Investigacion en Moléculas Bioactivas" (IQAC-CSIC). In addition, the group has worked in collaboration with the "Photosciences and Phtotonics" group of the National Institute for Interdisciplinary Science (India), supported by a Research Internationalization grant (MINECO), and with "Laboratorio de Fisiopatolgia Ortopédica e Medicina Regenerativa" (Insituto Ortopédico Rizzoli, Bolonia, Italy.



PROGRAMME:
Biomaterials and Tissue Engineering

Institute of Applied Ophthalmobiology (IOBA)

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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, Gene therapy.
- Inflammation. Target diseases: Dry Eye Syndrome, Allergy, Other immune-based diseases. Field of research: In vitro models development, 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 healthy individuals.
- 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 lens.

Most relevant scientific articles

- López-Paniagua M, Nieto-Miguel T, de la Mata A, Galindo S, Herreras JM, Corrales RM et al.. Consecutive expansion of limbal epithelial stem cells from a single limbal biopsy. Curr Eye Res. 2013 May;38(5):537-49.
- Nieto-Miguel T, Galindo S, Reinoso R, Corell A, Martino M, Pérez-Simón JA et al.. In vitro simulation of corneal epithelium microenvironment induces a corneal epithelial-like cell phenotype from human adipose tissue mesenchymal stem cells.Curr Eye Res. 2013 Sep;38(9):933-44.
- de la Mata A, Nieto-Miguel T, López-Paniagua M, Galindo S, Aguilar MR, García-Fernández L et al.. Chitosan-gelatin biopolymers as carrier substrata for limbal epithelial stem cells.J Mater Sci Mater Med. 2013 Dec;24(12):2819-29.
- Tesón M, González-García MJ, López-Miguel A, Enríquez-de-Salamanca A, Martín-Montañez V, Benito MJ et al.. Influence of a controlled environment simulating an in-flight airplane cabin on dry eye disease.Invest Ophthalmol Vis Sci. 2013 Mar 1;54(3):2093-9.
- Martín-Montañez V, López-Miguel A, Arroyo C, Mateo ME, González-Méijome JM, Calonge M et al.. Influence of environmental factors in the in vitro dehydration of hydrogel and silicone hydrogel contact lenses.J Biomed Mater Res B Appl Biomater. 2013 Oct 21;0(0):1-8.

Highlights

The IOBA-UVa group coordinated the intramural project BioScaff-EYE, designed to engineer the natural niche of corneal stem cells (SC) to treat ocular surface failure due to limbal SC deficiency (LSCD). At the very end of 2012, this intramural project was transferred to Ferrer, a leading Spanish pharmaceutical company. Since then, the three academic groups: IOBA-UVa, Valladolid (PI and coordinator, Margarita Calonge), IBEC, Barcelone (PI, Elisabeth Engel), and NanoBioCel, University of The Vasc Country in Vitoria (PI, José Luis Pedraz), have been closely working together with CIBER-BBN personnel and Ferrer Advanced Biotherapeutics to lead this project to the desired end at maximum speed. As a result, the in vitro and the in vivo experimental work have been intensified. Additionally, IOBA-UVa kept recruiting patients for the randomized double-masked clinical trial for the same pathology, LSCD syndrome, in which either limbal cells or bone marrow-derived stem cells are being tested and followed for one year after transplantation (ClinicalTrials.gov Identifier: NCT01562002). Results of this clinical trial will be available at the beginning of 2015.

PROGRAMME:
Bioengineering and Medical Imaging

Bioengineering and Telemedicine Group

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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.
- 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; Connexins in the Bone Marrow Hematopoietic Niche; Pathogenic Mechanisms in Myelin Disorders.
- 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, and the mechanical properties of cells adhesion to different substrates for the use as biomarkers and tissue engineering.
- 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.
- 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.

Most relevant scientific articles

- Photoacoustic effect measurement in aqueous suspensions of gold nanorods caused by low-frequency and low-power near-infrared pulsing laser irradiation. López de Pablo CS, Ramos Ávila JA, Fernández Cabada T, del Pozo Guerrero F, Serrano Olmedo JJ Applied optics 2013 Jul 1 Volume: 52 Issue: 19 Pages: 4698-705.
- Data mining applied to the cognitive rehabilitation of patients with acquired brain injury Alexis Marcano-Cedeño, Paloma Chausa, Alejandro García, César Cáceres, Josep M. Tormos, Enrique J. Gómez. Expert Systems with Applications. 2013, 40: 1054–1060.
- EVA: Laparoscopic instrument tracking based on endoscopic video analysis for psychomotor skills assessment. Oropesa I, Sánchez-González P, Chmarra MK, Lamata P, Fernández A, Sánchez-Margallo JA, Jansen FW, Dankelman J, Sánchez-Margallo FM and Gómez EJ. Surgical Endoscopy 2013 27(3): 1029-1039.
- How network operators can enhance Ambient Assisted Living applications through Next Generation Networks. P.A. Moreno, M.E. Hernando, A. Hernández, F. González, A. de Poorter, E.J. Gómez,. Journal of Ambient Intelligence and Smart Environments, 5(2): 237-250, 2013. ISSN: 1876-1364 IOS PRESS.
- TELMA: Technology enhanced learning environment for minimally invasive surgery. Sánchez-González P, Burgos D, Oropesa I, Romero, V Albacete A, Sánchez-Peralta LF, Noguera, J Sánchez-Margallo FM and Gómez EJ. Journal of Surgical Research. 2013 182(1):21-9.

Highlights

- Implementation and management of the global and meticentric project MAGIC-AD for the identification of objective early markers of Alzheimer's disease. The results (73.33 % PPV, 100 % NPV, 83:33 % Accuracy) at individual level are in press in very high impact journals and, due to its relevance, in multicentric replica process.
- First positive results in new rehabilitation therapies of STROKE by scaffolds and stem cells.
- Great impact contributions for new mathematical and computational models of brain networks for the characterization of pathological processes: EA, Epilepsy, Parkinson, phobias, etc.
- Development of the platform PERSONA to support personalized care in diabetes based on the integration of artificial intelligence methods and modeling and intermodal simulation techniques.
- Completion of a clinical trial on "artificial pancreas" showing that it is possible to achieve night normoglycemia during 95.8% of the length of the experiment ($p < 0.05$) without significant hypoglycemia in T1DM patients.
- Completion of the intramural project THEMIS, with 25 publications in journals and conferences, three doctoral theses and a prototype for a surgical planning and navigation system for liver resection in experimental evaluation in CCMIJU (Center for Minimally Invasive Surgery of Cáceres).
- Regarding strategic issues, the most relevant during this period has been the integration of a large number of researchers from the Centre for Biomedical Technology, CTB, directed by the PI of this CIBER-bbn group, in some of the CIBER activities. The CTB is a scientific and technological Center of the Technical University of Madrid, whose objectives, structure and activity can be found on the web site: www.ctb.upm.es.

PROGRAMME:
Biomaterials and Tissue Engineering

Group of Structural Mechanics and Materials Modeling (GEMM-I3A)

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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

- Altuna A, Bellistri E, Cid E, Aivar P, Gal B, Berganzo J, Gabriel G, Guimerà A, Villa R, Fernández LJ, Menéndez de la Prida L. SU-8 based microprobes for simultaneous neural depth recording and drug delivery in the brain.Lab on a chip. 2013;13(7): 1422-1430.
- Araña M1, Peña E, Abizanda G, Cilla M, Ochoa I, Gavira JJ, Espinosa G, Doblaré M, Pelacho B, Prosper F. Preparation and characterization of collagen-based ADSC-carrier sheets for cardiovascular applicationACTA BIOMATER. 2013;9(4):6075-6083.
- Acosta Santamaría VA, Malve M, Duizabo A, Mena Tobar A, Ferrer GG, García Aznar JM, Doblaré M, Ochoa I. Computational Methodology to Determine Fluid Related Parameters of Non Regular Three-Dimensional ScaffoldsANN BIOMED ENG. 2013;41(11):2367-2380.
- Hernández-Gascón B, Mena A, Peña E, Pascual G, Bellón JM, Calvo B. Understanding the passive mechanical behavior of the human abdominal wall.Ann Biomed Eng. 2013 Feb;41(2):433-44.
- Saez, P ; Pena, E ; Doblaré, M ; Martínez, MA. Hierarchical micro-adaptation of biological structures by mechanical stimuliINT J SOLIDS STRUCT. 2013;50(14-15):2353-2370.

Highlights

During 2013, the group maintained the research lines established in previous years but a strong effort has been carried out to focus its activity more to the private sector. Several research projects have been granted during 2013 to carry out research for life science applications. Thanks to that effort, the group obtained funding around EUR 200.000. Some of the projects are:

- Diseño, Fabricación y Caracterización de fichas microfluidicos párr Cultivo celular Que permita la Integración de gradientes Químicos -EBERS TECNOLOGÍA MÉDICA, SL.
- Autonomo prueba de estrés (CARDIOSTRESS) -LAB PANDFO.
- Caracterización mecánica de hidrogeles INSTITUTO DE BIOTECNOLOGÍA IMASD SL.
- Estudios de Viabilidad volumétricos biológica de la viruta obtenida óasea Tras el fresado de una irrigación pecado VELOCIDAD baja -AVINENT SISTEMA DE IMPLANTE, SL
- Fabricación de chips de microfluidicos MEDIANTE Técnicas de moldeo porción injection - MYPA MODELOS Y PLÁSTICOS ARAGÓN , SL.
- Desarrollo de la ONU lector Portátil Para La determination cuantitativa del Abuso de Drogas a Través del Análisis de saliva basado en el BSG de microfluídica y Sensores electroquímicos -ALPHASIP-01/01/2013-30/12/2014.
- DesarrollodelaONUSistemafluídicodediluciones-ALPHASIP-01/10/2013-30/05/2015
- Estudios de Resistencia Mecánica de mallas De poliésteres (PLGA , PCL , PHB) FABRICADOS porción elecrtospinning " - ASOCIACIÓN DE INVESTIGACIÓN DE LA INDUSTRIA TEXTIL - AITEX-01/05/2013-30/04/2015.

It is worth mentioning the participation in a European Project: Development of corneal biomechanical model. Dynamic topographical characterization based on 3D plenoptic imaging. PROJECT NO: POPCORN-606634. GRANT AGREEMENT No: FP7-SME-2013-606634.

One patent related with micro-technology devices for cell culture purposes have been obtained during 2013. As recognitions to the group, several companies are currently interested in their commercialization. Not only patents but also micro-technology based "know-how" is actually been transferred to local companies.

PROGRAMME:
Biomaterials and Tissue Engineering

Research Group in Biomaterials, Biomechanics and Tissue Engineering (GBBIT-IBEC)

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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

- Orenstein SJ, Kuo SH, Tasset I, Arias E, Koga H, Fernández-Carasa I et al.. Interplay of LRRK2 with chaperone-mediated autophagy.Nat Neurosci. 2013 Apr;16(4):394-406.
- González-García C, Cantini M, Moratal D, Altankov G, Salmerón-Sánchez M. Vitronectin alters fibronectin organization at the cell-material interface.Colloids Surf B Biointerfaces. 2013 Jul 12;111C:618-625.
- Álvarez Z, Mateos-Timoneda MA, Hyroššová P, Castaño O, Planell JA, Perales JC et al.. The effect of the composition of PLA films and lactate release on glial and neuronal maturation and the maintenance of the neuronal progenitor niche.Biomaterials. 2013 Mar;34(9):2221-33.
- Mateos-Timoneda, M.A., Punet, X., Mauchauffé, R., Giannotti, M., Rodríguez-Cabello, J.C., Sanz, F., Engel, E., Planell, J.. Enhaced Cell-material interactions through the biofunctionalization of polymeric surfacesBIOMACROMOLECULES. 2013;14:2690−2702.
- C. Canal, D. Pastorino, G. Mestres, Ph. Schuler, M.P. Ginebra.. Relevance of microstructure for the early antibiotic release of fresh and pre-set calcium phosphate cementsActa Biomaterialia. 2013;:8403–8412 .

Highlights

The group has developed basic and translational research in the framework of several national and international projects. Here we highlight the main projects:

- COST ACTION - Biomedical Applications of Atmospheric Pressure Plasma Technology (2011-2015). EU - MPNS COST Action.
- BIOMAT4BIOMED: Development of new biofunctionalized materials for application in regenerative medicine (2012-2015). EU-PEOPLE.
- INNOVABONE - Novel Biomimetic Strategy for Bone Regeneration (2011-2015). EU-FP7.
- REBORNE - Regenerating bone defects using new biomedical engineering approaches (2009 – 2014). EU-FP7.
- GRAIL – Tissue in Host Engineering Guided Regeneration of Arterial Intimal Layer (2012-2016). EU-FP7.
- FIBROGELNET - Network for Development of Soft Nanofibrous Construct for Cellular Therapy of Degenerative Skeletal Disorders (2013-2016).
- REGEN_HEART - Approximation of the bioengineering on the regeneraion/ heart reparation.
- Femoral head osteonecrosis treatment with advanced cell therapy and biomaterials in an experimental sheep animal model (Fundación La Marató de TV3, 2013-2015).

Two CIBER-BBN tissue regeneration projects coordinated by the GBBIT-IBEC group started last year with funding by the EU's ERA-NET EuroNanoMed initiative:

- nAngioFrac - materiales nanoestructurados angiogénicos para nonconsolidating fracturas óseas (2012-2014).
- STRUCTGEL - gel nanoestructurados para la terapia celular de trastornos óseos degenerativos (2012-2014).

Furthermore, the group has previously participated in seven projects of the CIBER-BNN:

- REWOUND (PI Josep A. Planell, GBBIT-IBEC).
- Bioscaff-Eye (PI Margarita Calonge, IOBA-UVA).
- Nacre (PI Francisco Blanco, CBTTC-CHUAC).
- ES-Cell Therapy (PI Jerónimo Blanco, TC-CIC).
- Scafftide 3D (PI María Vallet-Regí, COFIBIC-UCM).
- Bioproterial (PI Manuel Salmerón, CBM-UPV).
- TELTIS (PI Leonor Santos, LABRET-UMA).

PROGRAMME:
Nanomedicine

Nucleic Acid Chemistry Group

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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

- Tintoré M, Gállego I, Manning B, Eritja R, Fàbrega C. DNA origami as a DNA repair nanosensor at the single-molecule level.Angew Chem Int Ed Engl. 2013 Jul 22;52(30):7747-50.
- Terrazas M, Alagia A, Faustino I, Orozco M, Eritja R. Functionalization of the 3'-ends of DNA and RNA strands with N-ethyl-N-coupled nucleosides: a promising approach to avoid 3'-exonuclease-catalyzed hydrolysis of therapeutic oligonucleotides.Chembiochem. 2013 Mar 4;14(4):510-20.
- Ugarte-Uribe B, Grijalvo S, Busto JV, Martín C, Eritja R, Goñi FM et al.. Double-tailed lipid modification as a promising candidate for oligonucleotide delivery in mammalian cells.Biochim Biophys Acta. 2013 Oct;1830(10):4872-84.
- Gómez-Pinto I, Vengut-Climent E, Lucas R, Aviñó A, Eritja R, González C et al.. Carbohydrate-DNA interactions at G-quadruplexes: folding and stability changes by attaching sugars at the 5'-end.Chemistry. 2013 Feb 4;19(6):1920-7.
- Ferreira R, Artali R, Benoit A, Gargallo R, Eritja R, Ferguson DM et al.. Structure and stability of human telomeric G-quadruplex with preclinical 9-amino acridines.PLoS One. 2013;8(3):e57701.

Highlights

Development a novel modification for protecting the 3'- ends of oligonucleotides against degradation by nucleases. The modification, N-ethyl-N-coupled dinucleosides, has been tested in DNA and RNA yielding nuclease-stable oligonucleotides without disturbing the inhibitory properties of siRNA.

Identification of new compounds that inhibit human apurinic endonuclease (Ape1) by using docking-based virtual screening techniques. These compounds have activities in the low to the medium micromolar range and potentiate the cytotoxicity of the chemotherapeutic agents paving the road for improving chemotherapy by fighting drug resistant mechanisms.

In a recent work, DNA origami technology was used to visualize the effect of DNA structure on the binding of aptamers to thrombin. A number of aptamers that have a structure that provides quadruplex affinity to thrombin are arranged on the right side of a flat DNA structure. On the left side the same sequences are placed with a modification that prevents the formation of quadruplex. By atomic force microscopy (AFM) thrombin binding to quadruplex structures is observed. Chemical modification introduced in the left side of the origami can be repair by an enzyme involved in the resistance of cancer cells to chemotherapy. This system allows also visualizing the repair activity of this DNA repair enzyme involved in cancer.

Novel formulations based on cationic lipids developed by our group have been successfully used for gene therapy in eye diseases.

PROGRAMME:
Bioengineering and Medical Imaging

Neuroprosthesis and Neuroengineering Research Group - NN-UMH

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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, Zarate J, Díaz-Tahoces A, Avilés-Trigueros M, Fernández E, Pedraz JL. Oligo-chitosan polyplexes as carriers for retinal gene delivery.Eur J Pharm Sci. 2013 Jan 23;48(1-2):323-31.
- Llinares A, Badesa FJ, Morales R, García-Aracil N, Sabater JM, Fernández E. Robotic assessment of the influence of age on upper-limb sensorimotor function.Clin Interv Aging. 2013;8:879-88.
- Wark HA, Sharma R, Mathews KS, Fernández E, Yoo J, Christensen B et al.. A new high-density (25 electrodes/mm²) penetrating microelectrode array for recording and stimulating sub-millimeter neuroanatomical structures.J Neural Eng. 2013 Aug;10(4):045003.
- Sanges D, Romo N, Simonte G, Di Vicino U, Tahoces AD, Fernández E et al.. Wnt/β-catenin signaling triggers neuron reprogramming and regeneration in the mouse retina.Cell Rep. 2013;4(2):271-86.
- Markus Bongard, Daniel Micol, and Eduardo Fernández. NEV2lkit: A NEW OPEN SOURCE TOOL FOR HANDLING NEURONAL EVENT FILES FROM MULTI-ELECTRODE RECORDINGS International Journal of Neural Systems. 2013;Vol. 24:1450009 (10 pages).

Highlights

In the year 2013, the scientific activity of the group has led to the publication of 34 articles in national and international journals, 22 of which are indexed in the JCR and SJR. Also, the members of the group have participated actively in numerous national and international recognized prestigious conferences, with the highlight of receiving a prize in 2013 at the IEEE international Systems Conference.

Notably the group has acquired new funding and collaborations in transfer projects with private companies of important relevance such as the pharmaceutical group Ferrer International S.L. for the project "Toxicity and safety of a new therapy with adult stem cells designed to regenerate retinal neural cells, and in the continuation of the project " Development of a new generation of multifunctional intraocular lenses (HORUS)" co-financed with European funding carried out in collaboration with a consortium of companies oriented at applied R&D. Currently, public funding has been secured for 5 projects with a total budget of 1.113.9828€, for the continuation of projects launched in previous years.

During this year, the group has been involved in the participation of clinical trials in the field of epilepsy.

Equally noteworthy, was the interest shown in the group's active participation in the dissemination of scientific activities which is reflected by the numerous appearances in the national and international media.

PROGRAMME:
Nanomedicine

Dendrimer Group for Biomedical Applications

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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

- Vacas Córdoba E, Arnaiz E, Relloso M, Sánchez-Torres C, García F, Pérez-Álvarez L et al.. Development of sulphated and naphthylsulphonated carbosilane dendrimers as topical microbicides to prevent HIV-1 sexual transmission.AIDS. 2013 May 15;27(8):1219-29.
- Sepúlveda-Crespo D, Lorente R, Leal M, Gómez R, De la Mata FJ, Jiménez JL et al.. Synergistic activity profile of carbosilane dendrimer G2-STE16 in combination with other dendrimers and antiretrovirals as topical anti-HIV-1 microbicide.Nanomedicine.;.
- Córdoba EV, Arnáiz E, De La Mata FJ, Gómez R, Leal M, Pion M et al.. Synergistic activity of carbosilane dendrimers in combination with maraviroc against HIV in vitro.AIDS. 2013 Aug 24;27(13):2053-8.
- Fuentes-Paniagua E, Peña-González CE, Galán M, Gómez R, de la Mata FJ, Sánchez-Nieves J. Thiol-Ene Synthesis of Cationic Carbosilane Dendrons: a New Family of SynthonsORGANOMETALLICS. 2013;32(6):1789-1796.
- Ionov M, Ciepluch K, Moreno BR, Appelhans D, Sánchez-Nieves J, Gómez R, de la Mata FJ, Muñoz-Fernández MA, Bryszewska M. Biophysical Characterization of Glycodendrimers as Nano-carriers for HIV PeptidesCurrent Medicinal Chemistry. 2013;20(31): 3935-3943.

Highlights

The activity of the group during 2013 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 (EURONANOMED), national (CTQ2011-23245 (MINECO)) and regional (Consorcio NANODENMED-CM) projects . Research carried out, focused in the search of a new therapeutic approach towards the HIV treatment based on peptides-associated dendrimers in dendritic cells for the development of new nano-HIV vaccines within the framework of the European project EURONANOMED or the use of anionic dendrimers as HIV antiviral systems and their use in therapy of combination. In addition, new dendritic systems have been developed as carrier of double strand RNA in the treatment of melanoma cancer within the Consortium NANODENMED-CM from Community of Madrid, coordinated by our group.Results of the research have been presented in several conferences, notably in the VIII International dendrimers Symposium (IDS8) held in Madrid and organized by our group among others, and published works consisted of 13 publications and 3 books chapters. The group has continued intensifying its activities related to technology transfer applying for a PCT extension of one national patent based on the use of homo and hereto-functionalized carbosilane dendrimers in VIH and cancer diseases.

PROGRAMME:
Biomaterials and Tissue Engineering

Research Group on Microbial Adhesion

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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

- Vadillo-Rodríguez V, Pacha-Olivenza MA, Gónzalez-Martín ML, Bruque JM, Gallardo-Moreno AM. Adsorption behavior of human plasma fibronectin on hydrophobic and hydrophilic Ti6Al4V substrata and its influence on bacterial adhesion and detachment.J Biomed Mater Res A. 2013;101A(5):1397-1404.
- Galán-Ladero MA, Blanco-Blanco MT, Hurtado C, Pérez-Giraldo C, Blanco MT, Gómez-García AC. Determination of biofilm production by Candida tropicalis isolated from hospitalized patients and its relation to cellular surface hydrophobicity, plastic adherence and filamentation ability.Yeast. 2013 Sep;30(9):331-9.
- Pacha-Olivenza MA, Gallardo-Moreno AM, Vadillo-Rodríguez V, González-Martín ML, Pérez-Giraldo C, Galván JC. Electrochemical analysis of the UV treated bactericidal Ti6Al4V surfaces.Mater Sci Eng C Mater Biol Appl. 2013 Apr 1;33(3):1789-94.
- Rodríguez-Cano A, Cintas P, Fernández-Calderón MC, Pacha-Olivenza MÁ, Crespo L, Saldaña L et al.. Controlled silanization-amination reactions on the Ti6Al4V surface for biomedical applications.Colloids Surf B Biointerfaces. 2013 Jun 1;106:248-57.
- Saadeddin A, Rodrigo-Navarro A, Monedero V, Rico P, Moratal D, González-Martín ML et al.. Functional living biointerphases.Adv Healthc Mater. 2013 Sep;2(9):1213-8.

Highlights

The research activity during 2013 has focused on two different projects associated to private entities. In one case, the collaboration is carried out within the framework of a project INNPACTO, with the aim of characterizing different metal coatings that could potentially be used in prosthetic implants. This research makes use of the equipment provided by the "Plataforma de Calorimetría y Caracterización Superficial". In the other case, being fully financed by the company, the project is based on evaluating the response of a metal to possible infections after subjecting its surface to different treatments generated by the own company. In this line, a new contact with a third private entity was also established, the last details of a formal collaboration now being discussed.

Moreover, we have begun to work together with the "Servicio de Cirugía Oral y Maxilofacial del Hospital Universitario Infanta Cristina de Badajoz". Several studies have begun within this collaboration, one of them published already in a scientific journal, and also the initiation of a PhD dissertation on the characterization of explanted devices.

The research work associated to the project financed within the "Subprograma de Proyectos de Investigación Fundamental no Orientada" (Call 2012) has also been initiated. This project is based on a new polymer-metal composite on which the initial adhesion of different bacterial strains and the subsequent development of biofilms are being evaluated and related to its surface characteristics.

The influence of surface topography on bacterial adhesion has also been studied using spatially organized micro nano-topographic surface patterns generated on a polymeric material. In addition, studies have been carried out on the precursor layer of proteins on some metal surfaces. Also, the work related to the characterization of yeast biofilms associated to hospitalized patients continued. Finally, the research on the bactericide behavior of treated Ti6Al4V surface was advanced.

PROGRAMME:
Biomaterials and Tissue Engineering

Centre of Regenerative Medicine in Barcelona

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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

- Xia Y, Nivet E, Sancho-Martínez I, Gallegos T, Suzuki K, Okamura D et al.. Directed differentiation of human pluripotent cells to ureteric bud kidney progenitor-like cells.Nat Cell Biol. 2013 Dec;15(12):1507-15.
- Zhang K, Liu GH, Yi F, Montserrat N, Hishida T, Rodríguez Esteban C et al.. Direct conversion of human fibroblasts into retinal pigment epithelium-like cells by defined factors.Protein Cell. 2013 Jun 20;.
- Montserrat N, Nivet E, Sancho-Martínez I, Hishida T, Kumar S, Miquel L et al.. Reprogramming of human fibroblasts to pluripotency with lineage specifiers.Cell Stem Cell. 2013 Sep 5;13(3):341-50.
- Gu Y, Liu GH, Plongthongkum N, Benner C, Yi F, Qu J et al.. Global DNA methylation and transcriptional analyses of human ESC-derived cardiomyocytes.Protein Cell. 2013 Aug 27;.
- Marti M, Montserrat N, Pardo C, Mulero L, Miquel-Serra L, Cavaco Rodrigues AM et al.. M-cadherin-mediated intercellular interactions activate satellite cell division.J Cell Sci. 2013 Nov 15;126(Pt 22):5116-31.

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.

Besides, we have been collaborating with Dr. Elena Martínez (IBEC; CIBER-BBN), and from the CMR[B] we supervised a short stay of the predoctoral student Albert García. This collaboration culminated in the presentation of a poster at the 6th IBEC Symposium on Bioengineering and Nanomedicine (8/5/2013, Barcelona):

- Extended microcontact printing technique for the patterning of soft substrates: application to stem cell differentiation. Albert García, Verónica Hortigüela, Carme Cortina, Anna Lagunas, Josep Samitier, Nuria Montserrat, Elena Martínez

Two other posters were presented in this Symposium:

- Transdifferentiation of human Fibroblasts to cardiac fate. Lorena de Oñate, Montserrat Barragán, Núria Montserrat, Juan Carlos Izpisúa
- Generation of cardiac human reporter cell lines with BACs engineered by I-SceI stimulated recombineering methods. Lorena de Oñate, Rubén Peco, Núria Montserrat, Juan Carlos Izpisúa

These posters were also presented at the VII Jornadas Anuales CIBER BBN held on 21-22/11/2013, Torremolinos, Málaga.

INDEXED PUBLICATIONS

34 articles, 25 of them, published in scientific journals ranked in the first quartile.

PROGRAMME:
Bioengineering and Medical Imaging

Biomedical Systems and Signals research Group (SISBIO-UPC-IBEC)

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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

- Ziyatdinov A, Fernández Díaz E , Chaudry A , Marco S, Persaud K, Perera A. A software tool for large-scale synthetic experiments based on polymeric sensor arraysSENSORS AND ACTUATORS B-CHEMICAL. 2013;177:596-604.
- Jaramillo-Garzón JA, Gallardo-Chacón JJ, Castellanos-Domínguez CG, Perera-Lluna A. Predictability of gene ontology slim-terms from primary structure information in Embryophyta plant proteins.BMC Bioinformatics. 2013 Feb 26;14:68.
- Rojas-Martínez M, Mañanas MA, Alonso JF, Merletti R. Identification of isometric contractions based on High Density EMG maps.J Electromyogr Kinesiol. 2013 Feb;23(1):33-42.
- Sarlabous L, Torres A, Fiz JA, Morera J, Jané R. Index for estimation of muscle force from mechanomyography based on the Lempel-Ziv algorithm.J Electromyogr Kinesiol. 2013 Jun;23(3):548-57.
- Morgenstern C, Randerath WJ, Schwaibold M, Bolz A, Jané R. Feasibility of noninvasive single-channel automated differentiation of obstructive and central hypopneas with nasal airflow.Respiration. 2013;85(4):312-8.

Highlights

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

- "Multimodal invasive and non-invasive biomedical signal interpretation and modeling in cardiac, respiratory and neurological disorders" (TEC2010-21703-C03-01), 2011-2013. PI: Raimon Jané.
- "Herramientas de procesado de señal y bioinformática para la evaluación multinivel de desórdenes cardiovasculares y la monitorización de anestesia: Aproximación fenotípica" (TEC2010-20886-C02-01), 2011-2013. PI: Pere Caminal.
- "Herramientas de procesado de señal y bioinformática para la evaluación multinivel de desórdenes cardiovasculares y la monitorización de anestesia: Aproximación ómica" (TEC2010-20886-C02-02), 2011-2013. PI: Alexandre Perera.
- "Sistemas multicanal de análisis y sensorización no invasiva para la rehabilitación y monitorización clínica" (DPI2011-22680), 2012-2014. PI: Miguel Ángel Mañanas.

Furthermore, the group has participated in three projects of the CIBER-BBN (2012-2013):

- "Characterization and validation of novel ultrasensitive piezoresistive all-organic sensors for multimodal biomedical signals (ULTRASEN-4BIO) es un nuevo proyecto intramural, coordinado por este group (PI: Raimon Jané).
- "Multimodal Diagnosis by Interpretation of Multiscale Signals in the Respiratory System" (MUDIRES) es un proyecto traslacional, coordinado por este grupo (PI: Raimon Jané).
- "Indexes obtained from computational models and multiscale-multimodal biomedical signals for the diagnosis of cardiac pathologies" (INDI MUSICA), coord.por Pablo Laguna.

In these lines of biomedical signal processing and interpretation, 9 articles have been published in JCR indexed journals and 25 publications in IEEE/CinC conferences indexed in Pubmed / MEDLINE.

In addition, the following doctoral thesis have been presented:

- "Snoring and arousals in full-night polysomnographic studies from sleep apnea-hypopnea syndrome patients". Febrero 2013. Autor: Gil de Mesquita, Joana Margarida. Director: Raimón Jané Campos.
- "Evaluación no invasiva de la función muscular respiratoria mediante el análisis de la señal mecanomiográfica en pacientes con enfermedad pulmonar obstructiva crónica". Octubre 2013. Autor: Sarlabous Uranga, Leonardo. Director: Abel Torres Cebrián.
- "Genetic association analysis of complex diseases through inforamtion theoretic metrics and linear pleiotropy". Noviembre 2013. Autora: Brunel Montaner, Helena. Director: Alexandre Perera Lluna.
- "Protein function prediction with semi-supervised classification based on evolutionary multi-objective optimization". Noviembre 2013. Autor: Jaramillo Garzón, Jorge A. Director: Alexandre Perera Lluna.

PROGRAMME:
Bioengineering and Medical Imaging

Communication Technologies Group, Instituto de Investigación en Ingeniería de Aragón

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Main lines of research

- Non-invasive markers based on ECG pathology characterization and arrhythmia risk identification. The main target is the search for non-invasive indices for personalized malignant arrhythmia risk prediction, and to improve the decision making process, like at defibrillation implantation.
- Intra-cavitary electrogram signal processing (EGM) to improve surgery planning and therapy delivery. The main target is the ablation procedures guiding. (From FA, 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. It is propose a strategy to better dig into the knowledge of these bases by multi-scale computational modeling, so allowing drug design support for specific channel targeted drugs, and to improve the underlying information extraction from the ECG and EGM, by proposing specific biomarkers form this multi-scale knowledge.

- Evaluation and non-invasive quantification of the autonomic nervous system (ANS) . The ANS has a regulatory role very important in situations such as physiologic (exercise, stress, emotions ...) as well as pathologic (cardiovascular and mental disorders, obstructive sleep apnea, etc.). The variability of signal as heart rate (HRV) , blood pressure (BPV) or photopletismografy (PPG) is influence by the ANS activity, reason why their specific quantification and their interaction among the different signals, allows an 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. Solve 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

- Lázaro J, Gil E, Bailón R, Mincholé A, Laguna P. Deriving respiration from photoplethysmographic pulse width.Med Biol Eng Comput. 2013 Feb;51(1-2):233-42.
- Gil E, Laguna P, Martínez JP, Barquero-Pérez Ó, García-Alberola A, Sörnmo L. Heart rate turbulence analysis based on photoplethysmography.IEEE Trans Biomed Eng. 2013 Nov;60(11):3149-55.
- Bailón R, Garatachea N, de la Iglesia I, Casajús JA, Laguna P. Influence of running stride frequency in heart rate variability analysis during treadmill exercise testing.IEEE Trans Biomed Eng. 2013 Jul;60(7):1796-805.
- Bueno-Orovio A, Sánchez C, Pueyo E, Rodríguez B. Na/K pump regulation of cardiac repolarization: insights from a systems biology approach.Pflugers Arch. 2013 May;466(2):183-93.
- Pueyo E, Bailón R, Gil E, Martínez jp, Laguna P. Signal processing guided by physiology: making the most of cardio-respiratory signalsIEEE SIGNAL PROC MAG. 2013;30(5):136-142.

Highlights

During this period the research activity has led to the publication of 11 JCR articles in international journals, participation in more than 20 international and several national congresses. We should specifically highlight the achievements referreed at the five more relevant publications, we emphasis can be made a the position paper:

- E. Pueyo, R. Bailón, E. Gil, J. P. Martínez and P. Laguna (2013). Signal processing guided by physiology: making the most of cardio-respiratory signals, IEEE Signal Processing Magazine, vol.30, n.5, pp. 136-142; doi:10.1109/MSP.2013.2266961.

Physiology-oriented processing of biomedical signals is a powerful instrument in relevant areas such as the diagnosis, therapy, and follow-up of a wide range of diseases. In this work, there are presented examples of multimodal, multiscale, and multidisciplinary processing of cardiovascular signals. Some of those examples have illustrated how signal processing can aid in the identification of patients who are at high risk of developing cardiac arrhythmias as well as in the development of more effective strategies to treat them. Other examples have shown that signal processing of cardiovascular signals serves to noninvasively characterize the ANS activity and robustly derive respiratory information, both of which find great application in the clinical routine.

PROGRAMME:
Nanomedicine

NanoBiosensors and Bioanalytical Applications Group

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Main lines of research

Led by Full Professor Laura M. Lechuga, the NanoBiosensors and Bioanalytical Applications Group, focuses its activities inside the Nanomedicine area and is involved in the development of novel nanobiosensors devices based on plasmonics, nanoplasmonics, silicon photonics and 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

- D. Duval, J. Osmond, S. Dante, C. Domínguez, and L. M. Lechuga. Grating couplers integrated on Mach-Zehnder interferometric biosensors operating in the visible range IEEE PHOTONICS JOURNAL. 2013;5(2):3700108/1-8.
- de Juan-Franco E, Rodríguez-Frade JM, Mellado M, Lechuga LM.. Implementation of an SPR immunosensor for the simultaneous detection of the 22K and 20K hGH isoforms in human serum samplesTalanta. 2013;11:268-75.
- E. de Juan-Franco, A. Caruz, J.R. Pedrajas, and L. M. Lechuga. Site-directed antibody immobilization using a protein A-gold binding domain fusion protein for enhanced SPR immunosensingANALYST . 2013;138(7):2023-2031.
- B. Vega; A. Calle; A. Sánchez; L. M Lechuga; G. Armelles; J. M. Rodríguez Frade and M. Mellado. Real-time detection of the chemokine CXCL12 in urine samples by surface plasmon resonanceTalanta. 2013;15(109):209-15.
- Duval, Daphne; Lechuga, Laura M. 2012 Breakthroughs in Lab-on-a-chip & Optical biosensors IEEE PHOTONICS JOURNAL. 2013;5(2):00906-00906.

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. A technological transfer plan has been initiated in 2013. Several new projects have been granted in 2013 related to this research line: the national project EPISENS (TEC2012-34280) "Lab-on-a-chip integration of biophotonic devices to study gene expression alterations in cellular pathways" and two EU projects: BRAAVOO (FP7-OCEAN-201-614010) "Biosensors, Reporters and Algal Autonomous Vessels for Ocean Operation" and POCKET (FP7-ICT-2013-10-610389) "Development of a low-cost point-of-care test for Tuberculosis detection".
- 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), dry eye disease (INNPACTO national project); early detection of liver complications (CIBER internal project); novel sensor for in-situ doping control with a high level of sensitivity and accuracy; 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 initiated in 2013 a new 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 metilation or microRNA release).

2013 indicators to be noted: 11 international publications, 3 granted patents, 22 invited contributions to conferences and courses.

PROGRAMME:
Bioengineering and Medical Imaging

Endocrinology and Diabetes Research Group

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Main lines of research

THYROID CANCER

- Markers of prognostic prediction.

  - Implication of 21 genes in CDT. Development of data base, and a private collection of serum and tissue bank of epithelial thyroid cancer (more of 200 cases). We found he 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 e 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

- Jelsma JG, van Poppel MN, Galjaard S, Desoye G, Corcoy R, Devlieger R et al.. DALI: Vitamin D and lifestyle intervention for gestational diabetes mellitus (GDM) prevention: an European multicentre, randomised trial - study protocol.BMC Pregnancy Childbirth. 2013 Jul 5;13:142.
- Hawa MI, Kolb H, Schloot N, Beyan H, Paschou SA, Buzzetti R et al.. Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7.Diabetes Care. 2013 Apr;36(4):908-13.
- Mollo A, Hernández M, Marsal JR, Esquerda A, Rius F, Blanco-Vaca F et al.. Latent autoimmune diabetes in adults is perched between type 1 and type 2: evidence from adults in one region of Spain.Diabetes Metab Res Rev. 2013 Sep;29(6):446-51.
- Aulinas A, Ramírez MJ, Barahona MJ, Mato E, Bell O, Surrallés J et al.. Telomeres and endocrine dysfunction of the adrenal and GH/IGF-1 axes.Clin Endocrinol (Oxf). 2013 Aug 12;.

Highlights

- THYROID NEOPLASMS. A) The creation of a private collection of tissue samples and a serum bank of more than 200 patients with thyroid neoplasms, adequately characterized, recorded in the Endocrine Tumors Committee, Hospital de Sant Pau, chaired by the Principal Investigator. B) The results obtained in the transcriptomic and proteomic analysis in a cohort of 160 patients with epithelial thyroid carcinoma, suggesting the hyperexpression of genes TWIST1 and ANLN as new markers of undifferentiation and metastasis. C) The identification of a set of 120 proteins with a differential pattern between healthy thyroid, adenoma and thyroid epithelial carcinoma (papers invited to the International Congress on Thyroid Cancer, and to the American Association of Clinical Endocrinology). D) Original observation of the relationship between the expression of gene ABCG2/BCRP1 and the aggressiveness of a human cell line (CP-1) of thyroid follicular cancer, with loss of expression of NIS (regulatory gene of iodine uptake), of clinical importance in refractory cancer to I-131 treatment.
- DIABETES MELLITUS. Completion, within the European Project Action LADA, of a research activity coordinated (A.de Leiva) with the Hospital Universitario de Lérida (Didac Mauricio), that determines, for the first time, the prevalence and clinical, metabolic and immunological characterization of diabetes type LADA in Spain. Twelve per cent of patients initially diagnosed with DM-2 should be classified as DM-LADA, with a more severe metabolic alteration than classical DM-2 and early need for insulin therapy.
- INTERNATIONALIZATION. A. de Leiva named: A) Honorary Member of the Romanian Society of Diabetes, B) International Evaluator, Chair of Endocrinology of the University of Cluj-Napoca, C) Member of the International Honorary Committee for the inauguration of the Chair in History of Medicine, University of Yucatán (Mérida, Mexico). A.de Leiva and R.Corcoy D) were named members of the Steering Committee, International Project CONCEPTT-JDRF, that for the first time is going to analyse the benefits of Continuous Glucose Monitoring (CGM) during pregnancy in women with DM-1.

PROGRAMME:
Nanomedicine

Oncogenesis and Antitumour Drug Group

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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 resistance to therapy, metastasis and cancer stem cells
- Preclinical development of nanoconjugates for targeted delivery and receptor-mediated antitumor and antimetastatic therapy in solid and haematological neoplasias
- Identification of molecular markers for prognostication and personalized treatment of cancer.

Most relevant scientific articles

- Peña C, Céspedes MV, Lindh MB, Kiflemariam S, Mezheyeuski A, Edqvist PH et al.. STC1 expression by cancer-associated fibroblasts drives metastasis of colorectal cancer. Cancer Res. 2013 Feb 15;73(4):1287-97.
- Unzueta U, Saccardo P, Domingo-Espín J, Cedano J, Conchillo-Solé O, García-Fruitós E et al.. Sheltering DNA in self-organizing, protein-only nano-shells as artificial viruses for gene delivery.Nanomedicine. 2013 Nov 21;.
- Bosch R, Moreno MJ, Diéguez-González R, Céspedes MV, Gallardo A, Trias M et al.. A novel orally available inhibitor of focal adhesion signaling increases survival in a xenograft model of diffuse large B-cell lymphoma with central nervous system involvement. Haematologica. 2013 Aug;98(8):1242-9.
- Ryan CW, Matias C, Agulnik M, López-Pousa A, Williams C, de Alwis DP et al.. A phase II study of tasisulam sodium (LY573636 sodium) as second-line or third-line treatment for patients with unresectable or metastatic soft tissue sarcoma.Invest New Drugs. 2013 Feb;31(1):145-51.
- de Juan J, García J, López M, Orús C, Esteller E, Quer M et al.. Inclusion of extracapsular spread in the pTNM classification system: a proposal for patients with head and neck carcinoma.JAMA Otolaryngol Head Neck Surg. 2013 May;139(5):483-8.

Highlights

We have obtained a new project from the Instituto de Salud Carlos III for the development of animal models of colorectal cancer to study tumor relapse, and participated in a European Union COST Action on Hypoxia. We demonstrated selective biodistribution to CXCR4+ tumor and metastatic cells of a nanoconjugate that links the T22 nanoparticle to a fluoro-pyrimidine after intravenous administration in a metastatic colorectal cancer model, in collaboration with Villaverde's and Eritja's group. The increased concentration of the antitumor agent achieved in tumor tissue increases the number of DNA double strand breaks and apoptotic figures, leading to a significant reduction in CXCR4+ cells in tumor tissue. In collaboration with Arne Ostman (Karolinska Instituet) we demonstrated that PDGF-stimulated tumor-associated fibroblasts secrete SCT1, a glycoprotein that potentiate metastasis development in a colorectal cancer model. We have also developed a diffuse large B-cell Lymphoma model with central nervous system (CNS) involvement and demonstrated the capacity of an inhibitor of focal adhesion signalling in inhibiting metastatic growth in the CNS. We have also identified Rab25, a regulator of intracellular membrane trafficking, as a prognostic marker in head and neck squamous cell carcinoma patients. We have extended the patent we hold on nanoparticles targeting CXCR4-expressing cells to Europe, USA, Japan, China, Israel, India and Australia. We defended two doctoral dissertations and two visiting researchers form Brasil stayed in our laboratory during 2013. We continue our translational and industrial activities by carrying out contract work for the Pharmaceutical Industry in preclinical drug development using bioluminescent orthotopic models derived from lentivirus-transduced cancer cell lines.

PROGRAMME:
Nanomedicine

Nanobiotechnology for Diagnostics (Nb4D)

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Main lines of research

The Nanobiotechnology for Diagnostics (Nb4D) research group has been recognized and awarded by 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:

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

The scientific activity of the group started on year 1996 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 to develop immunoreagents and provide scientific support in the immunodiagnostic field. Since 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-KBBE-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 performed through the supervision of doctoral theses (more than 15 theses read) courses to PhD students and specialized technical personnel.

From a practical point of view, the research group is interested 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

- Alemany A, Sanvicens N, de Lorenzo S, Marco MP, Ritort F. Bond elasticity controls molecular recognition specificity in antibody-antigen binding.Nano Lett. 2013 Nov 13;13(11):5197-202.
- Conzuelo F, Campuzano S, Gamella M, Pinacho DG, Reviejo AJ, Marco MP et al.. Integrated disposable electrochemical immunosensors for the simultaneous determination of sulfonamide and tetracycline antibiotics residues in milk.Biosens Bioelectron. 2013 Dec 15;50:100-5.
- Esteban-Fernández de Ávila, Berta Escamilla-Gómez, Vanessa Campuzano, Susana Pedrero, María Salvador, J. Pablo Marco, M. Pilar; Pingarrón, José M.. Ultrasensitive amperometric magnetoimmunosensor for human C-reactive protein quantification in serumSENSOR ACTUAT B-CHEM. 2013;188:212-220.
- Muriano A, Pinacho DG, Chabottaux V, Diserens JM, Granier B, Stead S et al.. A portable electrochemical magnetoimmunosensor for detection of sulfonamide antimicrobials in honey.Anal Bioanal Chem. 2013 Sep;405(24):7885-95.
- Valera E, Muriano A, Pividori I, Sánchez-Baeza F, Marco MP. Development of a Coulombimetric immunosensor based on specific antibodies labeled with CdS nanoparticles for sulfonamide antibiotic residues analysis and its application to honey samples.Biosens Bioelectron. 2013 May 15;43:211-7.

Highlights

Among the most important results achieved during 2013, are the development of several diagnostic systems for cardiac biomarkers as result of our participation in projects of industrial orientation at European (ENIAC: CAJAL4EU) and National level (INNPACTO: Nanocardiococco). Furthermore, we have been able to develop electrochemical nanoprobes resulting from labeling of antibodies with metal nanoparticles, which allows us to increase performance of the amperometric biosensors. The use of electrochemical nanoprobes offers significant advantages over enzymatic labeling, improving detectability and shortening the analysis time.

From the point of view of transference and translation activities, it is worth mentioning the patent (PCT/ES2014070161) protecting the knowledge related to the production of antibodies to a specific biomarker of Pseudomonas aeruginosa, which have been used to develop an immunochemical method for the detection of infections caused by this microorganism. In this context, we have held discussions with various companies and a collaborative project (NanobioSepRes) between CIBERES, separ and CIBER-BBN,has initiated which aims to conduct a study on the clinical utility of this biomarker and immunochemical techniques developed. It is also noteworthy, the renewal of research contracts with companies Unisensor SA (Belgium) and Pharmasan (USA), with whom the group collaborates in the development of diagnostic methods for improving food security, and for the diagnosis of disorders neurological. In the same line, mention the operating agreement signed with the company Coorporation Bioo Scientific (USA).

PROGRAMME:
Nanomedicine

Applied Molecular Chemistry Group of the IDM (IQMA-IDM-UPV)

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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 load at will. For that purpose, nanometric mesoporous solids are used as support. Such gated mesoporous silica nanoparticles are able to retain a cargo inside of its 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 detection by colorimetric or fluorimetric methods 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

- Climent E, Mondragón L, Martínez-Máñez R, Sancenón F, Marcos MD, Murguía JR et al.. Selective, highly sensitive, and rapid detection of genomic DNA by using gated materials: Mycoplasma detection.Angew Chem Int Ed Engl. 2013 Aug 19;52(34):8938-42.
- Coll C, Bernardos A, Martínez-Máñez R, Sancenón F. Gated silica mesoporous supports for controlled release and signaling applications.Acc Chem Res. 2013 Feb 19;46(2):339-49.
- Mas N, Galiana I, Mondragón L, Aznar E, Climent E, Cabedo N et al.. Enhanced efficacy and broadening of antibacterial action of drugs via the use of capped mesoporous nanoparticles.Chemistry. 2013 Aug 19;19(34):11167-71.
- Aznar E, Villalonga R, Giménez C, Sancenón F, Marcos MD, Martínez-Máñez R et al.. Glucose-triggered release using enzyme-gated mesoporous silica nanoparticles.Chem Commun (Camb). 2013 Jul 21;49(57):6391-3.
- Oroval M, Climent E, Coll C, Eritja R, Aviñó A, Marcos MD et al.. An aptamer-gated silica mesoporous material for thrombin detection.Chem Commun (Camb). 2013 Jun 18;49(48):5480-2.

Highlights

In this year, we have continued our participation in the Intramural projects NANOCOMETS, MICHORMON, NANOHYPERTERMIA, and BIO-GATES. Within all this projects, we have prepared a collection of new gated materials for controlled release and sensing applications.

We have had an intense scientific activity during 2013 reporting more than thirty publications in international journals of high impact factor. We can highlight the preparation of new gated nanoparticles for the selective, highly sensitive, and rapid detection of genomic DNA (Angew. Chem. Int. Ed. 2013, 52, 8938). The developed innovative strategy for the detection of DNA sequences, is able to compete with classical methods which need PCR amplification, in important areas, such as point-of-care diagnostics or detection of specific biological contaminations with pathogens. Such comparatively simple and cheap yet highly selective and sensitive assays hold promise for use in less-developed areas of the world.

Moreover, we have also developed an aptamer-gated silica mesoporous material for thrombin detection in collaboration with Ramon Eritja's group (Chem. Commun. 2013, 49, 5480). The method, based on a simple competitive procedure, is undemanding and suggests that the use of aptamers can be a suitable approach to develop gated nanoparticles for simple chromo-fluorogenic assays for a wide range of bio-applications.

Finally, in 2013 our group has participated in the CIBER-BBN training program with two grants for initiation in research. Moreover, Alessandro Agostini, Inmaculada Campos, Yolanda Salinas and Tatiana Abalos have defended their PhD thesis during this year.

PROGRAMME:
Biomaterials and Tissue Engineering

Biomaterials Centre

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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

- Araque-Monrós MC, Gamboa-Martínez TC, Santos LG, Bernabé SG, Pradas MM, Estellés JM. New concept for a regenerative and resorbable prosthesis for tendon and ligament: physicochemical and biological characterization of PLA-braided biomaterial.J Biomed Mater Res A. 2013 Nov;101(11):3228-37.
- Lebourg M, Rochina JR, Sousa T, Mano J, Ribelles JL. Different hyaluronic acid morphology modulates primary articular chondrocyte behavior in hyaluronic acid-coated polycaprolactone scaffolds.J Biomed Mater Res A. 2013 Feb;101A(2):518-27.
- Vallés-Lluch A, Arnal-Pastor M, Martínez-Ramos C, Vilariño-Feltrer G, Vikingsson L, Castells-Sala C et al.. Combining self-assembling peptide gels with three-dimensional elastomer scaffolds.Acta Biomater. 2013 Dec;9(12):9451-60.
- Vallés-Lluch A, Poveda-Reyes S, Amorós P, Beltrán D, Monleón Pradas M. Hyaluronic acid-silica nanohybrid gels.Biomacromolecules. 2013 Dec 9;14(12):4217-25.
- Gamboa-Martínez TC, García Cruz DM, Carda C, Ribelles JL, Ferrer GG. Fibrin-chitosan composite substrate for in vitro culture of chondrocytes.J Biomed Mater Res A. 2013 Feb;101A(2):404-12.

Highlights

Work in current proyects has progressed during 2013. 36 published papers in high quality journals reflect this work. The most important single item during 2013, however, is the loss of qualified personnel leaving the group in the hope of finding abroad the opportunity for their careers that the current budgetary policy denies them here.

PROGRAMME:
Biomaterials and Tissue Engineering

Tissue Engineering Research Group, Health Unit TECNALIA (ITUS-Tecnalia)

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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

- Olalde B, Garmendia N, Sáez-Martínez V, Argarate N, Nooeaid P, Morin F et al.. Multifunctional bioactive glass scaffolds coated with layers of poly(D,L-lactide-co-glycolide) and poly(n-isopropylacrylamide-co-acrylic acid) microgels loaded with vancomycin.Mater Sci Eng C Mater Biol Appl. 2013 Oct;33(7):3760-7.
- Briz N, Antolinos-Turpin CM, Alió J, Garagorri N, Ribelles JL, Gómez-Tejedor JA. Fibronectin fixation on poly(ethyl acrylate)-based copolymers.J Biomed Mater Res B Appl Biomater. 2013 Aug;101(6):991-7.
- Braceras I, Oyarbide J, Azpiroz P, Briz N, Ipiñazar E, Álvarez N, Atorrasagasti G, Fratila RM, Aizpurura JM. "Plasma-click" based strategy for obtaining antibacterial surfaces on implants.Plasma Processes and Polymers. 2013;(10):328-335.

Highlights

2013 has been a consolidation year for the Biomaterials group in Tecnalia, both in terms of internal organization and focus of R&D activities. For human resources, Dr. Joseba oyarbide has been taken on by Tecnalia, and Dr. Nerea Argarate is now the assigned researcher to the Capacity Programme, reinforcing the team to face new future research challenges.

On the financial side, the group was granted several relevant Basque government projects in the field of 3D printing, strategic research on multifunctional Au nanoparticles for therapy and in vitro/in vivo diagnostics of cancer.

Several actions has been carried out to reinforce international cooperations (Brazilian students for trainning in San Sebastian, research project with Serbia, new proposal with Paraguay).

In the field of CIBER activities, the team has consolidated the commintment through two intramural projects (Teltis and Oligocodes) and try to obtain a third new one.

Furthermore, two European patent applications have been extended to PCT.

Finally, the group maintained the status of its authorizationfrom the Ministry of Health as Test Laboratory of the 0318 Notified Organism for "Biocompatibility UNE-EN-10993".

PROGRAMME:
Bioengineering and Medical Imaging

Biomedical Imaging Group

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Main lines of research

- Tracer synthesis: development of new tracer synthesis modules and optimization of radiotracer synthesis with 11C, 18F (PET) and 123I (SPECT).
- Monte Carlo Simulation: development and optimization of simulators.
- Tomographic reconstruction in emission tomography.
- Post-processing of human studies.
- Quantification of neurotransmission SPECT studies.
- 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

- Ribera J, Pauta M, Melgar-Lesmes P, Tugues S, Fernández-Varo G, Held KF et al.. Increased nitric oxide production in lymphatic endothelial cells causes impairment of lymphatic drainage in cirrhotic rats.Gut. 2013 Jan;62(1):138-45.
- Martí Fuster B, Esteban O, Planes X, Aguiar P, Crespo C, Falcon C et al.. FocusDET, a new toolbox for SISCOM analysis. Evaluation of the registration accuracy using Monte Carlo simulation.Neuroinformatics. 2013 Jan;11(1):77-89.
- Fuster BM, Falcon C, Tsoumpas C, Livieratos L, Aguiar P, Cot A et al.. Integration of advanced 3D SPECT modeling into the open-source STIR framework.Med Phys. 2013 Sep;40(9):092502.
- Gil-Navarro S, Lomeña F, Cot A, Lladó A, Montagut N, Castellví M et al.. Decreased striatal dopamine transporter uptake in the non-fluent/agrammatic variant of primary progressive aphasia.Eur J Neurol. 2013 Nov;20(11):1459-e126.
- Rodríguez M, Sempau J, Brualla L. PRIMO: a graphical environment for the Monte Carlo simulation of Varian and Elekta linacs.Strahlenther Onkol. 2013 Oct;189(10):881-6.

Highlights

PHD THESIS:

- Berta Martí Fuster. Universidad de Barcelona, 16/10/2013. "Image processing of emission tomography studies in refractory epilepsy".
- Víctor Hernández. Universidd Politécnica de Cataluña, 07/11/2013. "Optimization of field matching in external photon beam".

NEW PROJECTS:

- SYRA3 COST Action. Innovative Methods in Radiotherapy and Radiosurgery using Synchrotron Radiation. (2013-2017), Action TD1205.
- EUTEMPE-RX. EUropean Training and Education for Medical Physics. (2013-2016), EURATOM Coordination and support action Grant.
- Cuantificación de estudios de SPECT de neurotransmisión del sistema dopaminérgico nigroestriatal. Optimización para la utilización en la rutina clínica (FIS/PI12-00390).
- Development of an automated Monte Carlo-based linac simulator and radiotherapy treatment planning system for research: application to ion chambers in small off-axis fields (FIS/PI12-38480).

INTERNATIONAL COLLABORATIONS:

- Stay of two members of the group (Berta Martí and Carles Falcon) at the King's College London, Department of Imaging Sciences and Biomedical Engineering, School of Medicine.
- Agreement with King's College London University to launch a new STIR (Software for Tomographic Image Reconstruction) release including our SPECT reconstruction capabilities.

Notary registration of FocusDET software

PROGRAMME:
Nanomedicine

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

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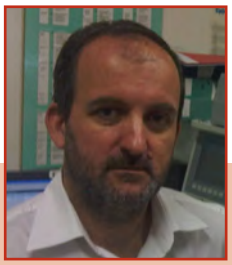

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Main lines of research

- MICROENCAPSULATION OF ALIVE CELLS: Design and optimization of polymeric systems for immobilization of cells with therapeutic activity. This system provides protection to cells against the host's immune response due to its technological design, and at the same time, it turns into a controlled release pharmaceutical system.
- MICRO AND NANO-PARTICLES AS VACCINE ADMINISTRATION SYSTEMS OF PEPTIDES AND PROTEINS: Promising results obtained by our research group support the use of these drug (antigen) carrier systems to develop vaccines, as demonstrated by the results after their administration by different routes in laboratory animals (mice and monkeys), inducing a sustained and strong immune response.
- NON VIRAL VECTORS FOR GENE THERAPY PURPOSES: Design and optimization of non-viral vectors based on lipidic and polymeric nanoparticles to transfect eukaryotic cells with therapeutic genes.
- DEVELOPMENT OF MODIFIED RELEASE FORMULATIONS: Development and optimization of drug delivery systems based on new polymers to obtain a sustained release profile of drugs.

- 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

- Santos E, Larzabal L, Calvo A, Orive G, Pedraz JL, Hernández RM.. Inactivation of encapsulated cells and their therapeutic effects by means of TGL triple-fusion reporter/biosafety gene.BIOMATERIALS. 2013;34(4):1442-51.
- Santos E, PedrazJL, Hernández RM, Orive G.. Therapeutic cell encapsulation: ten steps towards clinical translation.Journal Controlled Release. 2013;:1-14.
- Herran E, Pérez-González R, Igartua M, Pedraz JL, Carro E, Hernández RM.. VEGF-releasing biodegradable nanospheres administered by craniotomy: a novel therapeutic approach in the APP/Ps1 mouse model of Alzheimer's disease.Journal of Controlled Release. 2013;170(1):111-9.
- Orive G, Santos E, Pedraz JL, Hernández RM.. Application of cell encapsulation for controlled delivery of biological therapeutics.Advanced Drug Delivery Reviews. 2014;.
- Del Burgo LS, Hernández RM, Orive G, Pedraz JL.. Nanotherapeutic approaches for brain cancer management.Nanomedicine. 2014;.

Highlights

During 2013 year, we have obtained 4 new SAIOTEK projects from the ¨Departamento de Industria y Comercio del Gobierno Vasco¨, in different research areas such as: New strategies to transfect efficiently neurons with non-viral vectors; Delivering of neurotrophic factors to the brain for the treatment of Parkinson diseases; Cell containing scaffolds for bone regeneration and technologies for peptides purification.

Two patents have been developed for the Praxis Pharmaceutical S.A Company: "Lipidic nanoparticles for wound cicatrisation" and "Polymyxin containing lipidic nanoparticles".

The following patent has been developed in collaboration with the CIBERER, UAM, and the CSIC: "Biodegradable nanoparticles for the GSE24-2 peptide release, extraction and use procedure".

Two research members of our team had the opportunity to further develop their research skills in England (Bath University) and Germany (Institute for Biological and Medical Imaging (IBMI), Helmholtz Centre in Munich).

Three doctoral thesis were defended during 2013 year: "Optimization of cell microencapsulation in terms of biosafety, biomimesis and applicability in therapeutic targets of central nervous system", Microparticlulate systems as adjuvants of anti malaria synthetic antigens" and "Gastro-resistant microparticles as an oral cholera vaccine approach".

In 2013, 14 new articles and three book chapters have been published "Immobilization of Enzymes and Cells". Book chapters are:

"Biomedical Applications of Immobilized Enzymes: An update, Encapsulation of Cells in Alginate Gels" and "Therapeutic Applications of Encapsulated Cells".

PROGRAMME:
Nanomedicine

Biofunctional Nanomaterials Laboratory, CIC-Biomagune

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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

- Beloqui A, Calvo J, Serna S, Yan S, Wilson IB, Martín-Lomas M et al.. Analysis of microarrays by MALDI-TOF MS. Angew Chem Int Ed Engl. 2013 Jul 15;52(29):7477-81.
- Reichardt NC, Martín-Lomas M, Penadés S. Glyconanotechnology. Chem Soc Rev. 2013, May 21,42(10): 4358-76.
- Chiodo F, Marradi M, Tefsen B, Snippe H, van Die I, Penadés S. High sensitive detection of carbohydrate binding proteins in an ELISA-solid phase assay based on multivalent glyconanoparticles. PLoS One. 2013, 8(8): e73027.
- Etxebarria J, Serna S, Beloqui A, Martín-Lomas M, Reichardt NC. Three-dimensional arrays using glycoPEG tags: glycan synthesis, purification and immobilisation. Chemistry. 2013 Apr 8;19(15):4776-85.
- Guedes N, Czechura P, Echeverria B, Ruiz A, Michelena O, Martín-Lomas M et al.. Toward the solid-phase synthesis of heparan sulfate oligosaccharides: evaluation of iduronic acid and idose building blocks. J Org Chem. 2013 Jul 19;78(14):6911-34.

Highlights

In the frame of a contract with Midatech Biogune SL (CENIT-Advance Molecular Imaging Technique, AMIT) aiming at developing contrast agents to cross the blood brain barrier (BBB), 68Ga-based gold glyconanoparticles incorporating specific peptides have been evaluated by PET and gamma-counter techniques in healthy rats. The results are published in the J. Am. Chem. Soc. 2014, 136, 449-457 (68Ga-Labeled Gold Glyconanoparticles for Exploring Blood-Brain Barrier Permeability: Preparation, Biodistribution Studies, and Improved Brain Uptake via Neuropeptide Conjugation)

12 publications in 2013, 11 indexed, 4 in the first decile and 6 in the first quartile

Two PhD Theses have been presented:

- Gold glyconanoparticles as multivalent nanocarriers for carbohydrate antigens. Fabrizio Chiodo. Universidad del País Vasco (UPV-EHU). 11 de Marzo 2013.
- Exploring gold glyconanoparticles as multivalent carrier for specific molecules involved in HIV-1 infection. Paolo di Gianvincenzo. Universidad del País Vasco (UPV-EHU). 4 de Octubre 2013

PROGRAMME:
Biomaterials and Tissue Engineering

Health Technology Group (GTS-IBV)

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Main lines of research

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

- The main Healthcare Technology areas in which the IBV is active are:
  - Orthopaedic Implants Surgery: hip, knee and spine implants, osteosynthesis and personalized implants.
  - Dental implants and prosthesis.- Surgical instruments.
  - Applications for ophthalmology.- Personalization of medical devices to meet the anatomical and physiological needs of the patient.
  - Veterinary implants.

TECHNOLOGY CONSULTANCYThe 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

TRAININGTIC

APPLICATIONS

Most relevant scientific articles

- Gallego JÁ, Rocon E, Belda-Lois JM, Pons JL. A neuroprosthesis for tremor management through the control of muscle co-contraction.Journal of neuroengineering and rehabilitation. 2013;10:36.
- De Rosario, H., Page, T., Besa, A., Valera, T.. Propagation of soft tissue artifacts to the center of rotation: A model for the correction of functional calibration techniquesJ BIOMECH. 2013;:2619-2625.
- de Rosario H, Belda-Lois JM, Fos F, Medina E, Poveda-Puente R, Kroll M. Correction of Joint Angles From Kinect for Balance Exercising and Assessment.J Appl Biomech. 2013 Jul 22;.
- Chicote JC, Durá JV, Belda JM, Poveda R. A functional PCA model for the study of time series of pressure maps.J Appl Biomech. 2013 Apr;29(2):135-40.

Highlights

PROJECTS:

- A novel muscular micro-electro-stimulation device for the enhanced treatment of adolescent idiopathic scoliosis avoiding bracing and invasive open surgery.
- 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.
- Advanced BNCI Communication (ABC).
- ICT based System to Predict and Prevent Falls (ISTOPPFALLS).
- BNCI-driven Robotic Physical Therapies in Stroke Rehabilitation of Gait Disorders (BETTER).
- Development of a non-invasive and portable tissue viability measurement and intelligent actuation system for the prevention and early detection of Preassure Ulcer risk at Tetraplegic SCI users.
- Intelligent Motion analysis. Development of a novel technology that makes quantitative measurement of musculoskeletal problems available, in the interests of physiotherapists, patients and society.
- Flexible and on-demand manufacturing of customised spectacles by close-to-optician production clusters.

PATENTS:

- Maxillo-mandibular prosthesis and manufacturing method

PROGRAMME:
Nanomedicine

Small Biosystems Lab

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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

- Alemany A, Sanvicens N, de Lorenzo S, Marco MP, Ritort F. Bond elasticity controls molecular recognition specificity in antibody-antigen binding.Nano Lett. 2013 Nov 13;13(11):5197-202.
- Camunas-Soler, S. Frutos, C.V. Bizarro, S. de Lorenzo, M.E. Fuentes-Pérez, R. Ramsch, S. Vilchez, C. Solans, F. Moreno-Herrero, F. Albericio, R. Eritja, E. Giralt, S.B. Dev and F. Ritort. Electrostatic binding and hydrophobic collapse of peptide-nucleic acid aggregates quantified using force spectroscopyACS NANO. 2013;7(6): 5102-5113..
- M. Manosas, S. K. Perumal, P. Bianco, F. Ritort, S. J. Benkovic, V. Croquette. RecG and UvsW catalyse robust DNA rewinding critical for stalled DNA replication fork rescue-Nature Communications. 2013;4:1-11.
- M. Ribezzi, J. M. Huguet and F. Ritort. Counter-propagating dualtrap optical tweezers based on linear momentum conservationReview of Scientific Instruments. 2013;84:043104-1, 043104-10.
- A. Bosco, J. Camunas-Soler and F. Ritort. Elastic properties and secondary structure formation of single-stranded DNA at monovalent and divalent salt conditionsNucleic Acids Research. 2013;42(3):2064-74.

Highlights

Last year the group has succeeded in studding several problems combining theory and experiments to investigate the thermodynamics and non-equilibrium behavior of small systems using single molecule methods. By applying tiny forces in the piconewton range we use high-resolution optical tweezers to manipulate single molecules and mechanically dissociate molecular bonds to measure the energies of molecular reactions in nucleic acids, proteins and other molecular complexes with accuracy of tenths of kcal/mol. We apply the finest concepts and tools from statistical physics to extract precious information characterizing a wide range of molecular processes and phenomena: from the thermodynamics of nucleic acids to the kinetics of formation of molecular aggregates induced by anticancer drugs or the elasticity of antigen-antibody bonds in the immune system.

Motivated by my previous first experimental test of the Crooks fluctuation relation we found a new relation that recently paved the way to extract the free energies of kinetic states of finite lifetime in complex molecular structures. This work provides a new and powerful methodology to characterize the energetics and kinetics of non-native molecular structures (e.g. intermediate, misfolded) hardly accessible to most bulk based techniques. We have extended such method to the full characterization of intermolecular affinities between peptides and proteins binding to nucleic acids.

Beyond fundament research in biophysics I have led several applied-research collaborations with chemistry and biology groups and a drug company (Pharmamar) finding relevant results on the kinetics of DNA-peptide aggregation (Camunas-Soler et al) and the role of bond elasticity in antigen-antibody recognition (Alemany et al). I have also developed a novel dual-trap counter-propagating setup for pulling dumbbells with direct force measurement that can be used for pulling tethers with very short DNA handles (Ribezzi et al). Finally, we have built a new highly stable temperature controller for optical tweezers that allows us to face future challenges in this exciting field.

PROGRAMME:
Bioengineering and Medical Imaging

Biomedical Engineering Research Group (GIB-US)

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Main lines of research

- MULTISCALE COMPUTATIONAL MODELING FOR MULTIMODAL DIAGNOSIS: methods and technologies for the detection of biological and pathological events and to provide a quantitative understanding of the relationships between elements of complex biological systems through the integration of personalized knowledge in multiple scales: from genomic and proteomic level to whole body level.
- INTEGRATION ARCHITECTURES FOR HEALTH AND SOCIAL SERVICES: integration architectures for heterogeneous and distributed health services that allow the access, knowledge generation and management of personalized medical care delivery. Integration architectures for the provision of standard-based health and social services. Intermediation software technologies (middleware) to support service architectures for generating new medical/clinical knowledge in real-time.
- SMART DEVICES FOR AMBIENT ASSISTED LIVING: development of methods and techniques for designing and validating assisted living environments through distributed intelligent devices. Application to the elderly and chronic pathologies. Development of methodologies and techniques for the design

and validation of wearable systems based on the concepts of design-for-all and design space for citizens with special needs.

- METHODS AND TECHNIQUES OF ELECTROMAGNETISM APPLIED TO MEDICAL NANOTECHNOLOGY: modeling and characterization of the interactions of electromagnetic fields with biological tissues at different levels, and their applications; design of intelligent devices for therapy/diagnosis at micro-/nano level, and communications.

Most relevant scientific articles

- Callejon M, Reina-Tosina J, Naranjo D, Roa LM. Galvanic Coupling Transmission in Intrabody Communication: A Finite Element Approach.IEEE Trans Biomed Eng. 2013 Nov 7;.
- Calvillo J, Román I, Roa LM. How technology is empowering patients? A literature review.Health Expect. 2013 May 28;.
- Oliva JS, Roa LM, Lara A, Garrido S, Salgueira M, Palma A et al.. Survival and factors predicting mortality in hemodialysis patients over 75 years old.J Nephrol. 2013 Jan-Feb;26(1):129-35.
- Callejon M, Naranjo D, Reina-Tosina J, Roa LM. A comprehensive study into intrabody communication measurementsIEEE T INSTRUM MEAS. 2013;:2446-2455.
- Acha B, Serrano C, Fondón I, Gómez-Cía T. Burn depth analysis using multidimensional scaling applied to psychophysical experiment data.IEEE Trans Med Imaging. 2013 Jun;32(6):1111-20.

Highlights

Multiscale modeling for multimodal diagnosis: collaboration with the Biochemistry Department/ Infectious Diseases Unit at UHVM led to a joint publication (under review), another journal paper in preparation and two papers at international conferences. The PERSONA grant (CIBER-BBN) led to a paper at the Spanish Diabetes Society and an international journal (under preparation). Collaboration with Dr. Álvarez (Cardiology Unit, UHVR) includes two journal publications (accepted 2014) and two conference papers. Collaboration with the Nephrology Unit at UHVM led to three published chapters targeted to clinicians.

Regarding the integration architectures for health and social services, advances in virtual organizations and security issues of HISA-compliant architectures, and management of alarms with the DDS standard, led to two JCR papers (one under review) and four international conferences. Results are being transferred to the architecture of health information systems for ongoing projects. Research on E-NEFRO system architecture has already been transferred to UHVM for clinical validation, and has led to a paper in JCR journal.

With regard to smart devices for AAL, collaboration has been established with the Respiratory Unit at HUVR, and is being formalized through three grants (two funded by Neumosur and one at regional level). Results are being collected for preparation of two journal papers. Two papers are in review process covering related topics and two papers presented in international conferences. Two national patents have been submitted.

Regarding bioelectromagnetism, two JCR papers addressed the modeling of intrabody communications systems, with other two in preparation. Ongoing research in modeling skin wound healing from a bioelectric perspective has led to an international conference paper and is being redirected to regenerative medicine, with an international joint collaboration planned.

Two PF7 proposals were prepared in the subjects of AAL and empowerment of citizens, and lab-on-chip techniques for the early detection of bacteria, relying on international consortia including industry and academic partners.

We also highlight the active involvement of the group in the organization of the 13th Mediterranean Conference for Medical and Biological Engineering and Computing (MEDICON 2013), held in Seville from 25th to 28th September, 2013. The event counted on over 600 participants from 47 countries, 486 accepted papers, 5 keynote lectures, 54 oral sessions, 4 poster sessions and 16 parallel activities.

PROGRAMME:
Biomaterials and Tissue Engineering

BIOFORGE-Uva

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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

- Pierna M., Santos M., Arias F.J., Alonso M., Rodríguez- Cabello J.C.. Efficient cell and cell-sheet harvesting based on smart surfaces coated with a multifunctional and self-organizing Elastin-Like RecombinamerBIOMACROMOLECULES. 2013;14:1893−1903.
- Rui R. Costa, Catarina A. Custódio, Francisco J. Arias, José C. Rodríguez-Cabello, Joao F. Mano. Nanostructured and thermoresponsive recombinant biopolymer-based microcapsules for the delivery of active molecules.NANOMED-NANOTECHNOL. 2013;9(7):895-902.
- García-Arévalo C., Bermejo-Martín J.F., Rico L., Iglesias V., Martín L., Rodríguez-Cabello J. C., Arias F.J.. Immunomodulatory nanoparticles from elastin-like recombinamers: single-molecules for tuberculosis vaccine development.MOL PHARMACEUT. 2013;10(2): 586-97.
- Costa R.,Castro E., Arias F.J., Rodríguez-Cabello J.C., Mano J.. Multifunctional Compartmentalized Capsules with a Hierarchical Organization from the Nano to the Macro ScalesBIOMACROMOLECULES. 2013;14: 2403−2410.
- Mateos-Timoneda, M.A., Punet, X., Mauchauffé, R., Giannotti, M., Rodríguez-Cabello, J.C., Sanz, F., Engel, E., Planell, J.. Enhaced Cell-material interactions through the biofunctionalization of polymeric surfacesBIOMACROMOLECULES. 2013;14:2690−2702.

Highlights

In 2013 BIOFORGE's funding came from thirteen research projects and two networks with different funding sources. As for the Projects, BIOFORGE participated in: three European projects funded by the FP7-NMP-2010, FP7-Health-2011 and FP7-People-2012-ITN, three national projects (Programme of Non-oriented fundamental research projects), five regional projects (funded by the Ministries of Education and Health of the Regional Gonvernment of Castilla y León) and one international complementary action of the Spanish Ministry of Economy and Competitivity. As for the Networks, BIOFORGE took part in two Biomaterial Networks funded by the Instituto de Salud Carlos III (CIBER-BBN and Regenerative Medicine and Cell Therapy Network of Castilla y León).

In this period ten articles were published in international journals, eight of them in indexed high impact journals as well as one book chapters. Furthermore, one national patent applications was filled.

The group members attended many scientific meetings giving around sixteen oral presentations and two invited plenary talks. One PhD thesis with European mention was presented by the researcher Maria Pierna, who received the highest calification.

The training activities of the group included invited conferences and contributing to four master programs of the University of Valladolid.

PROGRAMME:
Biomaterials and Tissue Engineering

Tissue Bioengineering and Cell Therapy Group

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Main lines of research

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

Most relevant scientific articles

- Blanco FJ, Ruiz-Romero C. New targets for disease modifying osteoarthritis drugs: chondrogenesis and Runx1. Ann Rheum Dis. 2013 May;72(5):631-4.
- Magalhães J, Sousa RA, Mano JF, Reis RL, Blanco FJ, San Román J. Synthesis and characterization of sensitive hydrogels based on semi-interpenetrated networks of poly[2-ethyl-(2-pyrrolidone) methacrylate] and hyaluronic acid. J Biomed Mater Res A. 2013 Jan;101(1):157-66.
- Mateos J, De la Fuente A, Lesende-Rodríguez I, Fernández-Pernas P, Arufe MC, Blanco FJ. Lamin A deregulation in human mesenchymal stem cells promotes an impairment in their chondrogenic potential and imbalance in their response to oxidative stress. Stem Cell Res. 2013 Nov;11(3):1137-48.
- Cicione C, Muiños-López E, Hermida-Gómez T, Fuentes-Boquete I, Díaz-Prado S, Blanco FJ. Effects of severe hypoxia on bone marrow mesenchymal stem cells differentiation potential. Stem Cells Int. 2013;2013:232896.
- Mayan MD, Carpintero-Fernández P, Gago-Fuentes R, Martínez-de-Ilarduya O, Wang HZ, Valiunas V et al.. Human articular chondrocytes express multiple gap junction proteins: differential expression of connexins in normal and osteoarthritic cartilage. Am J Pathol. 2013 Apr;182(4):1337-46.

Highlights

During 2013, GBTTC-CHUAC group has published 12 peer-reviewed articles in which are described new regulators and the effect of biophysical stimuli, such as oxygen tension, in the differentiation of mesenchymal stem cells; the synthesis and characterization of hybrid hydrogels for their application in cartilage tissue engineering; and it was demonstrated that adults human chondrocytes communicate through gap junctions formed by connexin 43 and that the levels of this protein are expressed in a cartilage zonal structure-dependent manner which could affect the functional integrity of chondrocytes.

Moreover GBTTC-CHUAC group has generated 6 procedures, methodologies or techniques that affect processes of prevention, diagnosis and treatment of osteoarthritis such as the pharmacoproteomics of chondroitin culfate in osteoarthritis therapy; the use of biomarkers for the purposes of diagnosis and drug discovery programs, medical applications of hydrogen sulfide and the use of the human amniotic membrane as a potential tissue and cell source in the repair of cartilage lesions. The latest work has been prize awarded in the XIII Congress of the Spanish Association of Tissue Banking.

PROGRAMME:
Nanomedicine

Nanomedicine Group (NANOMED–IBEC)

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Website: www.ibecbarcelona.eu/nanobioengineering

Main lines of research

The main activities of the group involve the surface functionalization of materials integrated with microfluidics systems for the study of biomolecule and cell interactions to develop Organ on Chip or for the development of new biosensors that will be integrated in lab-on-a-chip devices. The goal is to fabricate microsystems containing living cells that recapitulate tissue and òrgan level functions in vitro and new portable diagnosis devices that can be used as Point-of-Care systems. The projects carried out by the group are focused on clinical and industrial problems and are related to three convergent research lines:

1). Biosensors and Lab-on-a-chip for clinical diagnosis and food safety applications

- DNA sensors for cancer biomarker detection
- Antibody-based sensors for detection of pathogenic microorganisms
- Olfactory receptor-based sensors for odorant and volatile compounds detection
- Polymer nanowires-based biosensors
  - Microfluidic chip for reagent handling in POC diagnosis devices
  - Microfluidic chip using hydrodynamic focusing for bacteria counting and sorting

2). Nanotechnology applied to biomolecule interaction studies and micro/nanoenvironments for biomedical studies and regenerative medicine applications.

- Design, production and characterization of micro/nanoenviroments with different biocompatible materials for cell behavior studies (adhesion, proliferation, differentiation)
- Design, production and characterization of scaffolds with a topography and chemical composition controlled at the nanoscale for ocular and cardiac tissue regenerative therapies based on stem cells
- Magnetic nanoparticles-biomolecules interactions and their Applications

3). Microfluidic systems for biological studies and Organ-on-Chip devices

- Microfluidic chip for blood/plasma filtering
- Spleen-on-a-Chip development
- Engineering microfluidic platforms for neurobiological studies

Most relevant scientific articles

- Prats-Alfonso, Elisabet; Oberhansl, Sabine; Lagunas, Anna; Martínez, Elena; Samitier, Josep; Albericio, Fernando. Effective and Versatile Strategy for the Total Solid-Phase Synthesis of Alkanethiols for Biological ApplicationsEur J Org Chem . 2013;(7):1233–1239.
- Lagunas A, Comelles J, Oberhansl S, Hortigüela V, Martínez E, Samitier J. Continuous bone morphogenetic protein-2 gradients for concentration effect studies on C2C12 osteogenic fate.Nanomedicine. 2013 Jul;9(5):694-701.
- Barreiros dos Santos M, Agusil JP, Prieto-Simón B, Sporer C, Teixeira V, Samitier J. Highly sensitive detection of pathogen Escherichia coli O157:H7 by electrochemical impedance spectroscopy.Biosens Bioelectron. 2013 Jul 15;45:174-80.
- Tahirbegi IB, Mir M, Samitier J. Real-time monitoring of ischemia inside stomach.Biosens Bioelectron. 2013 Feb 15;40(1):323-8.
- Novo S, Penon O, Barrios L, Nogués C, Santaló J, Durán S et al.. Direct embryo tagging and identification system by attachment of biofunctionalized polysilicon barcodes to the zona pellucida of mouse embryos.Hum Reprod. 2013 Jun;28(6):1519-27.

Highlights

During 2013, in collaboration with the group of Prof. CIBER- BBN Albericio (IRB) resulted in the publication of two scientific articles in international journals, one of them (European Journal of Organic Chemistry, 2013 (7): 1233-1239 (2013)) as the cover of the edition of the magazine. In addition, our group and groups of CIBER- BBN LABRET - UMA and NANOMEMB - UB began a collaboration. Also as part of CIBER intramural projects, the work carried out in the OLIGOCODES project has brought a national project and a presentation of European projects in the Horizon 2020. Since 2011, the group participates in a highly innovative project -FET program OPEN European whose objective is the development of robotic devices Inspired by the roots of plants for Monitoring Soil (PLANTOID). These achievements have helped to strengthen the team NANOMED - IBEC as a reference group in the development of integrated Nanobiosystems for biomedical applications.

The success of industrial projects in collaboration with GENOMICA SA, Enantia SL, SL PARTY TALLERS and BIOKIT SA, and successful collaboration with the Vall d' Hebron Hospital, in the field of diagnosis of prostate cancer (project funded by the FIS ISCIII) reflect the skills of the group in the transfer of knowledge to the market and into clinical practice. Finally, with regard to communication and training, 7 journal publications in the areas of biosensors, biomaterials and microfluidics, and successful completion of 2 doctoral thesis, are manifestations of the work of the group for Nanomedicine 2013 and set future goals.

PROGRAMME:
Biomaterials and Tissue Engineering

Biomaterials Group GBP-CSIC

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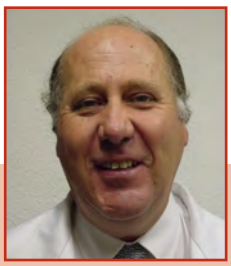

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Main lines of research

- 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 ANJD TARGETING SYSTEMS. Preparation of bioactive polymer systems with targeting properties for the application and release of well-known 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

- Fernández-Montes Moraleda B, San Román J, Rodríguez-Lorenzo LM. Influence of surface features of hydroxyapatite on the adsorption of proteins relevant to bone regeneration JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A. 2013;101:2332-2339.
- Magalhães J, Sousa RA, Mano JF, Reis RL, Blanco FJ, San Román J. Synthesis and characterization of sensitive hydrogels based on semi-interpenetrated networks of poly[2-ethyl-(2-pyrrolidone) methacrylate] and hyaluronic acid.J Biomed Mater Res A. 2013 Jan;101(1):157-66.
- Peniche H, Reyes-Ortega F, Aguilar MR, Rodríguez G, Abradelo C, García-Fernández L et al.. Thermosensitive macroporous cryogels functionalized with bioactive chitosan/bemiparin nanoparticles.Macromol Biosci. 2013 Nov;13(11):1556-67.
- Reyes-Ortega F, Rodríguez G, Aguilar MR, Lord M, Whitelock J, Stenzel MH, San Román J. Encapsulation of Low Molecular Weight Heparin (bemiparin) into Polymeric nanoparticles obtained from cationic block copolymers: Properties and cell activity.Journal of Materials Chemistry B. 2013;1:850-860.
- Reyes-Ortega F, Parra-Ruiz FJ, Averick SE, Rodríguez G, Aguilar MR, Matyjaszewski K, San Román J. Smart heparin-based bioconjugates synthesized by a combination of ATRP and click chemistryPolymer Chemistry. 2013;:2800-2814.

Highlights

- Preparation and application of bioactive nanoparticles for cáncer therapy.
- Design and preparation of abdominal meses with targeting antibiotic action.
- Preparation of bilayer dressings for activation of healing processes.
- New coating coronary stents with high stability and restenosis control.
- Organization of the XXV congference on Biomaterials for the European society for Biomaterials 8-12 September, with the participation of 956 registered felegates of 57 countries.

PROGRAMME:
Nanomedicine

Nanostructured Films and Particles (NFP)

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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 (direct heating by 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 (Hospital La Paz, Madrid - gene therapy and cell scaffolds), Dr Carles Arus (Autonomous University of Barcelona - Medical Imaging), Dr MA Gregory (Fac. Medicina, UZ - combination therapies in oncology) , Dr L. Luján (Fac. Veterinaria, UZ - bactericidal applications in trauma).
- NANOCOMPOSITES: Development of polymer based composites with different types of nanomaterials with mechanical reinforcement applications, bactericidal plastics, magnetic and barrier films. This field, we work with the Technological Institute of Aragon (ITA) .
- 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 na-

noparticles in various common handling operations with nanomaterials, as well as nanosafety procedures. An European project of the EU FP7 (Nanovalid) is ongoing in this field.

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

Most relevant scientific articles

- Cebrián V, Martín-Saavedra F, Gómez L, Arruebo M, Santamaría J, Vilaboa N. Enhancing of plasmonic photothermal therapy through heat-inducible transgene activity.Nanomedicine. 2013 Jul;9(5):646-56.
- Regiel A, Irusta S, Kyziol A, Arruebo M, Santamaría J. Preparation and characterization of chitosan-silver nano composite films and their antibacterial activity against Staphylococcus aureus NANOTECHNOLOGY. 2013;24(1):015101.
- Gómez V, Irusta S, Balas F, Santamaría J. Intense generation of respirable metal nanoparticles from a low-power soldering unit JOURNAL OF HAZARDOUS MATERIALS. 2013;256-257:84-89.
- Malumbres A, Martínez G, Mallada R, Hueso JL, Bomatí-Miguel O, Santamaría J. Continuous production of iron-based nanocrystals by laser pyrolysis. Effect of operating variables on size, composition and magnetic response.Nanotechnology. 2013 Aug 16;24(32):325603.
- Sebastian V, Calatayud MP, Goya GF, Santamaría J. Magnetically-driven selective synthesis of Au clusters on Fe3O4 nanoparticles.Chem Commun (Camb). 2013 Jan 25;49(7):716-8.

Highlights

PATENTS:

- "Hidrogeles de fibrina con nanopartículas plasmónicas", F. M. Martín Saavedra, N. Vilaboa Díaz, V. Cebrian Hernando, M. Arruebo Gordo, J. Santamaría Ramiro, L. Gómez Navascues, Entidades titulares: Fundación para la Investigación Biomedica del Hospital La Paz, CIBER-BBN, Universidad de Zaragoza. Solicitud de Patente española número P201330894, (2013).

PROJECTS:

- Synthesis and caracterization of nasotructured materials with luminiscent properties for diagnostic and therapeutic applications" (NANOLIGHT). Financiado por: UE (2011-2014)
- "Development of reference methods for hazard identification, risk assessment and LCA of engineered nanomaterials" (NANOVALID). Financiado por: el programa NMP del VII Programa Macro (2011-2015)
- "Microwave-assisted microreactors: development of a highly efficient gas phase contactor with direct catalyst heating (HECTOR)". Financiado por: UE (2011-2016)
- "Farolas Inteligentes con Nanosensores para Control de la Calidad del Aire". Financiado por: MINECO, proyecto INNpacto, IPT-2012-0749-310000, 2013-2015.
- "Investigación y desarrollo de un proceso de impresión basados en tintas constituídas por nanoparticulas para la securización de productos". Financiado por: MINECO, proyecto INNpacto, IPT-2012-0764-420000, 2013- 2014.
- "Development of a microfluidic platform to produce nanomaterials and assessment on new nanotechnology applications" (PLATFORM2NANO). Financiado por: UE, Marie Curie Action dentro del programa IDEAS del VII Programa Marco, 2012-2014.
- "Marcadores anti-falsificación basados en nanopartículas. DEsarrollo e identificación de tintas personalizadas". Financiado por: Tipolínea SAU, 2012-2014.
- "Desarrollo de suelas ignífugas libres de compuestos halogenados". Financiado por: el Centro Tecnológico del Calzado de La Rioja, 2012-13.

PROGRAMME:
Bioengineering and Medical Imaging

Biomedical Imaging Technology Group (BIT)

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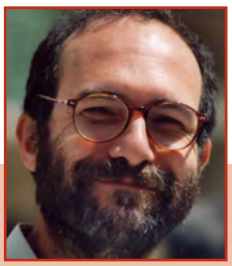

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Main lines of research

- 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

- Atienza F, Arenal Á, Pérez-David E, Elízaga J, Ortuño JE, Ledesma-Carbayo MJ, Sánchez-Quintana D, Fernández-Avilés F. New diagnostic and therapeutic approaches to treat ventricular tachycardias originating at the summit of the left ventricle: role of merged hemodynamic-MRI and alternative ablation sources.CIRC-ARRHYTHMIA ELEC. 2013;6(6):e80-4.
- Mikut R, Dickmeis T, Driever W, Geurts P, Hamprecht FA, Kausler BX, Ledesma-Carbayo MJ, Marée R, Mikula K, Pantazis P, Ronneberger O, Santos A, Stotzka R, Strähle U, Peyriéras N. Automated processing of zebrafish imaging data: a survey.ZEBRAFISH. 2013;10(3):20.
- Ortuño JE, Ledesma-Carbayo MJ, Simões RV, Candiota AP, Arús C, Santos A. DCE@urLAB: a dynamic contrast-enhanced MRI pharmacokinetic analysis tool for preclinical data. BMC Bioinformatics. 2013 Nov 4;14:316.
- Martí Fuster B, Esteban O, Planes X, Aguiar P, Crespo C, Falcon C et al.. FocusDET, a new toolbox for SISCOM analysis. Evaluation of the registration accuracy using Monte Carlo simulation.Neuroinformatics. 2013 Jan;11(1):77-89.
- García-Álvarez A, Fernández-Friera L, García-Ruiz JM, Nuño-Ayala M, Pereda D, Fernández-Jiménez R, Guzmán G, Sánchez-Quintana D, Alberich-Bayarri A, Pastor D, Sanz-Rosa D, García-Prieto J, González-Mirelis JG, Pizarro G, Jiménez-Borreguero LJ, Fuster V, Sanz J, Ibáñez B. Noninvasive monitoring of serial changes in pulmonary vascular resistance and acute vasodilator testing using cardiac magnetic resonance.J AM COLL CARDIOL. 2013;62(17):1621-31.

Highlights

The main results achieved during 2013 are:

- Research on a new automatic method for determining the prognosis of a patient suffering from pulmonary embolism from CT images has resulted in a US patent application and a research contract signed with Massachusetts Institute of Technology & Fundación madri+d para el Conocimiento.
- Research on image-guided radiotherapy has produced a technology transfer to the Spanish company GMV of a Monte Carlo simulation-based tool for treatment planning in Intraoperative Radiation Therapy.
- A new European research program has been started: BiopsyPen (7FP): Optical Biopsy Pen – A Compact and Low-Cost Diagnostic Tool for Dermatology based on High-performing Integrated OCT.
- A member of the group has been nominated ASHOKA fellow for his work on Games and Crowdsourcing for Medical Image Diagnosis.

PROGRAMME:
Nanomedicine

Nanomembrane Group (NANOMEMB-UB)

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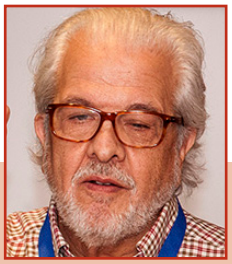

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Main lines of research

- 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

- Nevola L, Martín-Quirós A, Eckelt K, Camarero N, Tosi S, Llobet A et al.. Light-regulated stapled peptides to inhibit protein-protein interactions involved in clathrin-mediated endocytosis.Angew Chem Int Ed Engl. 2013 Jul 22;52(30):7704-8.
- Lima LM, Giannotti MI, Redondo-Morata L, Vale ML, Marques EF, Sanz F. Morphological and nanomechanical behavior of supported lipid bilayers on addition of cationic surfactants.Langmuir. 2013 Jul 30;29(30):9352-61.
- Izquierdo-Serra M, Trauner D, Llobet A, Gorostiza P. Optical control of calcium-regulated exocytosis.Biochim Biophys Acta. 2013 Mar;1830(3):2853-60.
- Madrigal MMP, Giannotti MI , Oncins G , Franco L , Armelin E, Puiggali J, Sanz F , del Valle LJ, Aleman C. Bioactive nanomembranes of semiconductor polythiophene and thermoplastic polyurethane: thermal, nanostructural and nanomechanical properties. Polymer Chemistry. 2013;4(3):568-583.
- Hoyo J, Guaus E, Oncins G, Torrent-Burgués J, Sanz F. Incorporation of ubiquinone in supported lipid bilayers on ITO.J Phys Chem B. 2013 Jun 27;117(25):7498-506.

Highlights

We have continued the research line on Scanning Tunneling Spectroscopy (STS) response of single proteins under electrochemical control. In particular, we have measured redox fluctuations in the tunneling current of azurin that suggest limits to the miniaturization of bioelectronic devices like single protein transistors.

In "Nanomechanics of biosystems" 2 new articles in the field have been published: one in lipid bilayer response in the presence of surfactants (http://dx.doi.org/10.1021/la400067n) and other in polymer scaffolds (http://dx.doi.org/10.1021/bm4005436) in collaboration with the GBBIT-IBEC group from CIBER-BBN.

Outstanding results in the application of light-activated nanoswitches are the development of photo switchable inhibitors of protein-protein interactions, synthetic peptides whose structure can be regulated by light that and we term traffic light peptides. These peptides allow controlling remotely clathrin mediated endocytosis an important pathway for cellular uptake of nutrients and/or membrane proteins. This research was published in Angewandte Chemie, being also featured in "faculty of 1000" and attracting substantial interest in general public media (e.g. Radio, newspapers). These results have served to apply for an ERC Proof of Concept grant in H2020.

During 2013 the capabilities developed by Nanoxen+ project (e.g. *in vivo* testing with small transparent animals) have been instrumental to demonstrate the pharmacological importance of a light-regulated drug, an allosteric modulator of metabotropic glutamate receptors. These results are currently under review and have served to submit an additional ERC Proof of Concept grant in H2020.

In the case of the "NanoFabry" CIBER-BBN project granted by La Marató TV3 (2011-2013), we have refined the nanoconjugate structure, finished the test of toxicology in the synthetic route, and began with the test in vivo murine models. In parallel, we have defined the best conditions for the cryogenic storage of the conjugate that responds fine to a temperature programmed sequence. Besides, we have started with the characterization –morphological, nanomechanical as well as the interactions between the nanoparticles decoration and their cargo of nanocarriers for antiapoptotic drug transport across the Blood-Brain-Barrier, within the CIBER-BBN project "NanoTransBrain".

PROGRAMME:
Nanomedicine

Drug Delivery and Targeting Group (GDLF-HUVH)

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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

- Cabrera I, Elizondo E, Esteban O, Corchero JL, Melgarejo M, Pulido D et al.. Multifunctional nanovesicle-bioactive conjugates prepared by a one-step scalable method using CO2-expanded solvents.Nano Lett. 2013 Aug 14;13(8):3766-74.
- Gomes-da-Silva LC, Fernández Y, Abasolo I, Schwartz S Jr, Ramalho JS, Pedroso de Lima MC et al.. Efficient intracellular delivery of siRNA with a safe multitargeted lipid-based nanoplatform.Nanomedicine (Lond). 2013 Sep;8(9):1397-413.
- Corchero JL,. Unconventional microbial systems for the cost-efficient production of high-quality protein therapeutics.Biotechnology advances. 2013;Número: 15 Volume: 31 Issue: 2 Pages: (15, 31, 2):140-153 .
- Fontrodona L, Porta-de-la-Riva M, Morán T, Niu W, Díaz M, Aristizábal-Corrales D et al.. RSR-2, the Caenorhabditis elegans ortholog of human spliceosomal component SRm300/SRRM2, regulates development by influencing the transcriptional machinery.PLoS Genet. 2013 Jun;9(6):e1003543.
- Mazzolini R, Rodrigues P, Bazzocco S, Dopeso H, Ferreira AM, Mateo-Lozano S, Andretta E, Woerner SM, Alazzouzi H, Landolfi S, Hernández-Losa J, Macaya I, Suzuki H, Ramón y Cajal S, Mooseker MS, Mariadason JM, Gebert J, Hofstra RM, Reventós J, Yamamoto H, Schwartz S Jr, Arango D. Brush border myosin Ia inactivation in gastric but not endometrial tumors.International journal of cancer. Journal international du cancer. 2013;132(8):1790-9.

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 two ERANET projects focused in nanomedicine applications involving SME's in which animal models are being used for preclinical validation of new therapies directed against tumor cells (IMMAPROT on Industrial biotechnology – ERA-IB; NANOSTEM – EuroNanoMed, coordinated by him), and an international project of the Iberian Nanotechnology Institute (OncoNanoTarget). Two additional projects from Marató TV3 (focused in drug delivery systems for the Fabry disease) and INNPACTO (also involving industry) were granted in 2013, and 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 and a new PCT has been issued on liposomal formulations. 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), and also a core member of the Nanomedicine networks "NanoBioMed Catalunya" and "CONNECT-EU". Dr Schwartz has also been appointed as Scientific Advisor by the Southern Denmark University of the excellence center NANOCAN for Nanomedicine. Further, Dr Schwartz's group published papers in top science journals in 2013. Dr Schwartz's has been also nominated associate editor of Nanomedicine NMB (FI:6,9)

PROGRAMME:
Nanomedicine

Colloidal and Interface Chemistry Group, Instituto de Química Avanzada de Cataluña (QCI-CSIC)

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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 nanoemulsion 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-Ruíz G, Melgar-Lesmes P, Solans C, García-Celma MJ. Multifunctional polyurethane-urea nanoparticles to target and arrest inflamed vascular environment: a potential tool for cancer therapy and diagnosis.J Control Release. 2013 Oct 28;171(2):163-71.
- Nestor J, Vílchez A, Solans C, Esquena J. Facile synthesis of meso/macroporous dual materials with ordered mesopores using highly concentrated emulsions based on a cubic liquid crystal.Langmuir. 2013 Jan 8;29(1):432-40.
- Llinàs M, Calderó G, García-Celma MJ, Patti A, Solans C. New insights on the mechanisms of drug release from highly concentrated emulsions.J Colloid Interface Sci. 2013 Mar 15;394:337-45.
- Serrà A, Gómez E, Calderó G, Esquena J, Solans C, Vallés E. Microemulsions for obtaining nanostructures by means of electrodeposition methodELECTROCHEM COMMUN. 2013;27:14-18.
- Vilanova N, Rodríguez-Abreu C, Fernández-Nieves A, Solans C. Fabrication of novel silicone capsules with tunable mechanical properties by microfluidic techniques.ACS Appl Mater Interfaces. 2013 Jun 12;5(11):5247-52.

Highlights

The research activities have mainly focused to the design of advanced multifunctional nanocarriers for the therapy of neurodegenerative diseases performed in the frame of the CIBER-BBN intramural project Nano-Trans-Brain. Polymeric nanoparticles with tuneable characteristics have been prepared by nano-emulsion templating and functionalized with carbosilane dendrons and monoclonal antibodies for the specific blood-brain barrier (BBB) targeting. Binding of oligonucleotides and encapsulation of antiapoptotic drugs to the nanoparticles have been successfully achieved.In vitro and in vivo evaluation of the designed nanocarriers has showed that they are appropriate for the intended application. The nano-emulsion templating technology developed in our group allows nanoparticle size control and high drug entrapment efficiency using biocompatible components. Moreover, this technology can be performed under mild processing conditions (e.g. at low temperature, 25ºC, allowing the preservation of pharmacological properties of drug molecules chemically unstable at high temperature), requires simple equipment and it is easily scalable. 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), "Nanoparticles in food: analytical methods for detection and characterization" FP7-245162, "Tecnologías de autoagregación de moléculas anfifílicas para aplicaciones terapéuticas" (CTQ2011-29336-C03-02), "Estudios experimentales y teóricos de procesos de autoagregación de compuestos anfifilicos biocompatibles para el diseño de nanomateriales avanzados"(CTQ2011-29336-C03-01) and 17) and "Formación de emulsiones de Pickering mediante métodos de baja energía para la preparación de nuevos materiales porosos nanocompuestos" (CTQ2011- 23842). The most important outcomes of the results obtained are reflected in 22 indexed publications and 3 book chapters, as well as in the presentation of 18 (two of them invited) oral and 23 poster presentations in national and international conferences. Five PhD and 3 Master thesis have been presented.

PROGRAMME:
Biomaterials and Tissue Engineering

Research Group in Intelligent Biomaterials

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Main lines of research

- Ordered mesoporous silica materials:
  - Functionalized with dendritic macromolecules
  - Biologically active molecule release systems.
  - Gene transfection.
  - Mesoporous bioactive glasses.
- Organic-inorganic hybrid materials: Nanostructured from dendritic networks.
- Intelligent supports for regenerative medicine. Manufacture of three-dimensional scaffolds for bone regeneration.
  - Functionalized calcium phosphates
  - Si-hidroxyapatite/biopolymers scaffolds for bone regeneration.
  - Incorporation in the surface of parathyroid hormone-related peptides (PTHrP).
  - Incorporation of antimicrobial agents.
  - Design of zwitterionic surface with antimicrobial activity.
- Stimuli-responsive systems based on mesoporous silica nanoparticles.

- Magnetic nanoparticles as thermoseeds for the treatment of tumors by hyperthermia.
- Magnetic nanoparticles-dendrimer systems for gene transfection.
- Controlled drug release systems in target tissues and organs.
- Nanoparticles for cancer treatment.

Most relevant scientific articles

- M. Colilla, B. González, M. Vallet-Regí. Mesoporous silica nanoparticles for the design of smart delivery nanodevices. biomaterials Science. 2013;:114-134.
- D. Arcos, M. Vallet-Regí. Bioceramics for drug deliveryacta mater. 2013;61(3): 890-911.
- S. Sánchez-Salcedo, M. Colilla, I. Izquierdo and M. Vallet-Regí. Design and preparation of biocompatible zwitterionic hydroxyapatite. J MATER CHEM. 2013;1(11):1595-1606.
- R. Mathew, C. Turdean-Ionescu, I. Izquierdo-Barba, A. García, D. Arcos, M. Vallet-Regí and M. Edén.. Direct probing of the spatial distribution of phosphate ions in bioactive silicate glasses by solid-state NMR. Chemistry of materials . 2013;25(9):1877-1885.
- González B, Colilla M, Vallet-Regí M. Design of in vitro bioactive hybrid materials from the first generation of amine dendrimers as nanobuilding blocks.Chemistry. 2013 Apr 8;19(15):4883-95.

Highlights

The most important achievements during 2013 include the preparation, optimization and implantation of three-dimensional scaffolds based on various bioceramics, as well as of new biologically functionalized mesoporous systems with osteogenic agents. The launch of a new research area in nanotechnology, for the development of non-viral magnetic vectors for gene transfection and antitumoral therapy, is also highlighted.

During 2013 GIBI group has developed different research lines in the frame of different national and international research projects including MAT2012-35556, S2009/MAT-1472, FP7-PEOPLE-2007-2-2-ERG, CSO2010-11384-E, AP/042845/11 and MAT2008-00736. GIBI group is member of the Research Institute of "Hospital 12 de Octubre (i+12)", Research Network of Excellence of Madrid Community (Spain) and the Spanish and European Network of Excellence for prevention and treatment of osteoporotic fractures (Agening). Moreover, GIBI group has been also involved in science spreading actions during 2013, specifically in organizing an International symposium on Agening and Osteosporosis (Fundación Ramón Areces).

During 2013, GIBI group has published 18 original research articles, 4 reviews, and 1 book chapters and 2 complete books enclosed in smart biomaterials for drug delivery and bone tissue regeneration purposes:

- "Biomedical Applications of Mesoporous Ceramics: Drug Delivery, Smart Materials and Bone Tissue Engineering" by María Vallet-Regí; Miguel Manzano García; Montserrat Colilla CRC Press, 2013. ISBN 9781439883075.
- "Biomaterials", from the series "What do we know about…?" from the Spanish National Research Council (CSIC) by Maria Vallet-Regí ISBN 978-84-00-09756-1.

Furthermore, recently the book "Bio-Ceramics with Clinical Applications" has just been published by John Wiley & Sons Ltd, Chichester, UK, edited by Prof. Maria Vallet-Regi (ISBN: 978-111840675). This book provides a cohesive, structured account of the advances and new applications of bioceramics in the clinical world.

Finally, María Vallet-Regí (IP) has been awarded with the IUPAC 2013 Prize as Distinguished Woman in Chemistry or Chemical Engineering and the Prize Miguel Catalán 2013.

PROGRAMME:
Nanomedicine

Molecular Nanoscience and Organic Materials Group

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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

- Mas-Torrent M, Rovira C, Veciana J. Surface-confined electroactive molecules for multistate charge storage information.Adv Mater. 2013 Jan 18;25(3):462-8.
- Cabrera I, Elizondo E, Esteban O, Corchero JL, Melgarejo M, Pulido D et al.. Multifunctional nanovesicle-bioactive conjugates prepared by a one-step scalable method using CO2-expanded solvents.Nano Lett. 2013 Aug 14;13(8):3766-74.
- Tatkiewicz WI, Seras-Franzoso J, García-Fruitós E, Vazquez E, Ventosa N, Peebo K et al.. Two-dimensional microscale engineering of protein-based nanoparticles for cell guidance.ACS Nano. 2013 Jun 25;7(6):4774-84.
- Seras-Franzoso J, Steurer C, Roldán M, Vendrell M, Vidaurre-Agut C, Tarruella A et al.. Functionalization of 3D scaffolds with protein-releasing biomaterials for intracellular delivery.J Control Release. 2013 Oct 10;171(1):63-72.
- Vera F, Mas-Torrent M, Avci C, Arbiol J, Esquena J, Rovira C et al.. Robust molecular micro-capsules for encapsulating and releasing hydrophilic contents.Chem Commun (Camb). 2013 Sep 14;49(71):7827-9.

Highlights

- 28 scientific publications in JCR journals with an average impact factor of 6,165.
- 20 invited lectures given in international conferences.
- Beginning of activities of the FP7 funded projects Nano2Fun and Common Sense.
- Participation in the INNPACTO ORALBEADS project coordinated by the PHARMAMAR company.
- Implementation of scientific activities of ERC Starting Grat project in 2012 "e-GAMES"
- Participation in the 2012 7th FP granted European project BERENICE.
- Execution of scientific activities of CIBER-BBN intramural projects: NANOFABRY II, PROGLIO II, NANOPROVIR, NANORETINA, ULTRASEN4BIO and NAINBO II.
- Prof. C. Rovira and Dr. M. Mas-Torrent have been awarded, respectively, with international prizes "IUPAC 2013 Distinguished Women in Chemistry or Chemical Engineering" and "Fourth Olivier Kahn International Award". Dr. N. Crivillers was awarded with the prize for young researchers of the "Real Sociedad Española de Química"
- The most remarkable scientific and technological results have been:

  a) 2- and 3-D microscale engineering of protein-based nanoparticles for cell guidance.

  b) Surface-confined electroactive molecules for multistate charge storage information.

  c) Study of bistability phenomena of molecule-based dyads with potential applications as memories and sensors.

  d) Photo-induced intramolecular charge transfer in an ambipolar field-effect transistor based on a π-conjugated donor–acceptor dyad.

  e) Synthesis and structural characterization of radical dendrimers with TEMPO Radicals for their use as MRI agents.

  f) Multifunctional nanovesicle-bioactive conjugates prepared by a one-step scalable method using CO2-expanded solvents.

  g) A PCT patent of a novel nanoliposome based nanomedicine candidate for the treatment of Fabry's rare disease, with promising pre-clinical results compared to current treatment.

  h) A PCT patent of an innovative nanomedicine, composed of EGF conjugated to new highly stable nanovesicular structures, branded Quatsomes, for topical treatment of diabetic foot ulcer which has been recently licensed.

  i) New organic field effect transistors as potential sensors.

PROGRAMME:
Biomaterials and Tissue Engineering

Research Group in Bone Physiopathology and Biomaterials, Hospital Universitario La Paz

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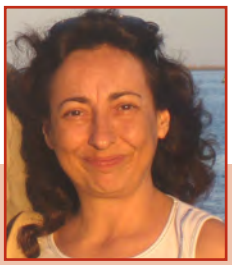

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Main lines of research

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

Most relevant scientific articles

- Cebrián V, Martín-Saavedra F, Gómez L, Arruebo M, Santamaria J, Vilaboa N. Enhancing of plasmonic photothermal therapy through heat-inducible transgene activity.Nanomedicine. 2013 Jul;9(5):646-56.
- Vegas MR, Martín-Hervas C. The superolateral thigh flap: cadaver and computed tomographic angiography studies with a clinical series.Plast Reconstr Surg. 2013 Feb;131(2):310-22.
- Vallés G, Pérez C, Boré A, Martín-Saavedra F, Saldaña L, Vilaboa N. Simvastatin prevents the induction of interleukin-6 gene expression by titanium particles in human osteoblastic cells.Acta Biomater. 2013 Jan;9(1):4916-25.
- Frutos E., González-Carrasco JL.. A method to assess the fracture toughness of intermetallic coatings by ultramicroindentation techniques: Applicability to coated medical stainless steelACTA MATER. 2013;61:1886-1894.
- Martín-Saavedra FM, Wilson CG, Voellmy R, Vilaboa N, Franceschi RT. Spatiotemporal control of vascular endothelial growth factor expression using a heat-shock-activated, rapamycin-dependent gene switch.Hum Gene Ther Methods. 2013 Jun;24(3):160-70.

Highlights

The group of Bone Physiopathology and Biomaterials has performed a thorough characterization of several modifications of medical 316 LVM steel and Ti64 alloys, including oxidation, thermolectrical power, mechanical and biocompatibility tests. The group has progressed in the development of gene switches for the spatial and temporal regulation of therapeutic transgenes, which are currently being adapted to control osteogenic and angiogenic growth factors in tissue engineering applications. Furthermore, the capacity of plasmonic nanoparticles to activate transgenes driven by hsp promoters upon near infrared laser irradiation has been demonstrated. In addition to their participation in 12 clinical trials for medical interventions in bone-related diseases, the clinical scientists of the group have continued their retrospective studies on total hip arthroplasties. Moreover, the group has shown that statins may ameliorate the wear debris-mediated periprosthetic osteolysis by down-regulating IL-6, a key player in this inflammatory process. The group funded its activities by means of grants from MINECO, ISCIII and research contracts with the industry.

PROGRAMME:
Nanomedicine

Nanobiotechnology

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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

- Corchero JL, . Unconventional microbial systems for the cost-efficient production of high-quality protein therapeutics.Biotechnology advances. 2013;Número: 15 Volume: 31 Issue: 2 Pages: (15, 31, 2):140-153 .
- Seras-Franzoso J, Peebo K, Luis Corchero J, Tsimbouri PM, Unzueta U, Rinas U et al.. A nanostructured bacterial bioscaffold for the sustained bottom-up delivery of protein drugs.Nanomedicine (Lond). 2013 Oct;8(10):1587-99.
- Tatkiewicz WI, Seras-Franzoso J, García-Fruitós E, Vazquez E, Ventosa N, Peebo K et al.. Two-dimensional microscale engineering of protein-based nanoparticles for cell guidance.ACS Nano. 2013 Jun 25;7(6):4774-84.
- Seras-Franzoso J, Steurer C, Roldán M, Vendrell M, Vidaurre-Agut C, Tarruella A et al.. Functionalization of 3D scaffolds with protein-releasing biomaterials for intracellular delivery.J Control Release. 2013 Oct 10;171(1):63-72.
- Unzueta U, Saccardo P, Domingo-Espín J, Cedano J, Conchillo-Solé O, García-Fruitós E et al.. Sheltering DNA in self-organizing, protein-only nano-shells as artificial viruses for gene delivery.Nanomedicine. 2013 Nov 21;.

Highlights

The group has devoted most of its activity in 2013 to the resolution of the molecular architecture of bacterial inclusion bodies as nanostructured materials. In particular, it has been determined that the capacity to act as slow release systems both as NANOPILLS or as BIOSCAFFOLDS depends on the proportion of amyloid protein that comprises then, organized in the a sponge-like form. By both regulating the temperature of production and by the right choice of the genetic background, the proportion of amyloid material can be increased (greater mechanical stability and lower protein release) or narrowed (less mechanical stability but greater release). This study is related to the use of the inclusion bodies in regenerative medicine and to their potential as therapeutic agents, which is around the activities associated with the licensed patent WO2010131117.

PROGRAMME:
Nanomedicine

Molecular Immunobiology

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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

- Sainz T, Serrano-Villar S, Díaz L, González Tomé MI, Gurbindo MD, de José MI et al.. The CD4/CD8 ratio as a marker T-cell activation, senescence and activation/exhaustion in treated HIV-infected children and young adults.AIDS. 2013 Jun 1;27(9):1513-6.
- Córdoba EV, Pion M, Rasines B, Filippini D, Komber H, Ionov M et al.. Glycodendrimers as new tools in the search for effective anti-HIV DC-based immunotherapies.Nanomedicine. 2013 Oct;9(7):972-84.
- Córdoba EV, Arnáiz E, De La Mata FJ, Gómez R, Leal M, Pion M et al.. Synergistic activity of carbosilane dendrimers in combination with maraviroc against HIV in vitro.AIDS. 2013 Aug 24;27(13):2053-8.
- Vacas Córdoba E, Arnaiz E, Relloso M, Sánchez-Torres C, García F, Pérez-Álvarez L et al.. Development of sulphated and naphthylsulphonated carbosilane dendrimers as topical microbicides to prevent HIV-1 sexual transmission. AIDS. 2013 May 15;27(8):1219-29.
- Sepúlveda-Crespo D, Lorente R, Leal M, Gómez R, De la Mata FJ, Jiménez JL et al.. Synergistic activity profile of carbosilane dendrimer G2-STE16 in combination with other dendrimers and antiretrovirals as topical anti-HIV-1 microbicide.Nanomedicine.;.

Highlights

The group has obtained funding to develop the proyects: EU-Belarus-Russia Network in Nanomaterials-Driven Anti-Cancer Gene Therapy. NANOGENE. SEVENTH FRAMEWORK PROGRAMME. Cooperation Work Programme: Health-2010. ERA-Net EuroNanoMedicine Identification: 316730 / PIRSES-GA-2012-316730. Proyect: Desarrollo y mecanismo de acción de dendrímeros como microbicidas para frenar la infección por VIH por transmisión sexual (vaginal y anal): prueba de concepto (FIS PI13/02016), from RED TEMÁTICA Iberoamericano de Ciencia y Tecnología para el Desarrollo (CYTED): Desarrollo de una vacuna frente a VIH: estudio de los cambios en la biología de células dendríticas humanas tras interacción con distintos sistema de liberación de péptidos de VIH (VIHVACD) (participate Chile, Argentina, Perú, Mexico, Portugal, Spain), also take part in SUBPROGRAMA RETICS (Redes Temáticas de Investigación Cooperativa en Salud). Identification: RD 12/0017/0037; and Redes Moleculares y Celulares en Enfermedades Inflamatorias proyect: INDISNET.Identification: S2010/BMD-2332

Molecular Immunobiology group develops the Coordination and Direction of HIV-HGM BioBank and its Reposity associated. HIV-HGM BioBank criopreserves very valuable collections in several pathologies as HIV, cancer, rare illness, respiratory, endocrine and infectious diseases.

RESEARCH PUBLICATIONS & H FACTOR

- 2013: 33 Articles in 1st Decilee/Quartile–2013 IF: 4,174– Accumulated IF: 4,364.
- Total articles: 186 Articles in 1st Decilee/Quartile – Accumulated 1994-2014 IF: 4,740
- IP H factor: 29

RESEARCH PROYECTS

- 2013 : 11 National & International Research Proyects as IP or Coordinator
- 4 National & International Research Proyects as collaborator
- Total proyects: 46 National & International Research Proyects as IP or Coordinator
- 22 National & International Research Proyects as collaborator

DIRECTED DOCTORAL THESIS

- 2014: 4 National & International doctoral thesis
- Total thesis: 39 National & International doctoral thesis

PATENTS & SPIN OFFS

- 14 patents or utility models as applicant or inventor.

PCT/ES2013/0705 ADMITED IN 2013

- 2 start ups (GENOMADRID SL, DendriCo SL) & 1 spin off (Ambiox Biotech SL) in active 2013.

PROGRAMME:
Nanomedicine

Cellular and Respiratory Biomechanics Group

Group Members

STAFF MEMBERS

Polo Tortola, Maeba

ASSOCIATED MEMBERS

Alcaraz Casademunt, Jordi
Campillo Agulló, Noelia
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Farre Ventura, Ramon
Garreta Bahima, Elena
Isseta, Valentina
Luque González, Tomás Alberto
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Main lines of research

- Pathophysiology of sleep apnea and acute lung injury in patients and in animal models.
- Cell and Tissue Mechanobiology in respiratory diseases.
- Instrumentation and diagnostic, therapeutic and monitoring methodologies for sleep apnea and acute lung injury.
- Nanotechnologies and lab-on-a–chip devices for the study and characterization of the mechanical behavior of cells and tissues.

Most relevant scientific articles

- Campos-Rodríguez F, Martínez-García MA, Martínez M, Durán-Cantolla J, Peña M de L, Masdeu MJ. Association between obstructive sleep apnea and cancer incidence in a large multicenter Spanish cohort.Am J Respir Crit Care Med. 2013 Jan 1;187(1):99-105.
- Franquesa M, Hoogduijn MJ, Reinders ME, Eggenhofer E, Engela AU, Mensah FK. Mesenchymal Stem Cells in Solid Organ Transplantation (MiSOT) Fourth Meeting: lessons learned from first clinical trials.Transplantation. 2013 Aug 15;96(3):234-8.
- Kim JH, Serra-Picamal X, Tambe DT, Zhou EH, Park CY, Sadati M. Propulsion and navigation within the advancing monolayer sheet.Nat Mater. 2013 Sep;12(9):856-63.
- Luque T, Melo E, Garreta E, Cortiella J, Nichols J, Farré R. Local micromechanical properties of decellularized lung scaffolds measured with atomic force microscopy.Acta Biomater. 2013 Jun;9(6):6852-9.
- Li Bassi G, Ranzani OT, Marti JD, Giunta V, Luque N, Isetta V. An in vitro study to assess determinant features associated with fluid sealing in the design of endotracheal tube cuffs and exerted tracheal pressures.Crit Care Med. 2013 Feb;41(2):518-26.

Highlights

The group belongs to the CIBER of Respiratory Diseases and is an associated group of CIBER of Bioengineering, Biomaterials, and Nanomedicine. In CiberES our research is currently focused on the Corporate Programs on Acute Lung Injury Program (ALI) and Sleep Apnea - Hypopnea Syndrome (SAHS). In CiberBBN we participate in the project Multimodal Diagnosis by Signal Interpretation of the Respiratory System oriented to Pulmonary Diseases and Sleep Disorders (MUDIRES-2PSD). Our research is interdisciplinary and is developed in collaboration with other groups of the CIBER. We transfer technology by means of contracts with companies of respiratory medical devices.

In SAHS program our group is active in the study of the pathophysiology and consequences of the disease. Members of the group have led two publications in 2013 based on a mouse model of melanoma and intermittent hypoxia, showing for the first time that intermittent hypoxia similar to OSA increases tumor growth - probably via overexpression of vascular endothelial growth factor – and promotes tumor metastasis to the lung. We have also published two studies in patients revealing a significant incidence/mortality of cancer in patients with SAHS. The group leads a Work Package of the European project CHROMED on home monitoring in patients with chronic respiratory diseases. We have also developed a platform for telematics control of CPAP treatment in patients with sleep apnea at home.

Within the ALI program and in order to understand the mechanisms that govern the cell-matrix interplay in lung repair/regeneration we have characterized the mechanical properties of the lung extracellular matrix by means of nanotechnologies. This work has revealed for the first time the mechanical heterogeneity of the cell niche in different lung structures. In addition, we have evaluated the effect of different decellularization procedures on the nanomechanics of lung matrix. Moreover, the mechanical forces governing collective migration involved in the tissue repair mechanisms have been identified. We have also developed a lab-on-a-chip device to study the cellular response to cyclic deformation.

6
Annex

Affiliated Publications CIBER-BBN

PI	Vancouver Citation	Pubmed Id	Quartile	IF	CIBER-BBN groups
Aguiló LLobet, Jordi	Altuna A, Bellistri E, Cid E, Aivar P, Gal B, Berganzo J, Gabriel G, Guimerà A, Villa R, Fernández LJ, Menendez de la Prida L. SU-8 based microprobes for simultaneous neural depth recording and drug delivery in the brain.Lab on a chip. 2013;13(7): 1422-1430.	23407672	1	5,67	Jordi Aguiló LLobet, Manuel Doblaré Castellano,
Aguiló LLobet, Jordi	Guimerà A, Illa X, Traver E, Plata-Cordero M, Yeste J, Herrero C et al. Flexible probe for in vivo quantification of corneal epithelium permeability through non-invasive tetrapolar impedance measurements.Biomed Microdevices. 2013 Oct;15(5):849-58.	23660841	1	2,718	Jordi Aguiló Llobet
Aguiló LLobet, Jordi	Martín-Fernández I, Gabriel G, Guimera A, Palomer X, Reig R, Sanchez-Vives MV, Villa R, Godignon P. Multi-walled carbon nanotube based multi-electrode arrays for the detection of the emergent activity in the cortical networkMICROELECTRON ENG. 2013;112:14-20.	-	2	1,224	Jordi Aguiló Llobet
Aguiló LLobet, Jordi	Viñas JL, Ventayol M, Brüne B, Jung M, Sola A, Pi F et al. miRNA let-7e modulates the Wnt pathway and early nephrogenic markers in mouse embryonic stem cell differentiation.PLoS One. 2013;8(4):e60937.	23593353	1	3,73	Jordi Aguiló Llobet
Aguiló LLobet, Jordi	Martí J, Fuster J, Solà AM, Hotter G, Molina R, Pelegrina A et al. Prognostic value of serum neutrophil gelatinase-associated lipocalin in metastatic and nonmetastatic colorectal cancer.World J Surg. 2013 May;37(5):1103-9.	23389669	2	2,228	Jordi Aguiló Llobet
Aguiló LLobet, Jordi	Prats-Alfonso, Elisabet; Oberhansl, Sabine; Lagunas, Anna; Martínez, Elena; Samitier, Josep; Albericio, Fernando. Effective and Versatile Strategy for the Total Solid-Phase Synthesis of Alkanethiols for Biological Applications. Eur J Org Chem. 2013;(7):1233–1239.	-	1	3,344	Josep Samitier Martí, Fernando Albericio Palomera, Jordi Aguiló Llobet
Albericio Palomera, Fernando	Cabrera I, Elizondo E, Esteban O, Corchero JL, Melgarejo M, Pulido D et al. Multifunctional nanovesicle-bioactive conjugates prepared by a one-step scalable method using CO2-expanded solvents.Nano Lett. 2013 Aug 14;13(8):3766-74.	23829208	1	13,025	Jaume Veciana Miró, Fernando Albericio Palomera, Simó Schwartz Navarro, Antoni Villaverde Corrales
Albericio Palomera, Fernando	Camunas-Soler, S. Frutos, C.V. Bizarro, S. de Lorenzo, M.E. Fuentes-Perez, R. Ramsch, S. Vilchez, C. Solans, F. Moreno-Herrero, F. Albericio, R. Eritja, E. Giralt, S.B. Dev and F. Ritort. Electrostatic binding and hydrophobic collapse of peptide-nucleic acid aggregates quantified using force spectroscopy. ACS NANO. 2013;7(6): 5102-5113.	23706043	1	12,062	Fernando Albericio Palomera, Concepción Solans Marsà, Félix Ritort Farran, Ramón Eritja Casadellà
Albericio Palomera, Fernando	Simón-Gracia L, Pulido D, Sevrin CH, Grandfils C, Albericio F, Royo M. Biocompatible, multifunctional, and well-defined OEG-based dendritic platforms for biomedical applications.Organic & Biomolecular Chemstry. 2013;11(24):4109-4121.	23673687	1	3,568	Fernando Albericio Palomera
Albericio Palomera, Fernando	Silvia Vilches, Cristina Vergara, Oriol Nicolas, Gloria Sanclimens, Sandra Merino, Sonia Varón, Gerardo A. Acosta, Fernando Albericio, Miriam Royo , Jose A. Del Río, Rosalina Gavin. Neurotoxicity of Prion Peptides Mimicking the Central Domain of the Cellular Prion Protein.PLOS One. 2013;8(8):e70881.	23940658	1	3,73	Fernando Albericio Palomera

Albericio Palomera, Fernando	Ángela Torres, Fernando Albericio, Miriam Royo. Polyproline–OEG Co-Oligomeric Dendrimers: A Family of Highly Branched Polyproline Macromolecules.Eur. J. Org. Chem. 2013;2013(36): 8279–8287.	-	1	3,344	Fernando Albericio Palomera
Albericio Palomera, Fernando	Pelay-Gimeno M, Meli A, Tulla-Puche J, Albericio F. Rescuing Biological Activity from Synthetic Phakellistatin 19.J. Med. Chem. 2013;56(23):9780-9788.	24252114	1	5,614	Fernando Albericio Palomera
Albericio Palomera, Fernando	Silvana L. Giudicessi, Juan M. Gurevich-Messina, María C. Martínez-Ceron,Rosa Erra-Balsells, Fernando Albericio,Osvaldo Cascone,Silvia A. Camperi. Friendly Strategy to Prepare Encoded One Bead-One Compound Cyclic Peptide Library.ACS Comb Sci. 2013;15(10):525-529.	23971518	1	3,636	Fernando Albericio Palomera
Albericio Palomera, Fernando	Ana I. Fernández-Llamazares, Jesús García, Jaume Adan, David Maunier, Francesc Mitjans, Jan Spengler, Fernando Albericio. The Backbone N-(4-Azidobutyl) Linker for the Preparation of Peptide Chimera.Organic Letters. 2013;15(17):4572-4575.	24006938	1	6,142	Fernando Albericio Palomera
Albericio Palomera, Fernando	Prabhakar Cherkupally, Gerardo A. Acosta, Lin Spengler-dia Nieto-Rodríguez, Hortensia Rodríguez. Sherine N. Khattab, Ayman El-Faham,Marina Shamis, Yoav Luxembourg, Rafel Prohens, Ramon Subiros-Funosas,and Fernando Albericio. K-Oxyma: A strong acylation-promoting, 2-CTC resin-friendly coupling additive.Eur J. Org Chem . 2013;(23):6372-6378.	-	1	3,344	Fernando Albericio Palomera
Albericio Palomera, Fernando	Xavier Just-Baringo,[Fernando Albericio, and Mercedes Álvarez*. From 2,6-Dichloronicotinic Acid to Thiopeptide Cores.Eur J. Org Chem. 2013;2013(28):6404–6419.	-	1	3,344	Fernando Albericio Palomera
Albericio Palomera, Fernando	Marta Paradís-Bas, Judit Tulla-Puche, Aikaterini A. Zompra, Fernando Albericio. RADA-16: A Tough Peptide – Strategies for Synthesis and Purification.Eur J. Org Chem. 2013;2013(26):5871-5878.	-	1	3,344	Fernando Albericio Palomera
Albericio Palomera, Fernando	Tobias M. Postma, Fernando Albericio. N-chlorosuccinimide, an efficient peptide disulfide bond-forming reagent in aqueous solution.RSC Advances. 2013;3(34):14277-14280.	-	2	2,562	Fernando Albericio Palomera
Albericio Palomera, Fernando	Fanny Guzmán, Sergio Marshall, Claudia Ojeda, Fernando Albericio, Patricio Carvajal-Rondanelli. Inhibitory effect of short cationic homopeptides against Gram-positive bacteria.J. Pept. Sci. 2013;19(12):792–800.	24243601	2	2,071	Fernando Albericio Palomera
Albericio Palomera, Fernando	Rajshekhar Karpoormath, Fernando Albericio, Thavendran Govender, Glenn E. M. Maguire, Hendrik G. Kruger. Synthesis and NMR elucidation of pentacycloundecane-derived hydroxy acid peptides as potential anti-HIV-1 agents.Struct Chem . 2013;24(5):1461–1471.	-	2	1,772	Fernando Albericio Palomera
Albericio Palomera, Fernando	Sara Preciado, Lorena Mendive-Tapia, Fernando Albericio, and Rodolfo Lavilla. Synthesis of C-2 Arylated Tryptophan Amino Acids and Related Compounds through Palladium-Catalyzed C-H Activation.J. Org. Chem. 2013;78(16):8129-8135.	23865986	1	4,564	Fernando Albericio Palomera
Albericio Palomera, Fernando	Ana I. Fernández-Llamazares, Jesús García, Vanessa Soto-Cerrato, Ricardo Perez-Tomas, Jan Spengler, Fernando Albericio. N-Triethylene glycol (N-TEG) as a surrogate for the N-methyl group: application to Sansalvamide A peptide analogs.ChemComm. 2013;49(57):6430-6432.	23752923	1	6,378	Fernando Albericio Palomera
Albericio Palomera, Fernando	Marta Pelay-Gimeno, Judit Tulla-Puche, Fernando Albericio . "Head-to-Side-Chain" Cyclodepsipeptides of Marine Origin. Marine Drugs. 2013;11(5):1693-1717.	23697952	1	3,978	Fernando Albericio Palomera
Albericio Palomera, Fernando	Xavier Just-Baringo, Paolo Bruno, Lars K. Ottesen, Librada M. Cañedo, Fernando Albericio, Mercedes Alvarez. Total Synthesis and Stereochemical Assignment of Baringolin. Angew. Chem. Int Ed. . 2013;52(30):7818 –7821.	2378064	1	13,734	Fernando Albericio Palomera
Albericio Palomera, Fernando	JuJudit Tulla-Puche, Sara Auriemma, Chiara Falciani, Fernando Albericio. Orthogonal Chemistry for the Synthesis of Thiocoraline--Triostin Hybrids. Exploring their Structure-Activity Relationship.Journal of Medicinal Chemistry . 2013;56(13):5587-5600.	3746132	1	5,614	Fernando Albericio Palomera
Albericio Palomera, Fernando	Vida Castro, Juan B. Blanco-Canosa, Hortensia Rodríguez, Fernando Albericio. Imidazole-1-sulfonyl Azide-Based Diazo-Transfer Reaction for the Preparation of Azido Solid Supports for Solid-Phase Synthesis.ACS Comb Sci. 2013;15(7):331-334.	23721561	1	3,636	Fernando Albericio Palomera

Albericio Palomera, Fernando	Ramon Subirós-Funosas, Lidia Nieto-Rodríguez, Knud J. Jensenc, Fernando Albericio. COMU: scope and limitations of the latest innovation in peptide acyl transfer reagents.J.Pept.Sci. 2013;19(7):408–414.	23712932	2	2,071	Fernando Albericio Palomera
Albericio Palomera, Fernando	Joan Camunas-Soler, Silvia Frutos, Cristiano V. Bizarro, Sara de Lorenzo, María Eugenia Fuentes-Perez, Roland Ramsch, Susana Vilchez, Conxita Solans, Fernando Moreno-Herrero, Fernando Albericio, Ramon Eritja, Ernest Giralt, Sukhendu B. Dev,Felix Ritort. Electrostatic Binding and Hydrophobic Collapse of Peptide.ACS Nano. 2013;7(6): 5102-5113.	-	1	12,062	Fernando Albericio Palomera, Concepción Solans Marsà, Félix Ritort Farran, Ramón Eritja Casadellà
Albericio Palomera, Fernando	Santiago Rojas, Pau Nolis, Juan D. Gispert, Jan Spengler, Fernando Albericio, Jose´ R. Herance, Sergio Abad. Efficient cysteine labelling of peptides with N-succinimidyl 4-[18F]fluorobenzoate: stability study and in vivo biodistribution in rats by positron emission tomography (PET). RSC Advances. 2013;3:8028–8036.	-	2	2,562	Fernando Albericio Palomera
Albericio Palomera, Fernando	Judit Tulla-Puche, Miriam Gongora-Benitez, Nuria Bayo-Puxan, AndrÉs M. Francesch, Carmen Cuevas, Fernando Albericio. Enzyme-Labile Protecting Groups for the Synthesis of Natural Products: Solid-Phase Synthesis of Thiocoraline.Angewandte Chemie International Edition . 2013;52(22):5726 –5730.	23619769	1	13,734	Fernando Albericio Palomera
Albericio Palomera, Fernando	Adura C, Guerrero S, Salas E, Medel L, Riveros A,‡ Mena J, Arbiol J, Albericio F, Giralt E, Kogan M. Stable Conjugates of Peptides with Gold Nanorods for Biomedical Applications with Reduced Effects on Cell Viability.ACS Appl. Mater. Interfaces. 2013;5(10):4076-4085.	23597259	1	5,008	Fernando Albericio Palomera
Albericio Palomera, Fernando	Jan Spengler, Anna-Iris Fernández-Llamazares, Fernando Albericio. Use of an Internal Reference for the Quantitative HPLC-UV Analysis of Solid-Phase Reactions: A Case Study of 2-Chlorotrityl Chloride Resin.ACS Comb. Sci. . 2013;15(5):229-234.	23521015	1	3,636	Fernando Albericio Palomera
Albericio Palomera, Fernando	Adriana Lorente, Janire Lamariano-Merketegi, Fernando Albericio,Mercedes Álvarez. Tetrahydrofuran-Containing Macrolides: A Fascinating Gift from the Deep Sea.Chem Rev. 2013;113(7):4567-4610.	23506053	1	41,298	Fernando Albericio Palomera
Albericio Palomera, Fernando	Prats-Alfonso, Elisabet; Oberhansl, Sabine; Lagunas, Anna; Martínez, Elena; Samitier, Josep; Albericio, Fernando. Effective and Versatile Strategy for the Total Solid-Phase Synthesis of Alkanethiols for Biological Applications. Eur J Org Chem. 2013;(7):1233–1239.	-	1	3,344	Josep Samitier Martí , Fernando Albericio Palomera, Jordi Aguiló LLobet
Albericio Palomera, Fernando	Custodio, Luisa; Patarra, Joao; Albericio, Fernando; Neng, Nuno Rosa; Nogueira, Jose Manuel Florencio; Romano, Anabela. Extracts from Quercus sp. acorns exhibit in vitro neuroprotective features through inhibition of cholinesterase and protection of the human dopaminergic cell line SH-SY5Y from hydrogen peroxide-induced cytotoxicity. Industrial Crops and Products. 2013;45:114–120.	-	1	2,468	Fernando Albericio Palomera
Albericio Palomera, Fernando	Postma, Tobias M.; Albericio, Fernando. N-Chlorosuccinimide, an Efficient Reagent for On-Resin Disulfide Formation in Solid-Phase Peptide Synthesis.Org Lett . 2013;15(3):616-619.	23320397	1	6,142	Fernando Albericio Palomera
Albericio Palomera, Fernando	astro, Vida; Rodríguez, Hortensia; Albericio, Fernando. Wang Linker Free of Side Reactions.ORG LETT. 2013;15(2):246-249.	23270537	1	6,142	Fernando Albericio Palomera
Albericio Palomera, Fernando	Cruz Luis J; Rueda Felix; Simon Lorena; Cordobilla Begona; Albericio Fernando; C Domingo Joan. Liposomes containing NY-ESO-1/tetanus toxoid and adjuvant peptides targeted to human dendritic cells via the Fc receptor for cancer vaccines.NANOMEDICINE-UK. 2013; 8028-8036.	24047283	1	5,26	Fernando Albericio Palomera
Albericio Palomera, Fernando	Pelay-Gimeno Marta; García-Ramos Yesica; Jesús Martín Maria; Spengler Jan; Molina-Guijarro Jose Manuel; Munt Simon; Francesch Andrés M; Cuevas Carmen; Tulla-Puche Judit; Albericio Fernando. The first total synthesis of the cyclodepsipeptide pipecolidepsin A.Nature Communications. 2013;4(2352):2352.	23989475	1	10,015	Fernando Albericio Palomera
Albericio Palomera, Fernando	Gongora-Benitez, M, Tulla-Puche J, Albericio F. Constella®(EU)-Linzess®(USA): the last milestone in the long journey of the peptide linaclotide and its implications for the future of peptide drugs.Future Medicinal Chemistry. 2013;5(3):291-300.	-	2	3,31	Fernando Albericio Palomera
Albericio Palomera, Fernando	Ramos-Tomillero, Ivan; Mendive-Tapia, Lorena; Gongora-Bentez, Miriam; Nicolas, Ernesto; Tulla-Puche, Judit; Albericio, Fernando. Understanding acid lability of cysteine protecting groups.Molecules. 2013;18(5):5155-5162.	-	2	2,428	Fernando Albericio Palomera

Albericio Palomera, Fernando	Custodio, Luisa; Escapa, Ana Luisa; Patarra, Joao; Aligue, Rosa; Albericio, Fernando; Neng, Nuno Rosa; Nogueira, Jose Manuel Florencio; Romano, Anabela. apwood of carob tree (Ceratonia siliqua L.) as a potential source of bioactive compounds.Records of Natural Products. 2013;7(3):225-229.	-	2	1,56	Fernando Albericio Palomera
Albericio Palomera, Fernando	Preciado, Sara; Mendive-Tapia, Lorena; Torres-García, Carolina; Zamudio-Vazquez, Rubi; Soto-Cerrato, Vanessa; Perez-Tomas, Ricardo; Albericio, Fernando; Nicolas, Ernesto; Lavilla, Rodolfo. Synthesis and biological evaluation of a post-synthetically modified Trp-based diketopiperazine. MedChemComm. 2013;4(8):1171-1174.	-	2	2,722	Fernando Albericio Palomera
Albericio Palomera, Fernando	Subiros-Funosas, Ramon; Khattab, Sherine N.; Nieto-Rodríguez, Lidia; El-Faham, Ayman; Albericio, Fernando. Advances in acylation methodologies enabled by oxyma-based reagents.Aldrichimica Acta. 2013;46(1):21-40.	-	1	12,231	Fernando Albericio Palomera
Albericio Palomera, Fernando	El-Faham, Ayman; Al Marhoon, Zainab; Abdel-Megeed, Ahmed; Albericio, Fernando. OxymaPure/DIC: An efficient reagent for the synthesis of a novel series of 4-[2-(2-Acetylaminophenyl)-2-oxo-acetylamino] benzoyl amino acid ester derivatives.Molecules. 2013;18(12):14747-14759.	-	2	2,428	Fernando Albericio Palomera
Arús Caraltó, Carles	Ortuño JE, Ledesma-Carbayo MJ, Simões RV, Candiota AP, Arús C, Santos A. DCE@urLAB: a dynamic contrast-enhanced MRI pharmacokinetic analysis tool for preclinical data.BMC Bioinformatics. 2013 Nov 4;14:316.	24180558	1	3,024	Carles Arús Caraltó, Andrés Santos Lleó
Arús Caraltó, Carles	Delgado-Goñi T, Campo S, Martín-Sitjar J, Cabañas ME, San Segundo B, Arús C. Assessment of a 1H high-resolution magic angle spinning NMR spectroscopy procedure for free sugars quantification in intact plant tissue.Planta. 2013 Aug;238(2):397-413.	23824526	1	3,347	Carles Arús Caraltó
Arús Caraltó, Carles	Ortega-Martorell S, Ruiz H, Vellido A, Olier I, Romero E, Julià-Sapé M et al. A Novel Semi-Supervised Methodology for Extracting Tumor Type-Specific MRS Sources in Human Brain Data.PLoS One. 2013;8(12):e83773.	24376744	1	3,73	Carles Arús Caraltó
Arús Caraltó, Carles	Rosell A, Morancho A, Navarro-Sobrino M, Martínez-Saez E, Hernández-Guillamon M, Lope-Piedrafita S et al. Factors secreted by endothelial progenitor cells enhance neurorepair responses after cerebral ischemia in mice. PLoS One. 2013;8(9):e73244.	24023842	1	3,73	Carles Arús Caraltó
Arús Caraltó, Carles	Chavarria L, Oria M, Romero-Giménez J, Alonso J, Lope-Piedrafita S, Cordoba J. Brain magnetic resonance in experimental acute-on-chronic liver failure.Liver Int. 2013 Feb;33(2):294-300.	23295057	1	3,87	Carles Arús Caraltó
Arús Caraltó, Carles	Albert Vilamala, Paulo J.G. Lisboa, Sandra Ortega-Martorell, Alfredo Vellido. Discriminant Convex Non-negative Matrix Factorization for the classification of human brain tumours.Pattern Recognition Letters. 2013;34(14):1734-1747.	-	2	1,266	Carles Arús Caraltó
Becerra Ratia, José	Bagó JR, Aguilar E, Alieva M, Soler-Botija C, Vila OF, Claros S et al. In vivo bioluminescence imaging of cell differentiation in biomaterials: a platform for scaffold development.Tissue Eng Part A. 2013 Mar;19(5-6):593-603.	23013334	1	4,065	José Becerra Ratia, Jerónimo Blanco Fernández
Becerra Ratia, José	Arrabal PM, Visser R, Santos-Ruíz L, Becerra J, Cifuentes M. Osteogenic molecules for clinical applications: improving the BMP-collagen system.Biological Research. 2013;46(4):421-9.	24510144	3	1,129	José Becerra Ratia
Becerra Ratia, José	Leal-Egaña A; Díaz-Cuenca A; Boccaccini AR. Tuning of cell-biomaterial anchorage for tissue regeneration.ADV MATER. 2013;25(29):4049–4057.	24063035	1	14,829	José Becerra Ratia
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