ANNUAL REPORT

2015

ciber-bbn

Centro de Investigación Biomédica en Red
Bioingeniería, Biomateriales y Nanomedicina

ciber

Centro de Investigación Biomédica en Red

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Scientific Director's Presentation

I am addressing you as the Scientific Director of the CIBER-BBN for the first time to give a short review of the work done in 2015.

The number of publications with CIBER- BBN affiliation, which had been rising over the last few years, dropped in 2015, possibly due to the reduction in resources through the economic situation. We can indeed affirm nevertheless that we keep up high quality levels in our scientific production, with over 65% of the articles published in journals of the first quartile and 30% in the first decile, these ratios improving in respect of previous years.

In 2015 we took the assessment given by the ISCIII, through an external panel of assessors, on the work done in the four-year period from 2011-2014. This was a highly demanding test which meant extra work and added effort for the groups. We are pleased with the result and take due note of the recommendations suggesting the need to improve in the transfer and translation indicators.

The most noteworthy cooperation work in our field continues to be our intramural projects. The 49 projects from the 2014-2015 period went on throughout 2015, all focussing on some specific pathology.

Four new projects have been got under way in cooperation with companies, in which these defray 50% of the cost of the project. This initiative represents a major thrust forward to take the results of research into the industrial setting. These transfer initiatives have been complemented with the onset of an action implying cooperation with consultancy companies to promote the search for outside investments.

In the field of cooperation with the clinic, I would like to stress the thematic forum arranged in May 2015 along with the Hospital Nacional de Parapléjicos and the start of the second edition of collaborative projects in respiratory pathologies along with the Fundación SEPAR and CIBERES. The collaborative projects in oncology with the Fundación ECO and with IMIBIC went on in 2015.

Other results from last year were the coordination by CIBER-BBN of one of the interCIBER excellence projects, intended to investigate into the relationship between diabetes and neurodegenerative disorders, the granting of the European project DRIVE to develop cell treatments and materials for diabetes and getting the Internationalisation Platform under way along with CIBERES and CIBERER.

The ICTS NANBIOSIS has started up, after signing the agreements required by the Ministry, and has started to develop its strategic plan, getting under way its own web page, which acts as the access portal for the infrastructure. Additional financing from MINECO has also been obtained in the call for Excellence Networks.

No group has had to leave CIBER-BBN as a result of the previous year's assessment, and furthermore, a new group joined in 2015, after the selection process in a competitive call launched by the ISCIII.

I would lastly like to thank all those of you who form part of the CIBER-BBN for your ongoing daily efforts, making such a decisive contribution to the consolidation of our centre's scientific excellence.

With best regards,

Ramón Martínez Máñez
Scientific Director

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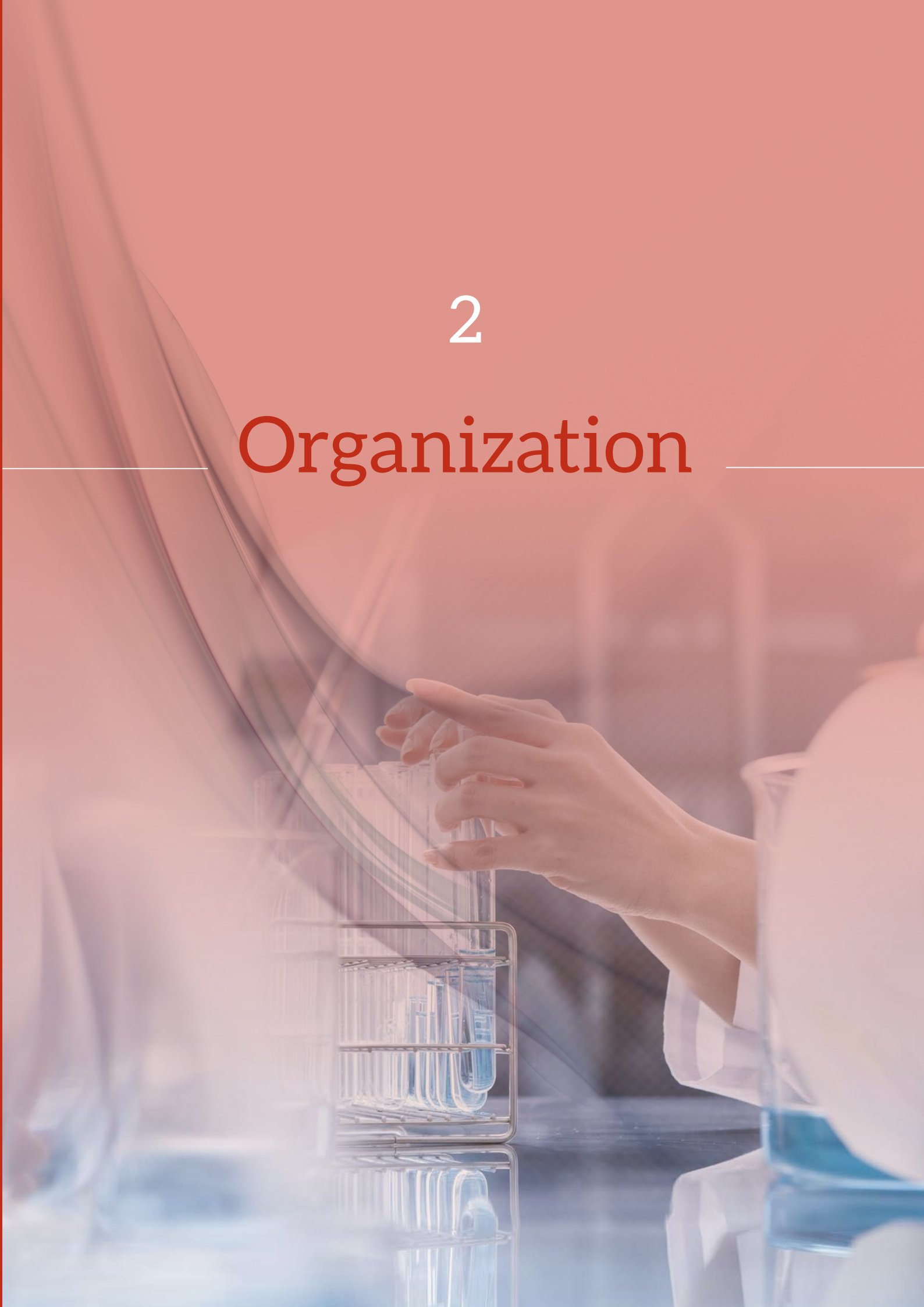
Organization



Organisational structure

The CIBER-BBN is one of the eight thematic areas forming the Centro de Investigación Biomédica en Red (CIBER), a Spanish research consortium in the field of biomedical research with great scientific potential, under the Instituto de Salud Carlos III (ISCIII) – Ministry of the Economy and Competitiveness.

The bioengineering, biomaterials and nanomedicine area is made up of 44 research groups, keeping its independence as regards scientific management. Its organisational structure is based on the research groups belonging to this and its activity revolves around the Research Programmes and Transversal Programmes, with a coordinator for each Programme belonging to the Steering Committee. Scientific decisions are made by the Scientific Director, advised by said Steering Committee and the External Scientific Committee.

The Steering Committee is presided over by the Scientific Director and made up of the coordinators of the programmes and Managing Director of the CIBER.

The External Scientific Committee is a body for scientific support and advice, made up of relevant personalities in the field of health sciences standing out for their professional or scientific careers in line with the objectives of the of the thematic area.

The senior administrative bodies of the CIBER-BBN are the Governing Body and the Permanent Commission, common for all the CIBER research areas.

The Governing Body is made up of three representatives of the ISCIII and by an institutional representative of each of the centres in the consortium. It is presided over by the Director of the ISCIII and meets every six months.

The Permanent Commission is an executive committee made up by the ISCIII and 8 members of the Governing Body, who can be renewed on an annual basis.

Both the operation and the purposes of the governing, support and advisory bodies are established in the statutes of the CIBER.

Members of the Steering Advisory Comittee of CIBER-BBN

NAME	POST HELD
Ramón Martínez-Máñez	Scientific Director
José Becerra	Deputy Scientific Director
Jordi Aguiló	Bioengineering and Medical Imaging Coordinator
Julio San Román	Biomaterials and Advanced Therapies Coordinator
M. Pilar Marco	Nanomedicine Coordinator
Jaume Veciana	ICTS / Platforms Coordinator
Simó Schwartz	Industrial Transfer Coordinator
Ramon Mangues	Translating Clinical Coordinator
Raimon Jané	Training Coordinator
Jesús Santamaría	Strategic Plan Coordinator
Manuel Sánchez	Managing Director

Scientific Director Assistant: Begoña Pérez

External Scientific Advisory Committee of CIBER-BBN

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

Medical Advisory Board

NAME	POST HELD
Joan Bigorra Llosas	Director of Innovation at Hospital Clínic, Barcelona.
Arcadi García Alberola	Arrhythmia Division Manager of the Cardiology Department at Hospital Universitario Virgen de la Arrixaca, Murcia.
Enrique Gómez Barrena	Specialist in the area of Traumatology and Orthopaedics at Hospital Universitario La Paz.
Mª José Martí Doménech	Neurology Department at Hospital Clínic, Barcelona.
José M. Ruíz Moreno	Specialist in the Area of Ophthalmology of the Complejo Universitario Hospitalario, Albacete.
Josep Tabernero Caturla	Onco-haematology Coordinator at Hospital Vall d´Hebrón.

Scientific Management

NAME	PROGRAMME
Theodora Tsapikouni	Bioengineering and Medical Imaging
Aída Castellanos Páez	Biomaterials and Advanced Therapies
Johanna Katharina Scheper	Nanomedicine
Fernando Santos Benito	Industrial Transfer
Jesús M. Izco Zaratiegui	Platforms (ICTS NANBIOSIS)

Technical Unit

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

Directory of groups and institutions

Group leader	Institution	Centre	Centre Prov
Aguiló Llobet, Jordi	Universitat Autònoma de Barcelona	Centro Nacional de Microelectrónica	Barcelona
Albericio Palomera, Fernando	Institut de Recerca Biomedica (IRB Barcelona)	Institut de Recerca Biomedica (IRB Barcelona)	Barcelona
Arús Caralto, Carles	Universitat Autònoma de Barcelona	Facultad de Biociencias	Barcelona
Becerra Ratia, José	Universidad de Málaga	Facultad de Ciencias	Málaga
Bellón Caneiro, Juan Manuel	Universidad de Alcalá	Facultad de Medicina	Madrid
Blanco Fernández, Jerónimo	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Calonge Cano, Margarita	Universidad de Valladolid	Instituto de Oftalmobiología Aplicada	Valladolid
Doblaré Castellano, Manuel	Universidad de Zaragoza	Instituto de Investigación en Ingeniería	Zaragoza
Engel López, Elisabeth	Fundación Instituto de Bioingeniería de Cataluña	Instituto de Bioingeniería de Cataluña	Barcelona
Eritja Casadellà, Ramon	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Fernández Jover, Eduardo	Universidad Miguel Hernández	Instituto de Bioingeniería	Alicante
Gómez Ramírez, Rafael	Universidad de Alcalá	Facultad de Farmacia	Madrid
Gómez Ribelles, José Luis	Universitat Politècnica de València	Centro de Biomateriales e Ingeniería Tisular	Valencia
González Martín, María Luisa	Universidad de Extremadura	Facultad de Ciencias	Badajoz
Jané Campos, Raimon	Fundación Instituto de Bioingeniería de Cataluña	Instituto de Bioingeniería de Cataluña	Barcelona
Laguna Lasaosa, Pablo	Universidad de Zaragoza	Instituto de Investigación en Ingeniería	Zaragoza
Lechuga Gómez, Laura María	Agencia Estatal Consejo Superior de Investigaciones Científicas	Institut Català de Nanociència i Nanotecnología	Barcelona
Leiva Hidalgo, Alberto	Instituto de Investigación del Hospital de la Santa Creu i Sant Pau	Instituto de investigación del Hospital de la Santa Creu i Sant Pau	Barcelona
Liz Marzán, Luis M.	CIC biomaGUNE	CIC biomaGUNE	Guipúzcoa
Mangues Bafalluy, Ramon	Instituto de Investigación del Hospital de la Santa Creu i Sant Pau	Instituto de investigación del Hospital de la Santa Creu i Sant Pau	Barcelona
Marco Colás, Mª Pilar	Agencia Estatal Consejo Superior de Investigaciones Científicas	Instituto de Química Avanzada de Cataluña	Barcelona
Martínez Máñez, Ramón	Universitat Politècnica de València	Centro de Reconocimiento Molecular y Desarrollo Tecnológico	Valencia
Muñoz Fernández, María Ángeles	Servicio Madrileño de Salud	Hospital Gregorio Marañón	Madrid

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

Budget

INCOME	6.976.525,02
NOMINAL ISCIII GRANT	3.800.160,00
INCOME FOR NEW GROUPS	60.000,00
COMPETITIVE INCOME	826.567,31
OWN FUNDS	2.289.797,71

EXPENDITURE	4.842.143,31
GROUPS	1.517.201,24
TRAINING	1.639.692,78
RESEARCH PROGRAMMES	152.795,61
TECHNICAL OFFICE	223.564,00
PLATFORMS	199.909,78
SCIENTIFIC MANAGEMENT AND STEERING COMMITTEE	114.799,89
INTRAMURAL P.	48.753,84
TECHNOLOGY TRANSFER	105.859,44
COMPETITIVE PROJECTS	839.566,73

Personnel

Personnel contracted during the year as of 31st December, separating by categories:

Category	Indefinite	Temporary	Work & service	Postdoctoral	Total Overall
Diploma holder	1				1
Doctor	41	1	13	6	61
Graduate	14	2	15		31
Technical	8		3		11
Total	**64**	**3**	**31**	**6**	**104**

Significant Activities

Projects

The projects under way in 2015 were as follows:

NATIONAL PROJECTS

Financing agency: Instituto de Salud Carlos III

- Miguel Servet Human Resources Contracting aid.
- STRUCTGEL. Nanostructured Gel for Cellular Therapy of Degenerative Skeletal Disorders.
- NANGIOFRAC. Angiogenic nanostructured materials for non-consolidating bone fractures.
- Role of monocytes/macrophages in the evolution of patients with acute kidney failure through cardio-renal syndrome 1 and their relation with the integration of renal epithelium.
- Molecular links between diabetes and neurodegenerative disorders.

Financing agency: Ministry of the Economy and Competitiveness

- NANOCARDIOCOCO. Nanotechnology for cardiology and pneumococcus.
- PHYTECH. Development of biomaterials coated with phytate to stimulate bone regeneration.
- 4 grants for contracting Technical Support staff.
- Ramón y Cajal aid for contracting Human Resources.
- PRONANBIOSIS. Consolidation of the management model and promotion of NANBIOSIS.
- ANSHEART. The autonomic nervous system as a modulator of the cardiac function: comprehensive research by signal processing and computational modelling.
- TERARMET. Development of therapies for treatment of congenital metabolic rare diseases.
- TERET. New treatments for degenerative diseases of the retina.
- INNCIDE. PETRA UVAT CIBER-BBN.

Other financing agencies

- FECYT and CAIXA: Biomedicine with and for Society.
- Junta de Castilla y León regional authority: Cell therapy in the failure of the ocular surface: development of a culture medium to improve the biosecurity of stem cell transplants.
- Ministry of Education, Culture and Sport: 2 José Castillejo grants for mobility.
- Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria: Optimisation of the cow's dry period by protein nanoparticles.

It should be stressed that CIBER-BBN coordinates one of the three CIBER interdisciplinary excellence projects financed by the AES, "Molecular links between diabetes and neurodegenerative disorders", with the aim of identifying common molecular mechanisms between diabetes and neurodegenerative diseases. Groups from the CIBER of Neurodegenerative Disease (CIBERNED), Rare Diseases (CIBERER) and from the CIBER of Diabetes and Associated Metabolic Diseases (CIBERDEM) are also taking part in the project.

INTERNATIONAL EUROPEAN COMMISSION PROJECTS

- BERENICE. Benznidazol and Triazol REsearch group for Nanomedicine and Innovation on Chagas disease.
- NEUROGRAPHENE. Neurological recordings with Graphene.
- DRIVE. Diabetes Reversing Implants with enhanced Viability and long-term Efficacy Project.
- E-MEDIVIP. E-learning platform for medical informatics to improve vocational and ict practice.

The CIBER-BBN's participation in the European DRIVE project should also be stressed. This project was got under way in June 2015 with the aim of developing biomaterials and new surgical devices to improve the transplant and survival of insulin-producing pancreatic islets for treating diabetes.

Technology transfer

One of the CIBER's main aims is the transfer of research results into clinical practice, and one of the best tools existing for this purpose is technology transfer. The Unit managing this at the CIBER sets out to act as a bridge between our researchers and other agents in the Science and Technology System (companies, business associations, other research organisations, etc.) to make cooperation with these bodies more effective. This means that research results will be efficiently developed and can succeed in being applied. Work is done in several lines to this end:

- **Training in innovation management and continuous contact with our researchers to monitor their results.**

  In this respect, last year the first general event of the CIBER in training on technology transfer and innovation was held, on 26th February 2015 and where national experts took part sharing their knowledge in matters such as industrial property, business creation or publication in open access, etc.

- **Protection of their research results and management of cooperation with other agents, as vouched for by applications for patents and signing licensing contracts, amongst other agreements.**

  Hence, over 20 new patent applications were made and seven licensing agreements were signed at the CIBER in 2015.

- **The presentation of research results and technological capacities of our groups.**

  Among many other measures and only as an example, in 2015, several projects were presented at the II Foro de Innovación en Diagnóstico in Vitro – FENIN in Barcelona (December 2015).

- **Support for technology-based business creation stemming from CIBER groups.**

  The CIBER has since 2014 taken part in Epidisease (http://www.epidisease.com/es/) which it continued to support in 2015.

- **Other activities connected with innovation, public-private cooperation and industrial and intellectual property.**

  For example, the registration of the "community trademark" of the CIBER has been processed, or steps have been taken for registering intellectual property rights for audio-visual projects, amongst many others.

Dissemination measures

The CIBER's Communication Department carried out different measures for dissemination and publicity in 2015 in order to improve the Centre's visibility, as well as to make known the research work done by groups in its eight thematic areas.

We will now give details of the milestones in Communication of the CIBER-BBN in 2015:

THE CIBER-BBN IN THE MEDIA:

50 CIBER press notes were sent out during the 2015 period, 5 of these from the CIBER-BBN and 4 in cooperation between several CIBER areas.

Date	Thematic Areas	Title
January	SEVERAL CIBER	El CIBER pone en marcha tres proyectos de excelencia interdisciplinares financiados con casi 2 millones de euros por la AES
February	SEVERAL CIBER	Investigadores del CIBER identifican diversos factores de riesgo de sufrir cáncer
November	SEVERAL CIBER	El CIBER acerca su investigación al público de la mano de la improvisación teatral en #ImproCiencia
December	SEVERAL CIBER	El CIBER incorpora 11 nuevos grupos en diversas áreas de investigación
March	CIBER-BBN	Reivindican la labor de las mujeres científicas con un espacio radiofónico de entrevistas y cuentos
April	CIBER-BBN	Ramón Martínez Máñez es nombrado Director Científico del CIBER de Bioingeniería, Biomateriales y Nanomedicine

Date	Thematic Areas	Title
May	CIBER-BBN	El CIBER-BBN y el Hospital Nacional de Parapléjicos estudian colaboraciones para conseguir aplicaciones clínicas en lesión medular
June	CIBER-BBN	Un consorcio europeo con participación española desarrollará materiales y tratamientos celulares para la diabetes
November	CIBER-BBN	Consiguen regenerar tejido nervioso en animales con implantes biodegradables tras lesiones cerebrales

378 appearances in the media were registered over this period:

CIBER-BBN	NEWS	AUDIENCE
Internet	340	39.882.800
Press	38	4.694.000
Total	**378**	**44.576.800**

NEW CIBER-BBN WEB SITE:

In September 2015 the new web page of the CIBER-BBN was launched in order to have a structure, image and contents manager in common for all the CIBER areas.

http://www.ciber-bbn.es/en

CIBER NEWSLETTER

5 CIBER newsletters were brought out and disseminated in this period, including relevant content about both the CIBER-BBN and the other thematic areas. These digital newsletters were sent to around 4000 subscribers.

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

SOCIAL NETWORKS

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

UPDATES		FOLLOWERS		FOLLOWING		KLOUT (influence, values from 1 to 100)	
JANUARY	DECEMBER	JANUARY	DECEMBER	JANUARY	DECEMBER	JANUARY	DECEMBER
856	1150	1636	2070	1274	1223	46	48

ANNUAL CIBER-BBN REPORT

The CIBER communication area, in cooperation with the CIBER-BBN, coordinated the content of the CIBER-BBN 2014 report in Spanish/English, preparing and disseminating 2 reports in interactive format (Flip- book) and PDF. These were distributed through the web page and the Twitter account:

http://www.ciberisciii.es/en/press/annual-report

CIBER #IMPROCIENCIA SCIENCE WEEK

The #ImproCiencia dissemination event, arranged by the CIBER in the framework of the Madrid Science Week 2015, took place on 3rd November at the Nave 73 rooms in Madrid. The event combined science and theatre improvisation to give a light-hearted explanation of the biomedical research done by the CIBER in its eight thematic areas.

Games and improvisations were alternated with live connections with CIBER researchers during the event. As far as the CIBER-BBN is concerned, we should stress the participation of Iñaki Ochoa, who explained from Zaragoza his daily work in tissue engineering, characterisation of biomaterials and microfluidics.

Scientific production

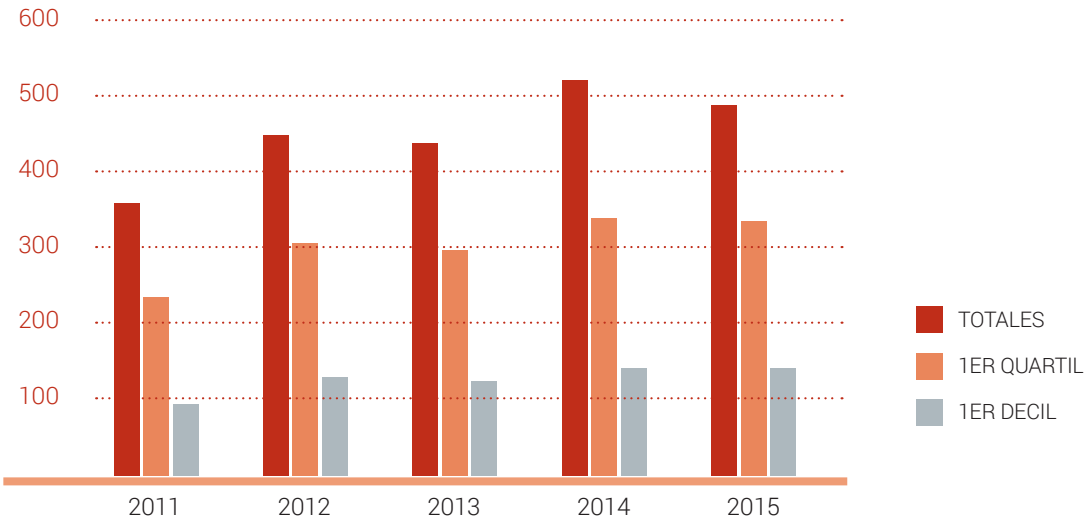
The evolution of CIBER-BBN publications can be appreciated from the following graphs, in which the data from 2010 to 2015 is analysed.

Details are also given of the publications per group for the current year, as well as interCIBER and intraCIBER cooperation work.

Publications:

No. of affiliated publications 2015	
Total publications	**491**
First quartile	338
First decile	142

EVOLUTION OF CIBER-BBN PUBLICATIONS 2010-2015



MOST RELEVANT PUBLICATIONS OF THE CIBER-BBN IN 2015 ACCORDING TO THE IMPACT FACTOR

Publication	Impact factor
INOSTROZA-BRITO K.E., COLLIN E., SITON-MENDELSON O., SMITH K.H., MONGE-MARCET A., FERREIRA D.S. ET AL. Co-Assembly, spatiotemporal control and morphogenesis of a hybrid protein-peptide system. Nature Chemistry. 2015; 7 (11):897-904.	25,325
BLAY J.-Y., PAPAI Z., TOLCHER A.W., ITALIANO A., CUPISSOL D., LOPEZ-POUSA A. ET AL. Ombrabulin plus cisplatin versus placebo plus cisplatin in patients with advanced soft-tissue sarcomas after failure of anthracycline and ifosfamide chemotherapy: A randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet Oncology. 2015; 16(5):531-540.	24,690
DIETERICH E., CAMUNAS-SOLER J., RIBEZZI-CRIVELLARI M., SEIFERT U., RITORT F. Single-molecule measurement of the effective temperature in non-equilibrium steady states. Nature Physics. 2015; 11(11):971-977.	20,147
BALSELLS M., GARCIA-PATTERSON A., SOLA I., ROQUE M., GICH I., CORCOY R. Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: A systematic review and meta-analysis. BMJ (Online). 2015; 350.	17,445

Publication	Impact factor
FRISENDA R., GAUDENZI R., FRANCO C., MAS-TORRENT M., ROVIRA C., VECIANA J. ET AL. Kondo effect in a neutral and stable all organic radical single molecule break junction. Nano Letters. 2015; 15(5):3109-3114.	13,592
PARIS J.L., CABANAS M.V., MANZANO M., VALLET-REGI M. Polymer-Grafted Mesoporous Silica Nanoparticles as Ultrasound-Responsive Drug Carriers. ACS Nano. 2015; 9 (11):11023-11033.	12,881
GARCIA I., SANCHEZ-IGLESIAS A., HENRIKSEN-LACEY M., GRZELCZAK M., PENADES S., LIZ-MARZAN L.M. Glycans as Biofunctional Ligands for Gold Nanorods: Stability and Targeting in Protein-Rich Media. Journal of the American Chemical Society. 2015; 137(10):3686-3692.	12,113
BLANCO-CANOSA J.B., NARDONE B., ALBERICIO F., DAWSON P.E. Chemical Protein Synthesis Using a Second-Generation N-Acylurea Linker for the Preparation of Peptide-Thioester Precursors. Journal of the American Chemical Society. 2015; 137(22):7197-7209.	12,113
UNZUETA U., CESPEDES M.V., VAZQUEZ E., FERRER-MIRALLES N., MANGUES R., VILLAVERDE A. Towards protein-based viral mimetics for cancer therapies. Trends in Biotechnology. 2015; 33(5):253-258.	11,958
ORIVE G., SANTOS E., PONCELET D., HERNANDEZ R.M., PEDRAZ J.L., WAHLBERG L.U. ET AL. Cell encapsulation: technical and clinical advances. Trends in Pharmacological Sciences. 2015; 36(8):537-546.	11,539

	PUBLICATIONS 2015		
Group- PI name	Total	1Q	1D
Aguiló Llobet, Jordi	3	2	1
Albericio Palomera, Fernando	37	24	15
Arús Caraltó, Carles	7	6	0
Becerra Ratia, José	7	3	0
Bellón Caneiro, Juan Manuel	12	4	1
Blanco Fernández, Jerónimo	6	4	1
Calonge Cano, Margarita	10	2	0
Del Pozo Guerrero, Francisco	12	5	2
Doblaré Castellano, Manuel	28	16	3
Engel López, Elisabeth	21	13	9
Eritja Casadellà, Ramon	11	7	2
Fernández Jover, Eduardo	6	5	1
Gómez Ramírez, Rafael	19	19	6
Gómez Ribelles, José Luis	28	21	5
González Martín, Mª. Luisa	1	1	1
Jané Campos, Raimon	14	10	2
Laguna Lasaosa, Pablo	14	9	2

	PUBLICATIONS 2015		
Group- PI name	Total	1Q	1D
Lechuga Gómez, Laura Mª	5	5	3
Leiva Hidalgo, Alberto	9	4	2
Liz Marzán, Luis M	14	11	4
Mangues Bafalluy, Ramon	14	10	7
Marco Colás, Mª. Pilar	4	4	2
Martínez Máñez, Ramón	28	24	10
Muñoz Fernández, Mª Ángeles	24	22	15
Pavía Segura, Javier	12	8	4
Pedraz Muñoz, José Luis	24	18	6
Peris Serra, José Luis	2	0	0
Raya Chamorro, Ángel	5	1	0
Ritort Farran, Félix	5	5	2
Roa Romero, Laura	3	1	1
Rodríguez Cabello, José C.	16	13	7
Ruiz Romero, Cristina	6	2	1
Samitier Martí, Josep	18	15	3
San Román del Barrio, Julio	12	8	4
Santamaría Ramiro, Jesús	20	18	11
Santos Lleó, Andrés	8	5	2
Sanz Carrasco, Fausto	9	8	2
Schwartz Navarro, Simó	11	11	6
Solans Marsá, Concepción	13	8	5
Vallet Regí, María	18	16	5
Veciana Miró, Jaume	15	11	5
Vilaboa Díaz, Nuria	7	6	1
Villaverde Corrales, Antonio	15	10	4

COOPERATION:

No. of intraCIBER publications 2015: **67**

No. of interCIBER publications 2015: **39**

Patents

INTERNATIONAL PATENTS APPLIED FOR

- Uso de un inhibidor de la adrenomedulina para la fabricación de un medicamento útil en la prevención y tratamiento de enfermedades que reducen la densidad ósea.
- Biopolímeros que comprenden polipéptidos quiméricos y las matrices obtenidas con los mismos.
- Agentes antivirales que comprenden un conjugado lípido-oligonucleótido con capacidad de formar G-cuádruplex.
- Biorreactor para co-cultivo celular.
- Dispositivo para medir la impedancia eléctrica transcelular en un modelo in vitro de barrera celular.
- Vidrios y andamiajes bioactivos, procedimientos de preparación y usos de los mismos.
- Liposomas funcionalizados útiles para la liberación de compuestos bioactivos.
- Liberación de sustancias en células senescentes.
- Mimético de 1,2,3-triazol 1,4,5-trisustituido de RGD y/u OGP10-14, procedimiento para obtenerlo y usos del mismo.
- Polímero de poliariletercetona modificado (PAEK) y procedimiento para obtenerlo.
- Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa.

NATIONAL PATENTS APPLIED FOR

- Material para implante moldeable biodegradable biocompatible y biorreabsorbible, prodedimiento de preparación y usos.
- Compuestos y sus usos como haptenos para la detección S. aureus.
- Chip microfluídico, dispositivo microfluídico, procedimientos y usos asociados.
- Dispositivo y sistema microfluídico, para el estudio de cultivos celulares.

NATIONAL PATENTS GRANTED

- Copolímeros anfifílicos portadores de alfa-tocoferol con propiedades antitumorales.
- Liberación de sustancias en células senescentes.
- Anticuerpos para la detección y cuantificación de agentes anticoagulantes.
- Cámara de cultivo celular sobre biomateriales.
- Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa.
- Hidrogeles plasmónicos basados en fibrina para la generación de hipertermia controlada.
- Sensor Inteligente de bioimpedancia para aplicaciones biomédicas.

Clinical guides

- Guía SECOT-GEIOS en osteoporosis y fractura por fragilidad. Actualización.
- SECOT-GEDOS consensus on pre-surgical pain management in knee and hip arthrosis.
- Giant cell tumour of bone: new treatments in development.
- Comprehensive T wave morphology assessment in a randomized clinical study of dofetilide, quinidine, ranolazine, and verapamil.
- Documento de consenso del CEVIHP/SEIP/AEP/SPNS respecto al tratamiento antirretroviral en niños y adolescentes infectados por el VIH.

3

Scientific Programmes

Bioengineering and Medical Imaging

Over 2015, the researchers from the Bioengineering and Medical Imaging programme of the CIBER BBN started up four projects with great impact Europe-wide: Neurographene, Modelage, RADAR-CNS and E-MEDIVIP, and have been given an award for Innovation.

Dr Rosa Villa from the GBIO-UAB group is taking part in the FET-Flagship Grafene with her Neurographene project, which sets out to synthesise graphene sensors to simultaneously detect electrical activity in different cortical regions of the brain. These devices are already being used in the study of sleep and epilepsy in animal models. These sensors could be incorporated in implantable devices which would for example enable the early detection of a crisis in epileptic patients at the same time as sending alerts to medical services. The results of this project will lead onto future brain-machine interfaces, an objective which will enable more efficient communication between persons and artificial electronic systems.

Dr Esther Pueyo's Modelage project (of the BSICoS group from the Universidad de Zaragoza) has been awarded a grant of 1.5 million euros from the European Research Council (Starting Grant category). Through this project, the researcher sets out to further the characterisation of the heart's aging and to shed light on the different paces of aging in different people, which can have major repercussions on an individual's predisposition to undergo heart arrhythmia. The results of the Modelage project will help to develop non-invasive tools for backing medical decisions, helping to make progress in personalised preventive medicine.

Professors Jordi Aguiló and Pablo Laguna take part along with CIBERSAM researchers in the consortium for the Remote Assessment of Disease And Relapse in Central Nervous System project (RADAR – CNS) which went in for the 3rd call for the Innovative Medicines Initiative 2 in 2015. The project focuses on improving patient care through the remote assessment of the evolution of diseases of the central nervous system, specifically epilepsy, multiple sclerosis and depression. To this end it is proposed to develop a platform enabling remote detection of biological signatures of early identification of relapse or cognitive deterioration.

As well as this, the "Liver on a chip" programme, coordinated by Dr Rosa Villa along with Dr Jordi Gràcia-Sancho from CIBEREHD, has obtained the second prize in the Innovation Competition at Salud del Vall d'Hebron Institut de Recerca (VHIR) in the category of innovation in research results. "Liver on a chip" is a microfluidic chamber which simulates liver microcirculation designed and made by this research team. The chamber will act as a tool for "in vitro" studies and diagnosis of cell function, pharmacology, toxicity and personalised medicine.

The E-MEDIVIP project: e-learning platform for medical informatics to improve vocational and information and communication technologies skills financed by the Erasmus+ programme of the European Commission has been got under way. Dr Margarita Julià, from the GABRMN-UAB group, is taking part in this. The project is designed to improve skills in information technology of healthcare students and workers, such as doctors, nurses, chemists and other professionals.

The programme's scientific production consists of 85 publications (articles, reviews, editorials and letters), with 62% in the first quartile and 19% in the first decile. As regards patents, two international patents have been applied for and a national patent has been granted.

Biomaterials and Advanced Therapies

The CIBER-BBN Programme for Biomaterials and Advanced Therapies encourages excellent science and the creation of innovation addressing the social challenges and technological requirements in a multidisciplinary approach, so as to obtain products with a great impact in the biomaterials area with applications in tissue engineering, nanomedicine and implants.

Different outcomes of importance as regards the transfer of research results have been obtained in 2015 as part of this programme. It should be stressed that the GEMM- I3A of the Universidad de Zaragoza has developed a new series of microfluidic devices for cell cultivation in biomimetic atmospheres which has led to creating the new BEONCHIP company. This business project was awarded the IDEA-PRODUCT award by the Centro Europeo de Empresas e Innovación (CEEI Aragón) thus receiving an economic endowment and support for its incorporation, which is intended to be for the end of the year. The promoting team is made up of researchers with different profiles such as Luis Fernández (physics), Ignacio Ochoa (biology) and Rosa Monge (engineering), thus demonstrating the need for multidisciplinary cooperation to manage to obtain products with real exploitation capacity on the market or with tangible impact in the health area. Experiments that were hitherto impossible can now be carried out with these be-on-chip polymeric devices.

The IOBA-UVA group led by Dr Margarita Calonge has developed a new polyethylene implant for patients with no eyeball. This new product has been successfully tested in a study on rabbits displaying the safety and biocompatibility of the orbital implant, which is porous and enables tissues to grow inside this. The company AJL Ophthalmic and the Centro de Medicina Regenerativa y Terapia Celular de Castilla y León took part in this project.

As part of this scientific programme the participation of clinical groups in intramural projects continues to be a priority, as well as the emergence of patents. 4 new patents were applied for in 2015, one European and three national, and a further two European patents which had been extended to PCT went into the national stages in the U.S.A., China and Korea.

Following on with the constant dialogue with regulatory agencies through this programme, the CIBER-BBN continues to be an Interested Party in the Committee for Advanced Therapies (CAT) of the European Medicines Agency (EMA), and there is similarly constant interaction with the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) to get advice and consultancy in different aspects of legislation connected with intramural projects and the scientific work of the CIBER-BBN in general.

One final point to be highlighted was the programme being joined by the Integrative cell and tissue dynamics group of the Instituto de Bioingeniería de Cataluña, led by Dr Xavier Trepat, that has also been selected from the eight finalists for the Science Award of La Vanguardia newspaper, which distinguishes the groups performing the most relevant research during the year.

The scientific production of articles, reviews, editorials and letters comes to 182 publications, with 62% in the first quartile and 21% in the first decile.

Since 2012, the Biomaterials Programme has been cooperating with the CIBER-BBN initiative Young Scientist Forum on Biomaterials furthered by CIBER-BBN researchers. This research programme annually grants an award to a young researcher coinciding with when the annual sessions are held, including a session on this Forum.

Nanomedicine

As far as the area's scientific programme is concerned, 25 scientific articles have been published in journals of great impact with the results stemming directly from the work done in the 18 intramural projects from the Nanomedicine area.

We should stress that the funds obtaining for carrying out some of these projects came from national and international publicly-financed calls. It should thus be pointed out that the following research projects have obtained external financing:

- PENTRI (*Personalized nanomedicine for triple negative breast cancer stem*). The project focusses on the treatment of triple negative breast cancer, with three CIBER-BBN groups taking part in this (Dr Ibane Abásolo, Dr Esther Vázquez and Dr Miriam Royo), which have obtained funding from La Marató on TV3 television channel, in its edition for the fight against cancer.
- NANOMETS (*Drug nanconjugates and nanovesicles for the treatment of metastatic colorectal cancer*). The project focusses on the treatment of metastatic colorectal cancer, with four CIBER-BBN groups participating in this (Dr Ramon Mangues, Dr Antonio Villaverde, Dr Ramon Eritja and Dr Jaume Veciana). The project, which is coordinated by Dr Mangues' group, has also obtained financing from La Marató on TV3 in its edition for the fight against cancer and from the call for excellence projects of the ISCIII. Funds have also been obtained from the AGAUR agency for valorisation and transfer of its results. This project also forms part of the COST action entitled "Chemical Approaches to Targeting Drug Resistance in Cancer Stem Cells".
- NANOXEN (*Xenopus Tropicalis as a platform to test light-regulated drugs with applications in nanomedicine*). This project uses Xenopus Tropicalis as a platform for testing the toxicity and efficacy of drugs/molecules. On a nationwide scale, financing for this was obtained from the RETOS Research call. In the field of international calls, the project has been awarded with a Marie Skłodowska-Curie action from the H2020 programme and it also receives financing through the ERA-Net EraSynBio. It has lastly also been financed by the FET Flagship Human Brain Project (HBP).

It is noteworthy that two of the junior CIBER-BBN researchers working on said project have received financing in parallel for undertaking the project in the call for R+D+I projects for young researchers.

The following events and congresses connected with the nanomedicine area were attended:

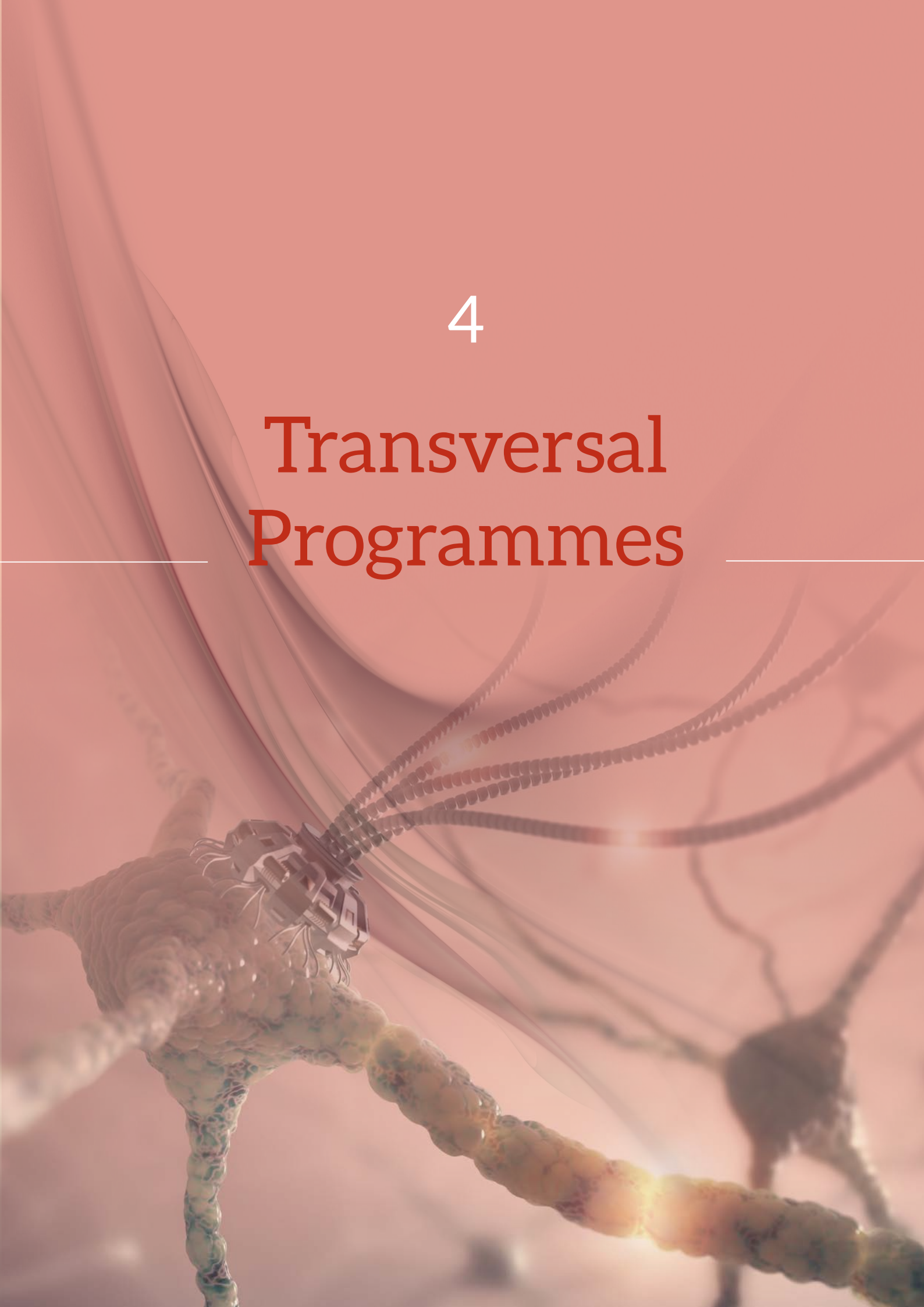
- CLINAM 2015 (European Foundation for Clinical Nanomedicine). Basle (Switzerland), 29th June – 1st July 2015. The CIBER-BBN and the ICTS NANBIOSIS were introduced at the event in both an oral presentation and in poster format.
- Annual meeting of the ETPN (European Technology Platform of Nanomedicine). Dublin (Ireland), 14 – 15th October 2015.
- X Conferencia Anual de las Platforms Tecnológicas de Investigación Biomédica. Madrid, 24 – 25th March 2015.

Lastly, the LIPOCELL transfer project was selected as part of the ENATRANS initiative of the ETPN, to participate at a session with the Translational Advisory Board to analyse the state of the project from the regulatory standpoint. This meeting took place during the annual sessions of the ETPN, and was defended by one of the researchers of the project and by the manager for the nanomedicine area. The project was selected to go on to phase II of the initiative, which will take place during 2016.

The programme's scientific production consists of 286 publications (articles, reviews, editorials and letters), with 80% in the first quartile and 38% in the first decile. As for patents, four international patents and one Spanish patent have been applied for, with three national patents being granted.

4

Transversal Programmes



Industrial Transfer Programme

In 2015 four Spanish patents, one Italian, two European patents and three PCT extensions were applied for and five patents went into national phases in several countries. Seven Spanish patents were granted and two licensing contracts were signed.

Three cooperation agreements were signed for carrying out transfer projects with three companies financing them. With the financing received in early 2015, a further two transfer projects were got under way, whose agreements with the companies involved were signed in late 2014. One last transfer project also received the second yearly sum of its financing. In all the cases, the companies undertake to co-finance half of the budget for the research project, while CIBER-BBN provides the other half.

In late 2015 a new strategic measure for furthering technology transfer started to be implemented, working with nine consultants. The latter will provide any of their contacts and customers (companies and investors) interested in our technologies, which will cooperate and invested in our projects, spin-offs, and acquire the licences for our patents. The CIBER-BBN research groups have been distributed among the consultants in keeping with the affinity of the working subjects and the work area and customer portfolio of those advisors. Each company will promote the technologies of the groups that they have been assigned and the CIBER-BBN will establish the framework for cooperation and investment with the companies and investors interested in the development and transfer of these technologies. Cooperation with these consultants has started by signing the relevant confidentiality agreements. In early 2016 the proper service-rendering contracts will be signed and the consultants will start their work.

With the advice of a specialised consultant, a study has also been made for prioritising and valorisation of 11 technologies (patents and projects), based on their transfer potential. The process consists of three phases: (a) analysis of eleven and selection of five technologies; (b) detailed analysis of these five and selection of the one with greatest potential for transfer to industry; (c) preparation of a development plan for this, intended to facilitate licensing it to an industrial partner. Each technology was valued from the standpoint of the technology offer (degree of development and technological competitiveness) and of the business demand (market needs, size of the market, value-generating potential).

Translational Research Programme

The CIBER-BBN - Hospital Nacional de Parapléjicos forum on medullar injury was arranged. Studies and progress were presented in such areas as neuroprotection, tissue engineering, regenerative medicine, neurorobotics, neuroprosthetics, transplants, neuro-repair and new devices for neuro-rehabilitation. Associated research topics and potential cooperation between both organisations which could result in projects addressing clinical applications were identified.

Three cooperation projects in respiratory pathologies have been got under way along with CIBERES and the Fundación SEPAR. These three projects, which are to be undertaken throughout 2015 and 2016, are respectively focussed on measuring stress in patients subject to mechanical ventilation, the use of nanoparticles as systems for releasing drugs for treatment of mycobacterium tuberculosis, and on the use of micro-CT technologies for the evaluation of 3D vascular structure in animal models of COPD.

CIBER-BBN has continued to be an Interested Party in the Committee for Advanced Therapies (CAT) of the European Medicines Agency (EMA), and constantly interacts with the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) to obtain advice and assessment in different aspects of legislation connected with intramural projects and the scientific work of the CIBER-BBN in general.

Each of the intramural projects in the course focusses on a particular pathology. More specifically, the diseases tackled by research done at the CIBER are: oncology (11 projects), neurological diseases (8), infectious diseases (7), diseases of the skeletal muscular system (5), implants (5), cardiovascular diseases (4), respiratory diseases (3), ophthalmology (3), chronic diseases (2) and rare diseases (1).

Training and Qualification Programme

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

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

TRAINING SUPPORT FOR INITIATION TO RESEARCH

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

Two calls were held in the months of July and October 2015. Limitations to contracting researchers as a result of the economic situation and the containment of salary volumes meant that both calls for grants came out for young researchers to join for a period of six months (unlike past calls, in which the support lasted for one year). The number of applications has been very high in each of the calls due to the interest aroused in the research groups by these grants. A total of 18 grants were given to the candidates with best academic records and whose proposals coincided most closely with the priority research lines of the CIBER-BBN.

Year	No. of "initiation to research" grants awarded
2011	19
2012	12
2013	15
2014	37
2015	18

AID FOR MOBILITY

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

In 2015 there were two mobility calls (March and September) and a total number of 18 grants for stays at groups outside the CIBER-BBN were awarded.

Three grants were awarded as support for mobility of research staff between groups in the CIBER-BBN, with a permanent call throughout the year.

Year	No. of intra-CIBER-BBN "mobility" grants awarded	No. of external "mobility" grants awarded	Total no. of "mobility" grants awarded
2011	6	10	16
2012	6	9	15
2013	1	20	21
2014	2	17	19
2015	3	18	21

Dissemination Programme

9TH ANNUAL CIBER-BBN CONFERENCE

The 9th Annual CIBER-BBN Conference were held at the Universitat Politècnica de València on 30th November and 1st December 2015, and attended by around 180 researchers.

The scientific encounter was preceded by a meeting of the Director with the principal investigators from all the groups the previous day, where relevant aspects on the running of the centre were brought up (scientific programme, budgetary aspects, assessment of the groups and assessment by the ISCIII, future actions planned, etc..)

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

The programme included two plenary sessions: "miRNA and Biomaterials for Musculoskeletal Regenerative Medicine", by professor Martijn van Griensven, from the University of Munich, and "Knowledge, Technology and Value in Health", by Joan Bigorra, from Barcelona Global Health Institute and the Hospital Clínico de Barcelona.

There was also a presentation of the Internationalisation Platform in which CIBER-BBN took part along with CIBERES and CIBERER and with a presentation of NANBIOSIS, the unique technical scientific infrastructure of CIBER-BBN.

The results of the 29 intramural research projects qualifying in the category of excellence which was about to conclude were given at the different scientific sessions of the first day, leaving time for debate and the discussion of results. On the second day a session known as "highlights" was held, intended to display relevant results or findings of some of the groups in the last two years. Other results were shown at the poster sessions.

Members of our External Advisory Scientific Committee took part at the event. The Management Committee had a meeting with the advisory committee at the end of the sessions.

Internationalization Programme

Last 11th May 2015 the CIBER programme for supporting internationalisation was set up, as a joint initiative of the areas of Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Rare Diseases (CIBERER) and Respiratory Diseases (CIBERES), of the Centro de Investigación Biomédica en Red (CIBER). Its purpose is to reinforce and coordinate endeavours intended to promote its researchers' participation in European programmes and to create a common structure for encouraging internationalisation and leadership of research and innovation in these three thematic areas.

Over these first six months of its action the platform has focussed its work on establishing a relationship of trust with the research groups. This started by holding bilateral interviews with the groups and the area leaders to get first-hand information on the research done and the internationalisation potential of the CIBER groups. The platform has also created profiles of specific area capacities so as to have a simple and comprehensive document acting as an introductory letter for the research done at the CIBER. This could be used at the different events for seeking partners. Likewise, the CIBER register of different tools for seeking existing partners has been completed (Cordis, IMI...).

As regards improving CIBER's international visibility, the CIBER has worked hard by attending over sixteen events (including conferences, infodays and partner-seeking events). One of the greatest accomplishments in this field was CIBER's invitation by CDTI to form part of the CDTI-SOST Manager Specialisation Course (CDTI, Brussels, BE). This course is intended to boost the international presence of invited organisations by substantially improving their international network of contacts and knowledge on

H2020 programmes. The platform also placed special stress on establishing smooth relations with the different national representatives, national points of contact by means of specific meetings, acting as a point of encounter on an institutional level.

The platform has also given awareness-raising talks on the relevance of internationalisation as part of the area conferences. The success of these events can be seen in the form of a significant increase in the number of enquiries from researchers (twenty specific enquiries, six requests for support for presentation, six requests for partnering, and six requests for valuing research proposals). This means the platform is already seen as an effective tool for aid and a reference point for settling doubts involving international programmes.

In the field of backing for submission of proposals, the platform has drawn up specific material providing support for writing and managing proposals. This year a practical guide has been drafted, entitled "How to write a European Proposal" as well as a practical guide for management and the "Quick guide for third parties" in order to provide researchers with understandable and reliable consultation material. As part of the support material the platform has also drawn up models and specific templates for managing and applying for H2020 proposals. These include the budget calculator, models of timesheets, letters for acceptance of participation in proposals, support letters, CIBER profile for European proposals as a partner and as third party and different forms for compiling all the data required for submitting a proposal. This material is intended to facilitate the process of submitting proposals for all our researchers. Thanks to this, in these six months of 2015 the CIBER has submitted four new proposals (three of these coordinated) while expressions of interest for the submission of ten new proposals have been received. In this area it should also be stressed that CIBER has received five new contacts from research groups or companies with the aim of reaching agreements for joint submission of proposals in the H2020 framework. For the time being two of these contacts have materialised in actual presentation of two H2020 proposals.

5

Platforms

Combined platforms of the CIBER-BBN/ ICTS NANBIOSIS

In 2015 the internal assessment of the units went on, in order to assign the economic incentives in accordance with the work done the previous year, as laid down in the established assessment protocol. Yet another year, the search for external financing, both from public and private sources, was a priority matter. The presentation of the programme of platforms was carried out at international bodies and partnering events, as well as at national companies, private research foundations and public research bodies. Promotion material was distributed on different visits to companies, research centres and industrial associations, as well as through participation at the Spanish Technology Platform MATERPLAT, the Spanish Biotechnology Platform and the Council for European BioRegions (CEBR). Similarly, participation at international initiatives and infrastructures such as ETP Nanofutures, Eurobioimaging, ARBRE and the Cost MOBIEU Action was promoted.

A large number of national and international events were attended: *Conferencia Anual de las Platforms de Investigación en Biomedicina*, *Jornada de Infraestructuras Europeas* and different brokerage events for seeking partners.

Operating as ICTS (Unique Technical Scientific Infrastructure) has been successfully consolidated. The framework agreement of the ICTS between the CIBER and the CCMIJU, containing the statutes of the ICTS NANBIOSIS, was approved during the first quarter of 2015. In July 2015 the official launching took place with the presentation of NANBIOSIS in Barcelona, with institutional representation of MINECO and ISCIII. The presentation of NANBIOSIS coincided with the launching of a web page and a dissemination dossier.

The cooperation schemes got under way with companies were followed up. Some examples of these are the PHYTECH (INNPACTO) project, in which two Spanish companies and a unit from the programme (Characterisation of surfaces and Calorimetry) are involved; the European project BERENICE, which includes two units (Biomaterial Processing and Nanostructuring Unit and Medicine Formulation Unit) or the TERET project (RETOS-COLABORACIÓN), in which two companies took part (Sylentis and LeadArtis) along with the Medicine Formulation Unit and a further two groups of the CIBER-BBN. The DRIVE project (H2020) was granted, in which one unit is involved. Financing from MINECO was also obtained for consolidating and promoting NANBIOSIS (call for Excellence Networks).

An application for cooperation projects with companies and units from the programme has been received.

In an attempt to promote cooperation with companies, making our services become more attractive, the support for units interested in certification to ISO 9001 standard has continued. In 2015 the protein production unit succeeded in obtaining ISO certification, the procedure for certifying the in vivo experimentation unit has been consolidated and the process for the Nanostructured Liquid Characterisation Unit and Surface Characterisation Unit has started.

Cooperation with other platforms:

- Platform of the Instituto Universitario en Nanociencia de Aragón (INA).
- Centro de Cirugía de Mínima Invasión Jesús Usón.
- Unidad de Imagen de CIC biomaGUNE.
- BIONAND (Centro Andaluz de Nanomedicine y Biotecnología).
- Laboratorio Internacional de Nanotecnología (INL). Braga, Portugal.

6

Research Groups

Biomonitoring Group

Programme: **Bioengineering & Medical Image**

Lead Researcher: **Aguiló Llobet, Jordi**

Group members

STAFF MEMBERS: García Pagès, Esther | Illa Vila, Xavier | Tsapikouni, Theodora.

ASSOCIATED MEMBERS: Gabriel Buguña, Gemma | Godignon, Philippe | Gómez Martínez, Rodrigo | Guimerà Brunet, Anton | Hotter Corripio, Georgina | Moya Lara, Ana | Palacios Raufast, Luis | Villa Sanz, Rosa.

CONTRIBUTORS: Arza Valdés, Adriana | Cerón Hurtado, Nathalie Marcela | Montero Suárez, Laura | Pérez Ladaga, Albert | Vinuesa Arroyo, Eugenia | Yeste Lozano, José.

Main lines of research

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

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

This is achieved through the development of:

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

GBIO group has developed during the last few years an outstanding expertise in the design and fabrication of Micro-Nano-Bio devices based either on silicon or biocompatible polymers. Biological signals obtained with these devices are usually subjected to post-acquisition conditioning and processing with the help of totally integrated systems.

Institution: Universitat Autònoma de Barcelona · **Contact:** Centro Nacional de Microelectrónica
Campus Universitat Autònoma de Barcelona · 08193 Bellaterra-Cerdanyola del Vallés
Tel.: +34 93 594 77 00 ext. 2459 · E.mail: jordi.aguilo@uab.es

Nanoparticle and Peptide Chemical Group

Programme: **Nanomedicine**

Lead Researcher: **Albericio Palomera, Fernando**

Group members

STAFF MEMBERS: Acosta Crespo, Gerardo Alexis | Pulido Martínez, Daniel.

ASSOCIATED MEMBERS: Álvarez Domingo, Mercedes | Blanco Canosa, Juan Bautista | Lavilla Grifols, Rodolfo | Royo Expósito, Miriam | Spengler, Jan | Tulla Puche, Judit.

CONTRIBUTORS: López Ibáñez, Alba | Lorente Crivillé, Adriana | Melgarejo Díaz, Marta | Pulido Villamil, Ximena Carolina.

Main lines of research

- Design and synthesis of bioactive low molecular weight compounds and peptides.
- Dendrimers based on defined units of olidoethylene glycol (OEG) as multifunctional systems for the creation of new biomaterials with application to drug delivery and tissue engineering (osteogenesis).
- Drugs-polymer conjugates based on polyglutamic (PGA) or OEG dendrimers, as nanomedicine for the advanced colorectal cancer treatment. Study of the use of these platforms on monotherapy and combined therapy.
- Multiple ligands as chemical tools to study various biological processes, for example: G protein-coupled receptors (GPCRs) oligomerization.
- Design and synthesis of a bicomponent thermoreversible hydrogel platform which combines the bioactive peptide dendrimer decorated hyaluronic acid with the thermoresponsive hyaluronic acid for developing scaffolds for tissue engineering with application to regenerative medicine (bone and cartilage regeneration).
- Development of protein drug delivery systems (PEGylation, peptide functionalized nanovesicles) for substitutive therapy (ie: Fabry disease).
- Design and synthesis of gamma peptides with capacity to cross biological barriers, such as the cytoplasmatic membrane of eukaryotic cells and parasites (Leishmania) and the blood brain barrier (BBB).
- Development of new target peptides for colorectal and triple negative breast cancer tissues.
- Vectorized multicomponent nanoparticles as drug delivery systems and modulators of pharmacokinetic properties.
- Multimodal imaging agents (SPECT, OI, CT and MRI). Nanoparticles for imaging diagnostic applications.
- Surface engineering for controlling cell proliferation on diverse materials.
- Development of solid phase methodology to synthesize biomolecules and other compounds.
- Bionanotechnologies as new strategy to save compounds that failed on clinical or preclinical phases.

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Website: http://www.irbbarcelona.org/index.php/en/research/programmes/chemistry-and-molecular-pharmacology/combinatorial-chemistry-for-the-discovery-of-new-compounds/people/fernando-albericio

Research Group in Biomedical Applications of Nuclear Magnetic Resonance

Programme: **Bioengineering & Medical Image**

Lead Researcher: **Arús Caralto, Carles**

Group members

STAFF MEMBERS: Candiota Silveira, Ana Paula | Juliá Sapé, Mª Margarita.

ASSOCIATED MEMBERS: Acebes Martín, Juan José | Aguilera Grijalbo, Carlos | Arias Ramos, Nuria | Baquero Munera, Miguel | Cabañas Egaña, Miquel | Capdevila Cirera, Antonio | Cos Domingo, Mónica | Fernández Flores, Francisco | Ferrer Font, Laura | Lope Piedrafita, Silvia | Majos Torro, Carlos | Mocioiu, Víctor | Moreno Torres, Ángel | Oriol Rocafiguera, Albert | Pumarola I Battle, Martí | Vellido Alcacena, Alfredo.

CONTRIBUTORS: Ciezka, Magdalena | Fernández Coello, Alejandro | Ortega Martorell, Sandra.

Main lines of research

The major research interest of our group is to improve the diagnosis, treatment and follow-up of therapy response of abnormal brain masses, with noninvasive monitoring tools based in Nuclear Magnetic Resonance (NMR). Within this major goal, several sublines related to MR methodology 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.
- Treatment and follow-up of preclinical brain tumour models with novel therapeutic agents.
- Search for molecular biomarkers of in vivo tumor therapy response, with the help of ex vivo and in vitro studies of cell models, animal models and their biopsies. Correlation with molecular and cellular parameters (histopathology, genomics).
- In vivo molecular phenotyping of tumor progression and therapy response.

Most relevant scientific articles

JULIA-SAPE M., GRIFFITHS J.R., TATE R.A., HOWE F.A., ACOSTA D., POSTMA G. ET AL. Classification of brain tumours from MR spectra: The INTERPRET collaboration and its outcomes. NMR in Biomedicine. 2015; 28(12):1772-1787.

SIMOES R.V., ORTUNO J.E., BOKACHEVA L., CANDIOTA A.P., LEDESMA-CARBAYO M.J., DELGADO-GONI T. ET AL. Effect of acute hyperglycemia on moderately hypothermic GL261 mouse glioma monitored by T1-weighted DCE MRI. Magnetic Resonance Materials in Physics, Biology and Medicine. 2015;28(2):119-126.

MAJOS C., COS M., CASTANER S., GIL M., PLANS G., LUCAS A. ET AL. Early post-operative magnetic resonance imaging in glioblastoma: correlation among radiological findings and overall survival in 60 patients. European Radiology. 2015.

MOCIOIU V., ORTEGA-MARTORELL S., OLIER I., JABLONSKI M., STARCUKOVA J., LISBOA P. ET AL. From raw data to data-analysis for magnetic resonance spectroscopy - the missing link: JMRUI2XML. BMC Bioinformatics. 2015;16(1).

FERRER-FONT L., ALCARAZ E., PLANA M., CANDIOTA A.P., ITARTE E., ARUS C.. Protein Kinase CK2 Content in GL261 Mouse Glioblastoma. Pathology and Oncology Research. 2015.

Highlights

During 2015, the GABRMN-UAB started the national project "Imagen molecular de glioma de alto grado para la mejora de la respuesta al tratamiento (MOLIMAGLIO)", granted by MINECO with code SAF2014-52332-R. This Project spans until 2017. Its key objective is to characterize non invasively the response of therapy, searching for early surrogate therapy response biomarkers with translational potential to clinics.

Also during 2015, the "e-MEDIVIP, E-Learning Platform for Medical Informatics to Improve Vocational and ICT Practice" project was awarded, led by the Bilecik Seyh Edebali University in which CIBER-BBN is a partner (PI Margarida Julià). This project has the objective to improve the acceptance of medical decision support systems in the clinical environment.

Regarding the postgraduate student training, Dr Magdalena Ciezka was awarded her PhD degree with a thesis entitled "Improvement of Protocols for Brain Cancer Diagnosis and Therapy Response Monitoring Using Magnetic Resonance Based Molecular Imaging Strategies", which received the Sobresaliente Cum Laude qualification. With respect to new personnel incorporations during 2015, Ms Lucía Villamañán who will follow the research line of noninvasive response assessment in preclinical brain tumour models and Mr Victor Mocioiu who develops artificial intelligence-based tools for both preclinical and clinical data.

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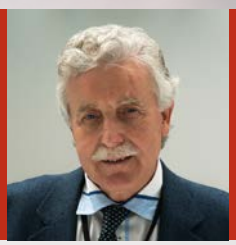
Tissue Bioengineering and Regeneration Laboratory

Programme: **Biomaterials & Advanced Therapies**

Lead Researcher: **Becerra Ratia, José**



Group members

STAFF MEMBERS: Santos Ruiz, Leonor | Visser, Rick.

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

Main lines of research

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

Most relevant scientific articles

DURAN I., RUIZ-SÁNCHEZ J., SANTAMARIA J.A., MARI-BEFFA M. Holmgren's principle of delamination during fin skeletogenesis. Mechanisms of Development. 2015;135:16-30.

VILLATORO A.J., FERNÁNDEZ V., CLAROS S., RICO-LLANOS G.A., BECERRA J., ANDRADES J.A. Use of adipose-derived mesenchymal stem cells in keratoconjunctivitis sicca in a canine model. BioMed Research International. 2015;2015.

DURAN I., CSUKASI F., TAYLOR S.P., KRAKOW D., BECERRA J., BOMBARELY A. ET AL. Collagen duplicate genes of bone and cartilage participate during regeneration of zebrafish fin skeleton. Gene Expression Patterns. 2015;19(1-2):60-69.

VISSER R., BODNAROVA K., ARRABAL P.M., CIFUENTES M., BECERRA J. Combining bone morphogenetic proteins-2 and -6 has additive effects on osteoblastic differentiation in vitro and accelerates bone formation in vivo. Journal of Biomedical Materials Research - Part A. 2015;104(1):178-185.

Highlights

In 2015 we have partnered with groups and companies from Italy, Switzerland, Netherlands and Spain to submit the proposal "NANODEV- NANO-sized Delivery systems for mesenchymal stem cells-derived Extracellular Vesicles" to the Horizon 2020 NMBP-10-2016. Nº 720821-1. We have as well applied to H2020-MSCA-IF-2015, presenting the proposal "OSTEOBIOMAT. Novel biomimetic peptides with specific binding domains for the functionalization of biomaterial surfaces for bone tissue engineering".

We have submitted two national project proposals to the MINECO: "Customized bioengineered implants of porous titanium for maxillofacial reconstructive surgery. Proofs of concept and preclinical assay" (BIO2015-66266-R); "Can Glass Nitridation Generate a New Scientific and Technologycal Pathway for Molecular Regognition and Efficient Osteoinduction?" (Explora).

We have applied for funding from the Andalusian Government "Desarrollo de un Preparado de Ingeniería Tisular para el tratamiento de Osteonecrosis Maxilar Aséptica" (PI-0339-2014).

Our group has hosted the Finnish postdoctoral Hertta Pulkkinen, whose 12-month stay was funded by Campus Excelencia Internacional Andalucía Tech and by CIBER-BBN. We also hosted short-stays of three Italian PhD students from the University of Pavía.

We have obtained the international extension for the patent "Bioactive glasses, bioactive glass scaffolds, and cell-seeded bioactive glass scaffolds; preparation methods; and uses thereof" (PCT/ES2015/070535), and published the results of this research in Acta Biomaterialia, although dated 2016 (Act Biom 29:424-34), the article was available online from 2015, quickly getting much attention from the media, and being Dr. Leonor Santos-Ruiz (CIBER-BBN researcher) interviewed in several radio and TV programmes.

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

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

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Translational Research Group in Biomaterials and Tissue Engineering

Programme: **Biomaterials & Advanced Therapies**

Lead Researcher: **Bellón Caneiro, Juan Manuel**

Group members

STAFF MEMBERS: González Chamorro, Diana | Martínez-Alcocer Fuerte, Soraya | Pascual González, Mª Gemma.

ASSOCIATED MEMBERS: Buján Varela, María Julia | García Honduvilla, Natalio.

CONTRIBUTORS: Pérez Köhler, Bárbara.

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 infection are currently being assayed. Tissue adhesives have recently been introduced in this line of research as a strategy for fixing prosthetic materials for hernia repair.
- **Repair of skin defects.** One of the alternatives for the repair of skin defects, especially in patients with compromised healing (diabetics, torpid vascular ulcers and pressure ulcers) can be improved through tissue engineering strategies. Essentially work is being conducted with two experimental models: muscle-derived stem cells for repairing excisional skin defects with encouraging results, and the design of polymers for the controlled release of healing modulating drugs.
- **Repair and vascular pathology.** Research has been conducted within this line in healing/ restenosis, with special interest in the modulation thereof. The problem of arterial substitution by means of biomaterials for clinical use and cryopreserved vessels has also been approached. Finally, tissue engineering techniques are used for the purpose of improving the viability of prosthetic materials through the creation of a cell coating and the incorporation of bioactive substances. Currently being working on venous insufficiency in pregnancy and in the search for predictive markers.
- **Osteogenic regeneration.** This research line

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

Most relevant scientific articles

PASCUAL G., SOTOMAYOR S., RODRIGUEZ M., ARTEAGA V., BELLON J.M. Extraperitoneal and intraperitoneal behavior of several biological meshes currently used to repair abdominal wall defects. Journal of Biomedical Materials Research - Part B Applied Biomaterials. 2015;103(2):365-372.

CORDERO A., HERNÁNDEZ-GASCON B., PASCUAL G., BELLON J.M., CALVO B., PENA E. Biaxial Mechanical Evaluation of Absorbable and Nonabsorbable Synthetic Surgical Meshes Used for Hernia Repair: Physiological Loads Modify Anisotropy Response. Annals of Biomedical Engineering. 2015;:1-8.

GARCÍA-MORENO F., PÉREZ-LÓPEZ P., SOTOMAYOR S., PÉREZ-KOHLER B., BAYON Y., PASCUAL G. ET AL. Comparing the host tissue response and peritoneal behavior of composite meshes used for ventral hernia repair. Journal of Surgical Research. 2015;193(1):470-482.

REYES-ORTEGA F., CIFUENTES A., RODRIGUEZ G., AGUILAR M.R., GONZÁLEZ-GÓMEZ A., SOLIS R. ET AL. Bioactive bilayered dressing for compromised epidermal tissue regeneration with sequential activity of complementary agents. Acta Biomaterialia. 2015;23:103-115.

PÉREZ-KOHLER B., GARCÍA-MORENO F., BAYON Y., PASCUAL G., BELLON J.M. Inhibition of Staphylococcus aureus adhesion to the surface of a reticular heavyweight polypropylene mesh soaked in a combination of chlorhexidine and allicin: An in vitro study. PLoS ONE. 2015;10(5).

Highlights

In connection with our research line in biomaterials for the repair of abdominal wall defects, a new national project under the call "R&D Excellence Projects" SAF2014-55022-P, "Bioassay of a new cyanoacrylate for internal use(n-octyl/CIAH) of implanted prosthetic materials for the repair of hernia defects"CIANOMESH", has been granted in 2015. In addition, the extension granted for the National Project DPI2011-27939-C02-02, as part of the intramural project BIOMIMESH, has been finished. A total of four transfer contracts have been signed with Sofradim Production and Assut Europe companies, in the field of prosthetic infection. This line has had a significant productivity, with a total of twelve publications (four Q1/six Q2). Several communications have been presented in the 1st World Congress on Abdominal Wall Surgery Conference and 28th European Congress on Surgical Infections, held in Milan and Oporto respectively.

In connection with our line in repair of skin defects, it has been published an article in Acta Biomaterialia (Q1) on the design and evaluation of new bilayered dressing for application in the healing of compromised wounds. The patent for this product was obtained a few years ago and during the 2015 extension to Europe, USA and Australia has been requested. During this year a major Art. 83 transfer contract with Novartis, in the field of drug healing, has been finished and a new one with Genzyme Corporation has been signed. Several communications have been presented at the XVIII SEHIT Congress, held in Bilbao.

Regarding the research line of repair and vascular pathology the second year of the National Project "Venous insufficiency in pregnancy: search of predictive markers", by the Instituto de Salud Carlos III (PI13/01513), has been carried out successfully. Several communications have been presented at 31st LIAC Meeting on Vascular Research, held in Lisbon, on the Gordon Research Conference on Elastin, Elastic Fibers and Microfibrils, in USA and in the XVIII Congress SEHIT/VI International Congress of Histology and Tissue Engineering, held in Bilbao.

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Cell Therapy Research Group

Programme: **Biomaterials & Advanced Therapies**

Lead Researcher: **Blanco Fernández, Jerónimo**

Group members

STAFF MEMBERS: Garrido López, Cristina Pilar.

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

Main lines of research

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

Most relevant scientific articles

MOLINAR-TORIBIO E., PÉREZ-JIMÉNEZ J., RAMOS-ROMERO S., ROMEU M., GIRALT M., TALTAVULL N. ET AL. Effect of n-3 PUFA supplementation at different EPA:DHA ratios on the spontaneously hypertensive obese rat model of the metabolic syndrome. British Journal of Nutrition. 2015;113(6):878-887.

ROURA S., SOLER-BOTIJA C., BAGO J.R., LLUCIA-VALLDEPERAS A., FERNÁNDEZ M.A., GALVEZ-MONTON C. ET AL. Postinfarction functional recovery driven by a three-dimensional engineered fibrin patch composed of human umbilical cord blood-derived mesenchymal stem cells. Stem Cells Translational Medicine. 2015;4(8):956-966.

MOLINAR-TORIBIO E., PÉREZ-JIMÉNEZ J., RAMOS-ROMERO S., GÓMEZ L., TALTAVULL N., NOGUES M.R. ET AL. D-Fagomine attenuates metabolic alterations induced by a high-energy-dense diet in rats. Food and Function. 2015;6(8):2614-2619.

GALVEZ-MONTON C., FERNÁNDEZ-FIGUERAS M.T., MARTI M., SOLER-BOTIJA C., ROURA S., PEREA-GIL I. ET AL. Neoinnervation and neovascularization of acellular pericardial-derived scaffolds in myocardial infarcts. Stem Cell Research and Therapy. 2015;6(1).

LLUCIA-VALLDEPERAS A., SÁNCHEZ B., SOLER-BOTIJA C., GALVEZ-MONTON C., PRAT-VIDAL C., ROURA S. ET AL. Electrical stimulation of cardiac adipose tissue-derived progenitor cells modulates cell phenotype and genetic machinery. Journal of Tissue Engineering and Regenerative Medicine. 2015;9(11):E76-E83.

Highlights

During the year 2015 the Cell Therapy Group has centered in the development of cell therapy strategies against tumors (gliomas) as well as in the advancement of our understanding of the interactions between therapeutic stem cells and tumor cells. The principal milestone achieved during this year has been the discovery that therapeutic mesenchymal stromal cells used for therapy agains gliomas do not undergo apoptosis upon administration of the Ganciclovir prodrug, but survive the treatment. Thus, we have to assume that tumor killing effect is mediated by secretion of Ganciclovir phosphate loaded exosomes or a similar mechanism. Moreover, we have also discovered that a consequence of anti-replication therapy against tumors is the appearance of a pool of therapy resistant glioma stem cells that we can detect and quantify by bioluminescence imaging; capable of recapitulating tumors upon release from therapy. We have also fine-tuned the CLARITY procedure that allows visualization of fluorescent tumors in transparent brains. Using this procedure together with confocal microscopy we have identified TR-GSC remnants. We believe that these are the last resource of therapy resistance, thus the main objective of this project in the near future will be its eradication.

During 2015 the research team has been supported by a project from MINECO, the Cell Therapy Network "TerCel" and an internationalization project with India for the use of photodynamic therapy against tumors. Additional support has been provided by a "Retos Colaboración" project with Instituto Químico de Sarria and the SAGETIS company. During this year, the group has obtained additional support from CIBER through Transfer Project "Multifunctional Nanoparticles for Cell Therapy (TRANSMAG).

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Ocular Surface Inflammation & Advanced Therapies Groups

Programme: Biomaterials & Advanced Therapies

Lead Researcher: Calonge Cano, Margarita

Group members

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Main lines of research

VERTICAL RESEARCH LINES:

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

HORIZONTAL RESEARCH LINES:

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

Most relevant scientific articles

RAMIREZ B.E., VICTORIA D.A., MURILLO G.M., HERRERAS J.M., CALONGE M. In vivo confocal microscopy assessment of the corneoscleral limbal stem cell niche before and after biopsy for cultivated limbal epithelial transplantation to restore corneal epithelium. Histology and Histopathology. 2015;30(2):183-192.

COCHO L., FERNÁNDEZ I., CALONGE M., MARTÍNEZ V., GONZÁLEZ-GARCÍA M.J., Caballero D. et al. Gene expression-based predictive models of graft versus host disease-associated dry eye. Investigative Ophthalmology and Visual Science. 2015;56(8):4570-4581.

ABENGOZAR-VELA A., CALONGE M., STERN M.E., GONZÁLEZ-GARCÍA M.J., ENRIQUEZ-DE-SALAMANCA A. Quercetin and resveratrol decrease the inflammatory and oxidative responses in human ocular surface epithelial cells. Investigative Ophthalmology and Visual Science. 2015;56(4):2709-2719.

LÓPEZ-MIGUEL A., TESON M., MARTÍN-MONTANEZ V., ENRIQUEZ-DE-SALAMANCA A., STERN M.E., GONZÁLEZ-GARCÍA M.J. ET AL. Clinical and Molecular Inflammatory Response in Sjögren Syndrome-Associated Dry Eye Patients Under Desiccating Stress. American Journal of Ophthalmology. 2015.

RAMIREZ B.E., SÁNCHEZ A., HERRERAS J.M., FERNÁNDEZ I., GARCÍA-SANCHO J., NIETO-MIGUEL T. ET AL. Stem Cell Therapy for Corneal Epithelium Regeneration following Good Manufacturing and Clinical Procedures. BioMed Research International. 2015;2015.

Highlights

IOBA-UVa group is working in three intramural projects:

1. BioScaff-EYE: "Bio-engineered stem cell niches in ocular surface reconstruction for corneal blindness", coordinated by IOBA-UVa was transferred to Ferrer Advanced Biotherapeutics (FAB). Three groups: IOBA-UVa-Valladolid, clinical group (PI M.Calonge, IBEC-Barcelona (PI E.Engel), and NanoBioCel-Vitoria (PI JL.Pedraz) are working and FAB to lead this project to the desired end at maximum speed. As a result, new in vitro studies are underway and new options are being tested in animals. Additionally, IOBA-UVa submitted for publication the first double-masked randomized clinical trial to report safety and efficacy of bone marrow-mesenchymal stem cells in human ocular surface. Due to the signed non-disclosure agreement, dissemination of results is not allowed.
2. EYE-PoC: "Point-of-care biosensor devices to detect biomarkers as evaluation end-points for therapeutic clinical trials in ocular surface inflammation" was granted in 2014. It is coordinated by IOBA-UVa, the clinical group (PI A.Enríquez-de-Salamanca) and teamed with NB4D-CISC (PI P.Marco, R.Galve), CIN2-CISC (PI L.Lechuga) and GQNA-CISC (PI R.Eritja). We developed a 4-molecule tear biomarker panel predictive for Dry Eye Disease (diagnosis) and differentiating severity grading, with excellent sensitivity and specificity values. These molecules will be integrated in amperometric and/or optical PoC devices and will be submitted for patentability. Additionally, we obtained preliminary data regarding differential microRNAs levels in tears samples from DED patients compared to those of healthy subjects.
3. NANO-OPHTHAL: "New si-RNA-nanoparticle conjugates for the treatment of ocular surface inflammations", granted as "excelent project" during 2014, is coordinated by Nanomol-CISC (PI S.Sala/J.Veciana) and teamed with GDAB-UAH (PI J.de-la-Mata), GQNA-CISC (PI R.Eritja), IOBA-UVa as clinical group (PI A.Enríquez-de-Salamanca) and external group (R.Herrero). We elaborate a protocol to test tolerance of nanoparticles in rabbits, approved by The Animal Welfare Committee of the University (CEEBA) and by the Regional Government.

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Group of Structural Mechanics and Materials Modeling

Programme: Biomaterials & Advanced Therapies
Lead Researcher: Doblaré Castellano, Manuel

Group members

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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.

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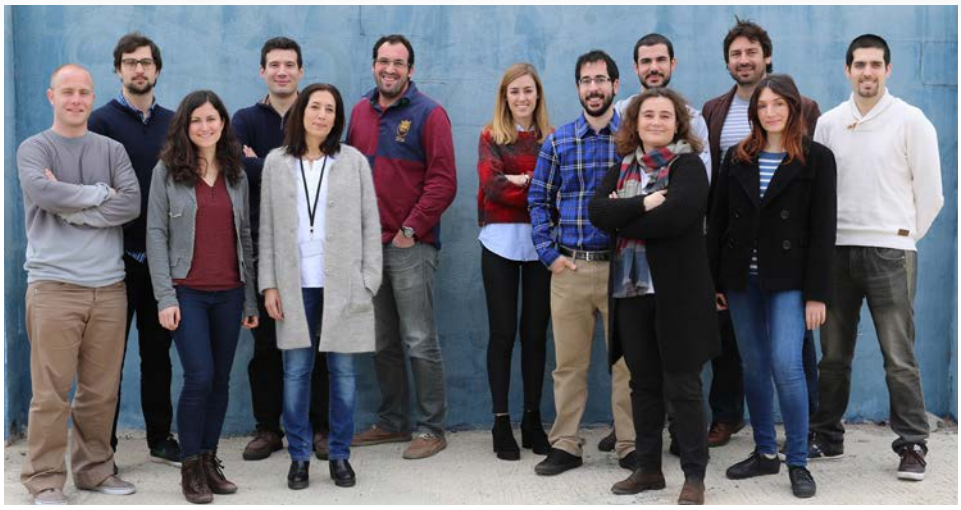
Research Group in Biomaterials, Biomechanics and Tissue Engineering

Programme: **Biomaterials & Advanced Therapies**
Lead Researcher: **Engel López, Elisabeth**

Group members



STAFF MEMBERS: González Marín, Belén | Mateos Timoneda, Miguel Ángel | Sánchez Ferrero, Aitor.

ASSOCIATED MEMBERS: Altankov, George | Cano Torres, Irene | Castaño Linares, Óscar | Koch, Martín Andreas | Lacroix, Damien | Levato, Riccardo | Martí Muñoz, Joan | Navarro Requena, Claudia | Noailly, Jerome | Planell Estany, Josep Anton.

CONTRIBUTORS: Álvarez, Zaida | Barreto, Sara | González Vázquez, Arlyng Gyveth | Gugutkov, Decnho | Malandrino, Andrea | Mattoti, Marta | Olivares, Andy Luis | Pérez, Soledad | Puñet Ortiz, Xavier | Sachot, Nadège.

Main lines of research

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

Most relevant scientific articles

LEVATO R., PLANELL J.A., MATEOS-TIMONEDA M.A., ENGEL E. Role of ECM/peptide coatings on SDF-1α triggered mesenchymal stromal cell migration from microcarriers for cell therapy. Acta Biomaterialia. 2015;18:59-67.

SÁNCHEZ-FERRERO A., MATA A., MATEOS-TIMONEDA M.A., RODRIGUEZ-CABELLO J.C., ALONSO M., PLANELL J. ET AL. Development of tailored and self-mineralizing citric acid-crosslinked hydrogels for in situ bone regeneration. Biomaterials. 2015;68:42-53.

SACHOT N., MATEOS-TIMONEDA M.A., PLANELL J.A., VELDERS A.H., LEWANDOWSKA M., ENGEL E. ET AL. Towards 4th generation biomaterials: A covalent hybrid polymer-ormoglass architecture. Nanoscale. 2015;7(37):15349-15361.

Won J.-E., Mateos-Timoneda M.A., Castano O., Planell J.A., Seo S.-J., Lee E.-J. et al. Fibronectin immobilization on to robotic-dispensed nanobioactive glass/polycaprolactone scaffolds for bone tissue engineering. Biotechnology Letters. 2015;37(4):935-942.

BAELO A., LEVATO R., JULIAN E., CRESPO A., ASTOLA J., GAVALDA J. ET AL. Disassembling bacterial extracellular matrix with DNase-coated nanoparticles to enhance antibiotic delivery in biofilm infections. Journal of Controlled Release. 2015;209:150-158.

Highlights

Production of polymeric biomaterials using different fabrication techniques. By using a polymer nanoprecipitation technique, the group produced nanoparticles for antibiotic drug delivery that effectively treated persistent bacterial infections. The use of a jet break-up polymer precipitation technique together with protein/peptide functionalization allowed the group to produce micro particles for effective cell delivery.

The production of structured bioactive nanocomposites that can enhance vascularization, bone and skin regeneration, either by electrospinning, rapid prototyping or microparticles production. Recent advances describe a novel hybrid material which faithfully mimics the structure of bone's extracellular matrix, recreating the molecular architecture

and biochemical environment to surround cells with the proper stimuli to spread and grow. Other biomaterials developed in the group such as hybrid fibrous mats with different contents of calcium-releasing nanoparticles are able to induce angiogenesis in in vivo models .In 2015, the Dermoglass project was selected for funding under the first CaixaImpulse call, a funding programme promoted by the Obra Social "la Caixa", that aims to promote technology transfer in science.

Institution: Fundación Instituto de Bioingeniería de Cataluña · **Contact:** Ins. de Bioingeniería de Cataluña
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Nucleic Acid Chemistry Group

Programme: **Nanomedicine**

Lead Researcher: **Eritja Casadellà, Ramon**

Group members

STAFF MEMBERS: Aviñó Andrés, Ana María | Grijalvo Torrijo, Santiago.

ASSOCIATED MEMBERS: Fábrega Claveria, Carmen | Pérez Rentero, Sonia | Tintoré Gazulla, Maria.

CONTRIBUTORS: Alagia, Adele.

Main lines of research

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

Most relevant scientific articles

AVINO A., HUERTAS C.S., LECHUGA L.M., ERITJA R. Sensitive and label-free detection of miRNA-145 by triplex formation. Analytical and Bioanalytical Chemistry. 2015;:1-9.

PÉREZ-RENTERO S., GARGALLO R., GONZÁLEZ C., ERITJA R. Modulation of the stability of i-motif structures using an acyclic threoninol cytidine derivative. RSC Advances. 2015;5(78):63278-63281.

FORNAGUERA C., GRIJALVO S., GALAN M., FUENTES-PANIAGUA E., DE LA MATA F.J., GÓMEZ R. et al. Novel non-viral gene delivery systems composed of carbosilane dendron functionalized nanoparticles prepared from nano-emulsions as non-viral carriers for antisense oligonucleotides. International Journal of Pharmaceutics. 2015;478(1):113-123.

GALAN T., PRIETO-SIMON B., ALVIRA M., ERITJA R., GOTZ G., BAUERLE P. ET AL. Label-free electrochemical DNA sensor using "click"-functionalized PEDOT electrodes. Biosensors and Bioelectronics. 2015;74:751-756.

AGIRRE M., OJEDA E., ZARATE J., PURAS G., GRIJALVO S., ERITJA R. ET AL. New Insights into Gene Delivery to Human Neuronal Precursor NT2 Cells: A Comparative Study between Lipoplexes, Nioplexes, and Polyplexes. Molecular Pharmaceutics. 2015;12(11):4056-4066.

Highlights

In collaboration with other CIBER-BBN (NANOBIOCEL, NN-UMH) groups we have developed formulations for transfection of nucleic acids for gene therapy of ocular diseases. This research is funded by a Collaborative project (TERET). Moreover and in collaboration with the NBT-UAB and GOA-HSCSP groups of CIBER-BBN, our group has prepared nanoconjugates made of cytotoxic oligonucleotides and proteins directed against cancer stem cells that are able to effectively kill metastatic cells. This project is funded by the Foundation "La Marató de TV3" and by the Institutes of Health. In collaboration with the group of Nanomedicine of IBEC we have developed a method for immobilizing DNA probes based on [2 + 2] cycloaddition reactions catalyzed by Cu. An important part of scientific activity has been focused on the evaluation of small RNA (siRNA) duplexes that are capable of silencing genes specifically. We have studied the introduction of small chemical modifications that increase the stability of siRNAs in serum and the ability to use nanostructured materials (prepared by other groups CIBER-BBN) for the development of new formulations that increase the efficiency of transfection. In collaboration with the group of CIBER-BBN (ICN2-CSIC) we have studied thedetection of microRNA by SPR using capture probes with high efficiency which are able to form triple helices with the target miRNA. Finally, we have developed derivatives forming oligonucleotides guanine quadruplex having a great antiviral activity against HIV-1 virus and Hepatitis C. These results have been protected with a patent. Two Ph. D. students have passed their Ph.D. dissertions with honours.

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Neuroprosthesis and Neuroengineering Research Group

Programme: **Bioengineering & Medical Image**

Lead Researcher: **Fernández Jover, Eduardo**

Group members

STAFF MEMBERS: Humphreys, Lawrence | Martínez Navarrete, Gema | Soto Sánchez, Cristina.

ASSOCIATED MEMBERS: Alfaro Sáez, Arantxa | Azorín Poveda, José María | Fimia Gil, Antonio | García Aracil, Nicolás Manuel | Marín Monerris, Cristina | Ortega Ascencio, Ilidia | Sabater Navarro, José María.

CONTRIBUTORS: Pérez Vidal, Carlos.

Main lines of research

- Genetic therapy:

  - Genetic therapy directed for reprogramming cells in vivo and in vitro for the regeneration of the retina.

  - Development of new nanoparticles to perform as vehicles for genes in genetic therapies.

- Development of biomedical technologies:

  - Development of robots to assist in surgery and surgery simulations.

  - Development of devices for neurorehabilitation and robot assisted rehabilitation.

  - Development of non-invasive brain-computer interfaces (BCI) based on electroencephalography (EEG) electrooculography (EOG for disabled people.

  - Development of technology for the detection of breast cancer.

  - Development of new generations of multifunctional intraocular lenses.

  - Development of software for neural signal analysis.

- Functional optimization and improvement of biocompatibility of long term neural interfaces.

- Study of cortical reorganization and associated changes to neural plasticity in the blind.

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Dendrimer Group for Biomedical Applications

Programme: **Nanomedicine**

Lead Researcher: **Gómez Ramírez, Rafael**

Group members

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

ASSOCIATED MEMBERS: De La Mata De La Mata, Francisco Javier | Gutiérrez Ulloa, Carlos Emilio | Maroto Díaz, Marta | Moreno Pinilla, Silvia.

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

Main lines of research

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

Most relevant scientific articles

SERRAMIA M.J., ALVAREZ S., FUENTES-PANIAGUA E., CLEMENTE M.I., SÁNCHEZ-NIEVES J., GÓMEZ R. ET AL. In vivo delivery of siRNA to the brain by carbosilane dendrimer. Journal of Controlled Release. 2015;200:60-70.

SEPULVEDA-CRESPO D., SÁNCHEZ-RODRIGUEZ J., SERRAMIA M.J., GÓMEZ R., DE LA MATA F.J., JIMÉNEZ J.L. ET AL. Triple combination of carbosilane dendrimers, tenofovir and maraviroc as potential microbicide to prevent HIV-1 sexual transmission. Nanomedicine. 2015;10(6):899-914.

SEPULVEDA-CRESPO D., SERRAMIA M.J., TAGER A.M., VRBANAC V., GÓMEZ R., DE LA MATA F.J. ET AL. Prevention vaginally of HIV-1 transmission in humanized BLT mice and mode of antiviral action of polyanionic carbosilane dendrimer G2-S16. Nanomedicine: Nanotechnology, Biology, and Medicine. 2015;11(6):1299-1308.

BRIZ V., SEPULVEDA-CRESPO D., DINIZ A.R., BORREGO P., RODES B., DE LA MATA F.J. ET AL. Development of water-soluble polyanionic carbosilane dendrimers as novel and highly potent topical anti-HIV-2 microbicides. Nanoscale. 2015;7(35):14669-14683.

MARTÍNEZ A., FUENTES-PANIAGUA E., BAEZA A., SÁNCHEZ-NIEVES J., CICUENDEZ M., GÓMEZ R. ET AL. Mesoporous Silica Nanoparticles Decorated with Carbosilane Dendrons as New Non-viral Oligonucleotide Delivery Carriers. Chemistry - A European Journal. 2015;21(44):15651-15666.

Highlights

The activity of the group during 2015 has been centered in the development of new dendritic nanosystems in two directions: (i) design of improved non-viral vectors for gene therapy in HIV and cancer and (ii) design of HIV antiviral, antibacterial, anticancer and antineurodegenerative agents, funded by european (IRSES), national (CTQ2014-54004-P, MINECO and PIE14/00061, INTERCIBER) and regional (Consorcio NANODENMED-CM) projects. The research carried out, focused in the search of a new therapeutic approach towards the HIV treatment based on the double and triple combined therapy of anionic dendrimers and retroviral drugs, achieving 100% of inhibition both in CCR5 and CXCR4 strains. Also, we are working in the use of combined therapy for bacteria and parasites, decreasing the concentration of the drug while keeping the activity when dendrimers are added as adjuvants. In addition, new cationic dendritic systems have been developed based on the dendronization of silica and gold nanoparticles to carry short nucleic acid (antisense oligonucleotides or siRNA) within different intramural CIBER-BBN projects.

Results of the research has led to 20 publications The group has continued intensifying its activities related to technology transfer applying for a national Spanish patent based on the use of metallic nanoparticles stabilized with carbosilane dendrons for biomedical applications. In this sense, in April 2015, we were awarded a second prize for the best patent of the Comunity of Madrid, from the Madrid+d Foundation.

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Biomaterials Centre

Programme: Biomaterials & Advanced Therapies
Lead Researcher: Gómez Ribelles, José Luis

Group members

STAFF MEMBERS: Rico Tortosa, Patricia | Teruel Biosca, Laura.

ASSOCIATED MEMBERS: Gallego Ferrer, Gloria | Gómez Tejedor, José Antonio | Meseguer Dueñas, José María | Monleón Pradas, Manuel | Sabater i Serra, Roser | Salmerón Sánchez, Manuel | Vidaurre Garayo, Ana.

CONTRIBUTORS: Araque Monrós, Carmen.

Main lines of research

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

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

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

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

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

Most relevant scientific articles

ANTOLINOS-TURPIN C.M., MORALES ROMAN R.M., RODENAS-ROCHINA J., GÓMEZ RIBELLES J.L., GÓMEZ-TEJEDOR J.A. Macroporous thin membranes for cell transplant in regenerative medicine. Biomaterials. 2015;67:254-263.

MNATSAKANYAN H., RICO P., GRIGORIOU E., CANDELAS A.M., RODRIGO-NAVARRO A., SALMERON-SÁNCHEZ M. ET AL. Controlled Assembly of Fibronectin Nanofibrils Triggered by Random Copolymer Chemistry. ACS Applied Materials and Interfaces. 2015;7(32):18125-18135.

GAMIZ-GONZÁLEZ M.A., PISKIN A.E., PANDIS C., CHATZIMANOLIS-MOUSTAKAS C., KYRITSIS A., MARI B. ET AL. Determining the influence of N-acetylation on water sorption in chitosan films. Carbohydrate Polymers. 2015;133:110-116.

LOZANO PICAZO P., PÉREZ GARNES M., MARTÍNEZ RAMOS C., VALLES-LLUCH A., MONLEON PRADAS M. New semi-biodegradable materials from semi-interpenetrated networks of poly(ε-caprolactone) and poly(ethyl acrylate). Macromolecular Bioscience. 2015;15(2):229-240.

BALLESTER-BELTRÁN J, LEBOURG M, RICO P, SALMERÓN-SÁNCHEZ M. Cell migration within confined sandwich-like nanoenvironments.Nanomedicine (London, England). 2015;10(5):815-28.

Highlights

TRASLATIONAL RESEARCH:

- Tissue Engineering for Bone Augmentation for Dental Implant Fixation, in collaboration with Zvit Medica SL. and the LABRET-UMA group. CIBER-BBN Technology Transfer Program Proposals
- Creation of the spin-off IKASIA Technologies SL in which Universitat Politècnica de València ia a partner.

EUROPEAN RESEARCH PROJECTS:

- Nanostructured Gel for Cellular Therapy of Degenerative Skeletal Disorders (STRUCTGEL). EuroNanoMed 2011 (PI11 / 03032).
- Network for Development of Soft Nanofibrous Construct for Cellular Therapy of Degenerative Skeletal Disorders (FIBROGELNET). EU Marie Curie IAPP (PIAP-GA-2012-324386).

NATIONAL RESEARCH PROJECTS:

- Local mechanical stimulation of mesenchymal stem cells to enhance oteogenic and chondrogenic differentiation in regenerative medicine. (MAT2013-46467-C4-1-R).
- Material-driven fibronectin fibrillogenesis to Engineer Synergistic Growth Factor Microenvironments. (MAT2012-38359-C03-01).
- Enteroscopy in humans by Endoworm system ISCIII-FIS (PI12 / 01000).
- "Network of Excellence" research for the development of functionalized titanium implants. (MAT2014-52905-REDT).

REGIONAL RESEARCH PROJECTS:

- New biomaterials for improving predictive models based on liver cell cultures. HEPATIBIOMAT (Projects UPV-Hospital La Fe).
- Construction of a semidegradable hybrid system with applications in bone regeneration. BIOSCAFF. (Projects UPV-Hospital La Fe).
- Three-dimensional supports based on biodegradable microparticles for the regeneration of articular cartilage (IIS INCLIVA Foundation Hospital of Valencia - UPV).
- New Endoscopy System Endoworm 3.0 (Projects UPV-Hospital La Fe).
- Development of biomimetic three-dimensional environments for myeloma cells culture (Project UPV-Hospital La Fe).

THESIS AWARDS: JJosé Ballester Beltran "Sandwich to engineer systems like the cellular microenvironment".

- Award: Specialized Group of Polymers (GEO) of the Spanish Royal Chemistry and Physic Royal Societies.
- 2015 European doctoral award-European Society for Biomaterials (ESB).

7 doctoral theses in 2015.

39 scientific articles published in 2015.

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Research Group on Microbial Adhesion

Programme: Biomaterials & Advanced Therapies

Lead Researcher: González Martín, María Luisa

Group members

STAFF MEMBERS: Fernández Calderón, Mª Coronada | Pacha Olivenza, Miguel Ángel.

ASSOCIATED MEMBERS: Blanco Roca, María Teresa | Gallardo Moreno, Amparo M. | Gómez García, Antonio Candido | Labajos Broncano, Luis | Morales Bruque, José | Pérez Giraldo, Ciro.

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

Main lines of research

The research line of the AM-UEx group is directed to the issue of the biomaterial-associated infections, BAI. These infections appear because of the microorganisms ability for the surfaces colonization. They are one of the main reason behind the need of replacement of implants, prosthesis, catheters, etc. because the lower efficacy of antibiotics to BAI in respect other infections. In this line, we are interested on the initial behavior of the interaction of microorganisms with surfaces, that is, the rate and initial extension of their adhesion, and also, the biofilm growth on the material. We look for different behaviors related to the conditions of growth and / or suspension of microorganisms. Within our specialty, we analyze physical and chemical properties of the surfaces of bacteria and substrate, in order to identify the most relevant characteristics for the beginning of the bacterial colonization of the material. We look into surface electrical properties, free energy and hydrophobicity for substrata and microorganisms, as well into the changes in the surface chemical composition. We devote special interest to the study of the consequences of the different topographical issues of the substrate surface on the bacterial adhesion. Also, we work on the genetic bases for biofilm production and the effect of antiseptics and antibiotics on them.

In a direct collaboration with the clinic practice, we work together with the Maxillofacial Surgery Service of the Infanta Cristina University Hospital in Badajoz. We study characteristics of the explanted devices in relation with patient history.

Most relevant scientific articles

CÓRDOBA A., MONJO M., HIERRO-OLIVA M., GONZÁLEZ-MARTÍN M.L., RAMIS J.M. Bioinspired Quercitrin Nanocoatings: A Fluorescence-Based Method for Their Surface Quantification, and Their Effect on Stem Cell Adhesion and Differentiation to the Osteoblastic Lineage. ACS Applied Materials and Interfaces. 2015;7(30):16857-16864.

Highlights

An important part of the activity of the research group along the 2015 has been focused on the collaboration with several research groups, contributing with our knowledge on bacterial colonization of surfaces and on surface characterization. We have been working together with other groups from CIBER-BBN, within the framework of the internal projects or not, but also with some other external groups in the University of Illes Balears and in the National Hospital for Paraplegic. Also we continue in the consolidation of some other collaborations within our environment that are especially relevant for us. They are with two Services in the Hospital Infanta Cristina in Badajoz, those of Maxillofacial Surgery and Interventional Radiology.

Also, we have registered two patents. One of them, on a new biodegradable material, in cooperation with other CIBER-BBN group. A second patent is on a procedure for obtaining specific topographical features on surfaces. This is very useful for the research on the consequences of topography of substrate on the bacterial adhesion.

Besides, we have taken part in several applications in European calls and maintained an intense formative activity.

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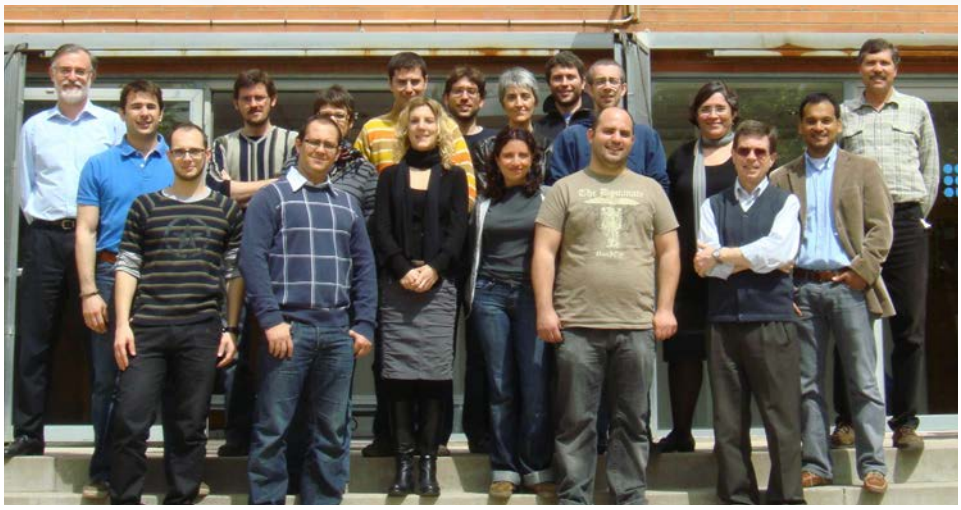
Biomedical Systems and Signals Research Group

Programme: **Bioengineering & Medical Image**

Lead Researcher: **Jané Campos, Raimon**

Group members



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ASSOCIATED MEMBERS: Alonso López, Joan Francesc | Arcentales Viteri, Andrés Ricardo | Caminal Magrans, Pere | Fiz Fernández, José Antonio | Giraldo Giraldo, Beatriz | Gomis Román, Pedro | Mañanas Villanueva, Miguel Ángel | Perera Lluna, Alexandre | Ruiz de Alda Cañamares, Mª Puy | Torres Cebrián, Abel | Vallverdú Ferrer, Montserrat.

CONTRIBUTORS: Estrada Petrocelli, Luis Carlos | Romero Lafuente, Sergio | Serna Higuita, Leidy Yanet | Solá Soler, Jordi.

Main lines of research

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

Most relevant scientific articles

SARLABOUS L., TORRES A., FIZ J.A., GEA J., MARTÍNEZ-LLORENS J.M., JANE R. Efficiency of mechanical activation of inspiratory muscles in COPD using sample entropy. European Respiratory Journal. 2015;46(6):1808-1811.

VIZOSO M., PUIG M., CARMONA F.J., MAQUEDA M., VELASQUEZ A., GÓMEZ A. ET AL. Aberrant DNA methylation in non-small cell lung cancer-associated fibroblasts. Carcinogenesis. 2015;36(12):1453-1463.

GUAITA M., MELIA U., VALLVERDU M., CAMINAL P., VILASECA I., MONTSERRAT J.M. ET AL. Regularity of cardiac rhythm as a marker of sleepiness in sleep disordered breathing. PLoS ONE. 2015;10(4).

MELIA U., VALLVERDU M., BORRAT X., VALENCIA J.F., JOSPIN M., JENSEN E.W. ET AL. Prediction of nociceptive responses during sedation by linear and non-linear measures of EEG signals in high frequencies. PLoS ONE. 2015;10(4).

MIGLIORELLI C., ALONSO J.F., ROMERO S., MAANAS M.A., NOWAK R., RUSSI A. Automatic BSS-based filtering of metallic interference in MEG recordings: Definition and validation using simulated signals. Journal of Neural Engineering. 2015;12(4).

Highlights

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

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

Furthermore, the group has coordinated three intramural projects of the CIBER-BBN (2014-2015):

- MUDIRES-2PSD: "Multimodal Diagnosis by Signal Interpretation of the Respiratory System oriented to Pulmonary Diseases and Sleep Disorders".
- ULTRASEN-4BIO-2MD: "Characterization and evaluation of novel ultrasensitive piezoresistive all-organic sensors for biomedical signals applied to multimodal diagnosis".
- ROBERT: "ROBotic arm and high density Electromyography for upper- limb Rehabilitation and Therapy".

and has participated in:

- INTER-CARDIO: "Computer-assisted interpretation of electrical signals: a step forward in understanding and treating cardiac diseases".

The group have published 19 articles in JCR indexed journals and 10 publications in IEEE/CinC conferences indexed in Pubmed / MEDLINE / IEEEXplore..

In addition, the following doctoral thesis have been presented:

- "Detection of Transcription Factor Binding Sites by Means of Multivariate Signal Processing Techniques", 21/07/2015, Universitat de Barcelona. Autor: Erola Pairó. Director: Santiago Marco, Alexandre Perera.
- "Análisis de la interacción cardíaca y respiratoria en pacientes con cardiomiopatía y pacientes en proceso de extubación", 27-10-2015, Universitat Politècnica de Catalunya. Autor: Andrés Ricardo Arcentales Viteri. Director: Beatriz F. Giraldo Giraldo.

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Website: http://www.ibecbarcelona.eu/biomedsignal · http://futur.upc.edu/176413

Biomedical Signal Interpretation & Computational Simulation

Programme: Bioengineering & Medical Image

Lead Researcher: Laguna Lasaosa, Pablo

Group members

STAFF MEMBERS: Bolea Bolea, Juan Ramón | Martínez Carballo, M. Ángeles | Ramírez García, Julia.

ASSOCIATED MEMBERS: Bailón Luesma, Raquel | Gil Herrando, Eduardo | Martínez Cortes, Juan Pablo | Vergara Ugarriza, José María.

CONTRIBUTORS: Alcaine Otín, Alejandro | Borges de Almeida, Rute Alexandra | Carro Fernández, Jesús | Hernando Jumilla, David | Lazaro Plaza, Jesús | Llamedo, Mariano | Orini, Michele | Sánchez Tapia, Carlos.

Main lines of research

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

(PPG) is influenced by the ANS activity, reason why their specific quantification and their interaction among the different signals, allows a non-invasive evaluation of the ANS status.

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

Most relevant scientific articles

LAZARO J., NAM Y., GIL E., LAGUNA P., CHON K.H. Respiratory rate derived from smartphone-camera-acquired pulse photoplethysmographic signals. Physiological Measurement. 2015;36(11):2317-2333.

VICENTE J, JOHANNESEN L, MASON JW, CRUMB WJ, PUEYO E, STOCKBRIDGE N ET AL. Comprehensive T wave morphology assessment in a randomized clinical study of dofetilide, quinidine, ranolazine, and verapamil.Journal of the American Heart Association. 2015;4(4).

MARTÍN-YEBRA A., CAIANI E.G., MONASTERIO V., PELLEGRINI A., LAGUNA P., MARTÍNEZ J.P. Evaluation of T-wave alternans activity under stress conditions after 5 d and 21 d of sedentary head-down bed rest. Physiological Measurement. 2015;36(10):2041-2055.

HERNANDO D., SORNMO L., SANDBERG F., LAGUNA P., LLAMEDO M., BAILON R. Identification of patients prone to hypotension during hemodialysis based on the analysis of cardiovascular signals. Medical Engineering and Physics. 2015;37(12):1156-1161.

RAMIREZ J., MONASTERIO V., MINCHOLE A., LLAMEDO M., LENIS G., CYGANKIEWICZ I. ET AL. Automatic SVM classification of sudden cardiac death and pump failure death from autonomic and repolarization ECG markers. Journal of Electrocardiology. 2015;48(4):551-557.

Highlights

- Awarded Funding for a project from the Spanish National Research Agency, led by Prof. Raquel Bailón Luesma: "TIN2014-53567-R: Noninvasive assessment of autonomic nervous system through the analysis of biosignals variability. Application to stress-related clinical problems."
- Prof. Juan Pablo Martínez Cortés was invited keynote speaker at the "Atrial Signals 2015: Quantitative analysis and diagnostics, predictive and therapeutic values" Symposium, where he presented a "Review" on signal processing techniques for ablation guiding in atrial fibrillation entitled "Advanced processing of intracardiac atrial signals - get more out of the data ".
- The group had hosted six researchers from other research labs (3 Predoc, and 3 Postdoc). They have done short research stays, in periods going from 3 weeks to 6 months. These researchers come from: Lithuania, India, Italy, Greece, Germany and Spain.
- During this year the group IP, Prof. Pablo Laguna, has hold the Presidency of the "Board of Director Computing in Cardiology", see report at:

  P. MacFarlane, P. Laguna, G. Krastacic (2015): "Computing in Cardiology (CinC)" A report from the 41st Annual CinC meeting in Cambridge", MA, USA, head on 7-10 September 2014, Cardiopulse, doi:10.1093/eurheartj/ehu483, pp. 331.
- As research production the group has published a total of 12 papers and 20 conference proceedings, and has defended a doctoral Ph. D. thesis.

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NanoBiosensors and Bioanalytical Applications Group

Programme: **Nanomedicine**
Lead Researcher: **Lechuga Gómez, Laura Mª**

Group members

STAFF MEMBERS: Estévez Alberola, María del Carmen.

ASSOCIATED MEMBERS: Caro Salazar, Carlos | Herranz Andrés, Sonia | Zinoviev, Kirill.

CONTRIBUTORS: González Guerrero, Ana Belén | Maldonado Váquez, Jesús Manuel | Márquez Villalobos, Salomón Elieser | Sánchez Huertas, César | Solís Tinoco, Veronica Irais.

Main lines of research

Led by Full Professor Laura M. Lechuga, the Nano-Biosensors 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.

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Endocrinology and Diabetes Research Group

Programme: **Bioengineering & Medical Image / Nanomedicine**

Lead Researcher: **Leiva Hidalgo, Alberto**

Group members

STAFF MEMBERS: Bell Ramírez, Olga Lidia | Mato Matute, Mª Eugenia.

ASSOCIATED MEMBERS: Chico Ballestero, Ana Isabel | Corcoy Pla, Rosa.

CONTRIBUTORS: Cubero Marcos, José María | González Blanco, Cintia.

Main lines of research

THYROID CANCER

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

- Diabetes Mellitus Autoinmune: 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

BALSELLS M., GARCÍA-PATTERSON A., SOLA I., ROQUE M., GICH I., CORCOY R. Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: A systematic review and meta-analysis. BMJ (Online). 2015;350.

MATO E, BARCELÓ-BATLLORI S, ORERA I, SELVA L, CORRA M, GONZÁLEZ C ET AL. The proteomic 2D-DIGE approach reveals the protein voltage-dependent anion channel 2 as a potential therapeutic target in epithelial thyroid tumours. Molecular and cellular endocrinology. 2015;404:37-45.

SIMMONS D, JELSMA JG, GALJAARD S, DEVLIEGER R, VAN ASSCHE A, JANS G ET AL. Results From a European Multicenter Randomized Trial of Physical Activity and/or Healthy Eating to Reduce the Risk of Gestational Diabetes Mellitus: The DALI Lifestyle Pilot.Diabetes care. 2015;38(9):1650-6.

FEIG D.S., CORCOY R., JENSEN D.M., KAUTZKY-WILLER A., NOLAN C.J., OATS J.J.N. ET AL. Diabetes in pregnancy outcomes: A systematic review and proposed codification of definitions. Diabetes/Metabolism Research and Reviews. 2015;31(7):680-690.

AULINAS A, COLOM C, GARCÍA PATTERSON A, UBEDA J, MARÍA MA, ORELLANA I ET AL. Smoking affects the oral glucose tolerance test profile and the relationship between glucose and HbA1c in gestational diabetes mellitus.Diabetic medicine : a journal of the British Diabetic Association. 2015.

Highlights

Main results of research activities

To demonstrate, for the first time, VDAC2 gene as a new therapeutic target for epithelial thyroid neoplasia. B-In collaboration with NanoBioCel, we have reported that sorafenib incorporated PGLA nanoparticles, surface modified with cetuximab, represent a new targeting approach for the treatment of epithelial thyroid cáncer. C-Type 1 Diabetes Genome. EDUAB-HSP (A. de Leiva) belongs to the International Consortium "Type 1 Diabetes Genetics Network" (426 investigators from Europe and USA), supported by NIH, JDRF and Wellcome Trust Laboratory. The recent publication "Fine mapping of type 1 diabetes susceptibility loci and evidence for colocalization of causal variants with lymphoid gene enhancers", Nature Genetics 2015 Apr; 47(4): 381-6.doi:10.1038/ng.3245, has identified 4 genetic areas associated with autoimmune diabetes, and provided support for three additional novel T1DM loci (full list of investigators available from www.wtccc.org.uk)

Organization of 47th Annual Meeting, DPSG-EASD, October 2015.

The most relevant scientific European event in the field of Diabetes and Pregnancy (Alberto de Leiva, Chairman of the Meeting). Program-Book edited by EDUAB-DIABEM. EDUAB-HSP contributed with the Inaugural Lecture by Alberto de Leiva (Old and New Controversies on the Discovery of Insulin: Pancreatic Extracts") and 6 exhibited and discussed posters. Congress participation included experts from most European countries, USA, Canada, Australia, Japón, Venezuela, Méjico, Chile and Argentina. (CME Accreditation by UEMS).

Academic Coordination, Master of Clinical Andrology (UAB).

Academic Program for the specialization as clinical andrologist (accredited by the European Academy of Andrology), organized by UAB and Fundació Puigvert. Academic Director and Coordination by Prof. Alberto de Leiva, EDUAB-HSP. Graduated students were medical specialists (urologists and endocrinologists) from Mexico, Venezuela, Colombia, Costa Rica, Cuba and Spain).

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Biofunctional Nanomaterials Laboratory

Programme: Nanomedicine

Lead Researcher: Liz Marzán, Luis M.

Group members

STAFF MEMBERS: García Martín, Isabel.

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Main lines of research

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

Most relevant scientific articles

GARCÍA I., SÁNCHEZ-IGLESIAS A., HENRIKSEN-LACEY M., GRZELCZAK M., PENADES S., LIZ-MARZAN L.M. Glycans as Biofunctional Ligands for Gold Nanorods: Stability and Targeting in Protein-Rich Media. Journal of the American Chemical Society. 2015;137(10):3686-3692.

GARCÍA I., HENRIKSEN-LACEY M., SÁNCHEZ-IGLESIAS A., GRZELCZAK M., PENADES S., LIZ-MARZAN L.M. Residual CTAB ligands as mass spectrometry labels to monitor cellular uptake of Au nanorods. Journal of Physical Chemistry Letters. 2015;6(11):2003-2008.

ECHEVERRIA B, ETXEBARRIA J, RUIZ N, HERNÁNDEZ Á, CALVO J, HABERGER M ET AL. Chemo-Enzymatic Synthesis of (13) C Labeled Complex N-Glycans As Internal Standards for the Absolute Glycan Quantification by Mass Spectrometry.Analytical chemistry. 2015;87(22):11460-7.

BRZEZICKA K., ECHEVERRIA B., SERNA S., VAN DIEPEN A., HOKKE C.H., REICHARDT N.-C. Synthesis and Microarray-Assisted Binding Studies of Core Xylose and Fucose Containing N-Glycans. ACS Chemical Biology. 2015;10(5):1290-1302.

DO NASCIMENTO A.S.F., SERNA S., BELOQUI A., ARDA A., SAMPAIO A.H., WALCHER J. ET AL. Algal lectin binding to core (α1-6) fucosylated N-glycans: Structural basis for specificity and production of recombinant protein. Glycobiology. 2015;25(6):607-616.

Highlights

During 2015, the activities within the intramural projects and Glyco-HIV3 NANOSENFIBRO have continued. In the frame of the latter project, a set of new formulations based on gold nanoparticles have been prepared and tested for the induction of immune responses in samples from infected patients.

Among the most notable achievements of the group it is worth to mention the ERC- Proof of Concept Project (READCELL) approved by the European Research Council, based on the development of a system for the efficient and non-invasive harvesting and Release of Adherent Cells controlled by light. The objective of this call is to fund ideas to be brought to a pre-demonstration stage where potential commercialization opportunities have been identified. The results obtained with this methodology have been protected by a patent.

Within a translational medicine research line we collaborate with the laboratory of Dr. Charles Lawrie at Biodonostia Health Research Institute (accredited by the ISCIII) in the detection of tumor markers. This project focuses on the development of a lateral flow device for the specific detection of nucleic acids in the blood of cancer patients.

Also, Dr. Reichardt's team has developed CarboQuant, a technology platform for the absolute quantification of glycans by mass spectrometry with applications in clinical diagnostics and quality control of biopharmaceuticals. A market study and business plan for the commercialization of the technology through a spin-off company, for which investors are being sought, has been developed.

We have participated in several European projects, including the Marie Curie Network IMMUNOSHAPE, coordinated by Niels Reichardt. In addition, we have received and trained more than 26 students from different countries.

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Oncogenesis and Antitumour Drug Group

Programme: **Nanomedicine**

Lead Researcher: **Mangues Bafalluy, Ramon**

Group members

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CONTRIBUTORS: Álamo Vargas, Patricia | Arroyo Solera, Irene | Del Canto González, Alexandra | Moreno Jiménez, María José | Navas Jiménez, Luis Carlos | Suárez Vasallo, Cristina.

Main lines of research

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

Most relevant scientific articles

MORENO M.J., BOSCH R., DIEGUEZ-GONZÁLEZ R., NOVELLI S., MOZOS A., GALLARDO A. ET AL. CXCR4 expression enhances diffuse large B cell lymphoma dissemination and decreases patient survival. Journal of Pathology. 2015;235(3):445-455.

UNZUETA U., CESPEDES M.V., VAZQUEZ E., FERRER-MIRALLES N., MANGUES R., VILLAVERDE A. Towards protein-based viral mimetics for cancer therapies. Trends in Biotechnology. 2015;33(5):253-258.

PAVON M.A., PARRENO M., TELLEZ-GABRIEL M., LEON X., ARROYO-SOLERA I., LÓPEZ M. ET AL. CKMT1 and NCOA1 expression as a predictor of clinical outcome in patients with advanced-stage head and neck squamous cell carcinoma. Head and Neck. 2015.

RUEDA F., CESPEDES M.V., CONCHILLO-SOLE O., SÁNCHEZ-CHARDI A., SERAS-FRANZOSO J., CUBARSI R. ET AL. Bottom-Up Instructive Quality Control in the Biofabrication of Smart Protein Materials. Advanced Materials. 2015.

BLAY J.-Y., PAPAI Z., TOLCHER A.W., ITALIANO A., CUPISSOL D., LÓPEZ-POUSA A. ET AL. Ombrabulin plus cisplatin versus placebo plus cisplatin in patients with advanced soft-tissue sarcomas after failure of anthracycline and ifosfamide chemotherapy: A randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet Oncology. 2015;16(5):531-540.

Highlights

During this year, we have raised additional funding for the development of the CIBER-BBN Intramural project Nanomets, having obtained an Integrated Project of Excellence from the Instituto de Salud Carlos III (PIE/00028) and a Coordinated Project from the FIS (PI15/00378). We have also obtained an industrial transference project (2014 PROD 00055) that has allowed starting a negotiation for a possible license agreement involving the WO2012/095527 patent that protects the nanoconjugate developed in the Nanomets project, in which CIBER-BBN is a partner. We have renew our recognition as a consolidated research group (2014-SGR-1041) and have bee accepted as members of the EU COST Action CM1106 working on drug resistance and cancer stem cells. The CIBER-BBN Nanotoxicology Unit, that our group coordinates, which is integrated in the Nanbiosis Network has been recognized as a Singular Infrastructure (ICTS) and obtained funding for its promotion from MINECO (SAF2015-69388).

Our group has incorporate a new Miguel Servet Researcher (CP/00163), who will direct a new project on a nanoconjugate for the treatment of pancreatic carcinoma, a new Sara Borrell postdoctoral researcher (CD14/00055) and a new technician for giving support to the Nanotoxicology Platform (PTA2013-8426-I). We have also incorporated to the Group two new pre-doctoral students and a Specialist in Surgery from the Hospital de Sant Pau to carry out their thesis project. Over this year, we have developed a new colorectal carcinoma model with enhanced metastatic efficiency. We have used this model to demonstrate a selective biodistribution to primary tumor and metastases of the nanoconjugate developed in the Nanomets intramural project, and we have also demonstrated a potent antimetastatic effect especially regarding liver, lung and peritoneal foci.

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Nanobiotechnology for Diagnostics

Programme: **Nanomedicine**

Lead Researcher: **Marco Colás, Mª Pilar**

Group members

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CONTRIBUTORS: Colom Sanmartí, Gloria | Petanas Esteban, Salvador.

Main lines of research

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

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

La actividad científica del grupo comenzó en 1996, The scientific activity of the group began in 1996 and was particularly focused on the development of antibodies and on the establishment of immunochemical methods. In this respect, the group has an important collection of immunoreagents for environmental pollutants including endocrine disruptors, pesticides or pharmaceuticals. The group is running the CAbS (Custom Antibody Service), a facility that provides internal and external services addressed at developing immunoreagents and providing scientific support in the immunodiagnostic field. For more than eight years the scientific objectives have been expanded to the biosensor and nanobiotechnology fields. The associated increase of the know-how, expertise and capabilities of the Nb4D group has been achieved through its participation in a significant number of Spanish and FP European research projects (FP4-FP7: INEXsPORT- ENV4-CT97-0476, TECACOR- FAIR-CT98-9586; RADAR-GLK1-CT-2001-01670,

ELISHA- NMP2-CT-2003-505485, GOODFOOD- IST-2003-508774, Conffidence-KBBE-2008-211326, CA-JAL4EU- 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) or the giving of courses to PhD students and specialized technical personnel.

From a practical point of view, the research group is interested in and develops projects in the following areas

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

Most relevant scientific articles

TUFA R.A., PINACHO D.G., PASCUAL N., GRANADOS M., COMPANYO R., MARCO M.P. Development and validation of an enzyme linked immunosorbent assay for fluoroquinolones in animal feeds. Food Control. 2015;57:195-201.

PASTELLS C., ACOSTA G., PASCUAL N., ALBERICIO F., ROYO M., MARCO M.-P. An immunochemical strategy based on peptidoglycan synthetic peptide epitopes to diagnose Staphylococcus aureus infections. Analytica Chimica Acta. 2015;889:203-211.

MURIANO A., CHABOTTAUX V., DISERENS J.-M., GRANIER B., SÁNCHEZ-BAEZA F., MARCO M.-P. Rapid immunochemical analysis of the sulfonamide-sugar conjugated fraction of antibiotic contaminated honey samples. Food Chemistry. 2015;178:156-163.

BROTO M., MATAS S., BABINGTON R., MARCO M.-P., GALVE R. Immunochemical detection of penicillins by using biohybrid magnetic particles. Food Control. 2015;51:381-389.

AHADIAN S., YAMADA S., RAMON-AZCON J., ESTILI M., LIANG X., NAKAJIMA K. ET AL. Hybrid hydrogel-aligned carbon nanotube scaffolds to enhance cardiac differentiation of embryoid bodies. Acta Biomaterialia. 2015.

Highlights

Throughout 2015, the Nanobiotechnology for Diagnostics Group continued with its research lines, namely food safety, environmental monitoring and in keeping with the objectives of CIBER-BBN - clinical diagnosis.

We have developed an ELISA for the detection of sepsis caused by Pseudomonas aeruginosa. The samples used were provided to us by the Microbiology Department of the University Hospital of Germans Trias i Pujol (HUGTiP) in collaboration with CIBER projects. With the speific immunoreagents that we produced in the group we were capable of detecting infections with this bacteria in the samples of patients with tell-tale symptoms. In 2015, we presented our patent P201530780 in the Spanish Office for Patents and Brands. The patent is titled “Compunds and their uses as haptens for the detection of Staphylococcus aureus”. This patent, along with another for the detection of Pseudomonas aeruginosa have had a lot of interest from companies and groups dedicated to point-of-care diagnosis and we are currently in negotiations with several companies for the possibility to exploit them.

Since 2011 we have been collaborating with an American company in the development of immunoreagents for the detection of neurodegenerative disease biomarkers and in 2015 we extended this agreement to include two new lines of investigation - the preparation of oxidised cardiolipines and the detection and quantification of pterins.

We are developing and validating immunoreagents for the detection of citotoxic agents such as fluoracil and cyclophosphamide for the therapeutic monitoring of these drugs in treated pacients.

We now have a catalogue of the principal biomarkers involved in cardiovascular diseases and we are optimising the conditions to create a multiplexed system that can recognise various biomarkers together.

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Applied Molecular Chemistry Group of the IDM

Programme: **Nanomedicine**

Lead Researcher: **Martínez Máñez, Ramón**

Group members

STAFF MEMBERS: Aznar Gimeno, Elena | Lozano Torres, Beatriz | Pérez Magallón, Begoña.

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Main lines of research

Development of nanometric devices with 'molecular gates" for controlled release.

Our objective is to develop nano-systems containing "molecular gates" for releasing a certain payload at will. For that purpose, nanometric mesoporous solids are used as support. Such gated mesoporous silica nanoparticles are able to retain a cargo inside the pore system and deliver it upon the application of a target chemical (redox molecules, selected anions, pH changes, etc.), physical (such as temperature, magnetic fields or light) or biochemical (such as enzymes, antigens, DNA) stimuli.

Molecular probes.

We have experience in developing molecular chemical probes in which the recognition process is coupled to signaling. This applies to the design of probes for the in vitro or in vivo chromo-fluorogenic detection of molecules of interest.

Transverse capacities.

- Organic and inorganic synthesis.
- Preparation/functionalization of mesoporous materials.
- Preparation/functionalization of inorganic nanoparticles (gold, silver, oxides, silica, etc).

Most relevant scientific articles

PASCUAL L., BAROJA I., AZNAR E., SANCENON F., MARCOS M.D., MURGUIA J.R. ET AL. Oligonucleotide-capped mesoporous silica nanoparticles as DNA-responsive dye delivery systems for genomic DNA detection. Chemical Communications. 2015;51(8):1414-1416.

DE LA TORRE C., MONDRAGON L., COLL C., GARCÍA-FERNÁNDEZ A., SANCENON F., MARTÍNEZ-MANEZ R. ET AL. Caspase 3 Targeted Cargo Delivery in Apoptotic Cells Using Capped Mesoporous Silica Nanoparticles. Chemistry - A European Journal. 2015;21(44):15506-15510.

SANCENON F., PASCUAL L., OROVAL M., AZNAR E., MARTÍNEZ-MANEZ R.. Gated Silica Mesoporous Materials in Sensing Applications. ChemistryOpen. 2015;4(4):418-437.

GORBE M., BARBA-BON A., DE LA TORRE C., GIL S., COSTERO A.M., SANCENON F. ET AL. Synthesis and in Vitro Evaluation of a Photosensitizer-BODIPY Derivative for Potential Photodynamic Therapy Applications. Chemistry - An Asian Journal. 2015;10(10):2121-2125.

TOSCANI A., MARIN-HERNÁNDEZ C., MORAGUES M.E., SANCENON F., DINGWALL P., BROWN N.J. ET AL. Ruthenium(II) and Osmium(II) Vinyl Complexes as Highly Sensitive and Selective Chromogenic and Fluorogenic Probes for the Sensing of Carbon Monoxide in Air. Chemistry - A European Journal. 2015;21(41):14529-14538.

Highlights

During 2015, we started with activities in the SEPAR Project TARMAC. We have also continued with the Intramural Projects NANOHYPERTERMIA, NEURO-MON, TBIO-GATE SPRING and NANOSENFIBRO and in the transfer project MICHORMON-PRO. Within all these projects, we have prepared a collection of new gated materials for controlled release applications and as sensors. Apart from continuing our current regional and National Plan projects, in 2015 we have been granted with a European Project related with the development of a novel Titanium based alloy for additive manufacturing in special applications and also with a two RETOS project, one of them for the detection of Human Papiloma Virus, and with a project involving researchers from the Polytechnic University of Valencia and the Instituto de Investigación Sanitaria La Fe, for the support of the mixed research units UPV/IIS La Fe.

Also this year, we have continued with an intense scientific activity publishing twenty eight articles in international journals of high impact factor. In these works we have demonstrated that it is possible to develop a new delivery system for anticancer substances directed to CXCR4 receptor (overexpressed in lymphoma cells) using silica nanoparticles that are loaded with doxorubicin and capped with a derivative of the T22 peptide. Also, new hybrid oligonucleotide-capped mesoporous silica nanoparticles able to detect genomic DNA have been designed.

At the international level, we have participated in the preparation of various European projects proposals. In addition, we hosted four PhD students from Cuba, Honduras, Syria and Egypt. In addition, three of our PhD students have spent several months in England and Brazil.

Finally, in 2015 our group has participated in the CIBER-BBN training program being granted with one scholarship and three students have defended their PhD thesis during this year.

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Molecular Immunobiology – Grupo Asociado

Programme: Nanomedicine

Lead Researcher: Muñoz Fernández, María Ángeles

Group members

ASSOCIATED MEMBERS: Alonso García, Esther | Clemente Mayoral, María Isabel | Díaz Muñoz, Laura | Gurbindo Gutiérrez, María Dolores | Jiménez Fuentes, José Luis | Pion, Marjorie | Serramia Lobera, María Jesús.

CONTRIBUTORS: Perisé Barrios, Ana Judith | Sánchez Rodríguez, Javier | Vacas Córdoba, Enrique.

Main lines of research

HIV/Aids, Paediatric, Immunology, Age, Inflammation, Viral Latency, Microbicides Against HIV; HCV, HSV, HIV Vaccine, Carbosilane Dendrimers, Nanomedicine, Gene Therapy, Transfection, Dendritic Cells, Immunogens, New Therapies, Animal Models, Hiv Cohort, HIV Biobank, Biobanks.

Most relevant scientific articles

BRIZ V., SEPULVEDA-CRESPO D., DINIZ A.R., BORREGO P., RODES B., DE LA MATA F.J. ET AL. Development of water-soluble polyanionic carbosilane dendrimers as novel and highly potent topical anti-HIV-2 microbicides. Nanoscale. 2015;7(35):14669-14683.

SEPULVEDA-CRESPO D., SERRAMIA M.J., TAGER A.M., VRBANAC V., GÓMEZ R., DE LA MATA F.J. ET AL. Prevention vaginally of HIV-1 transmission in humanized BLT mice and mode of antiviral action of polyanionic carbosilane dendrimer G2-S16. Nanomedicine: Nanotechnology, Biology, and Medicine. 2015;11(6):1299-1308.

SEPÚLVEDA-CRESPO D, GÓMEZ R, DE LA MATA FJ, JIMÉNEZ JL, MUÑOZ-FERNÁNDEZ MÁ. Polyanionic carbosilane dendrimer-conjugated antiviral drugs as efficient microbicides: Recent trends and developments in HIV treatment/therapy.Nanomedicine : nanotechnology, biology, and medicine. 2015;11(6):1481-98.

SERRAMIA M.J., ALVAREZ S., FUENTES-PANIAGUA E., CLEMENTE M.I., SÁNCHEZ-NIEVES J., GÓMEZ R. ET AL. In vivo delivery of siRNA to the brain by carbosilane dendrimer. Journal of Controlled Release. 2015;200:60-70.

SEPULVEDA-CRESPO D., SÁNCHEZ-RODRIGUEZ J., SERRAMIA M.J., GÓMEZ R., DE LA MATA F.J., JIMÉNEZ J.L. ET AL. Triple combination of carbosilane dendrimers, tenofovir and maraviroc as potential microbicide to prevent HIV-1 sexual transmission. Nanomedicine. 2015;10(6):899-914.

Highlights

In 2015 we improved nanotechnology used in infectious diseases. HSV-2 as HIV-1 is acquired during sexual transmission and affects the genital area. Studies have shown that HSV-2 genital ulceration is associated with increased risk of acquiring HIV infection. Our vaginal microbicide polianionic carbosilan dendrimers gel impeded 85% of HIV-1 infection in a humanized mouse model (BLT-mice) as a concept proof. We showed that combination of the polianionic carbosilan dendrimers with tenofovir/maraviroc, working in the first steps of HIV viral replication cycle as microbicide, stopped 100% the HIV -1 infections. We have shown that this dendrimer inhibit 100% of HSV-2 in vaginal and in rectum. We went from traslational to clinical research having developed a vaginal and rectal microbicide for topical application. This proved to be a breakthrough in our research not only in the use of dendrimers as microbicides, also in the use of dendrimers as delivery systems, biodistribution, toxicology, etc in animal models. We used these nanosytems and other new such as different nanoparticles as anti-latency drugs in HIV infection, therapeutic vaccines against HIV-1 infection with dendritic cells. We established the in vitro and in vivonanobioguiaded platform with the objective to test new nanosystems against other infectious diseases caused by HSV-2, HCV, Chijungunya, ebola...We got very promising results, showing how various nanosystems depending on their synthesis, nucleus, peripheral charges, generation, etc act against different virus. This clarifies that inhibition of HIV/HSV-2 entry carries on to be a promising target for drug development due to the fact that nanotechnology can transform the field of HIV/HSV-2 prevention by improving the efficacy of the currently available antiviral treatments. We contributed to develop a new treatments against HIV-1, HSV-2, HCV and to the search of potential cure for viral infections. We begun a new line of research on tumor and degenerative diseases.

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Cellular and Respiratory Biomechanics Group – Linked group

Programme: **Biomaterials & Advanced Therapies**

Lead Researcher: **Navajas Navarro, Daniel**

Group members

STAFF MEMBERS: Polo Tortola, Maeba.

ASSOCIATED MEMBERS: Alcaraz Casademunt, Jordi | Almendros López, Isaac | Campillo Agullo, Noelia | Carreras Palau, Alba | Farré Ventura, Ramon | Luque González, Tomás Alberto | Melo Herráiz, Esther | Rodríguez Lázaro, Miguel Ángel | Rotger Estapé, Maria del Mar.

Main lines of research

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

Most relevant scientific articles

MORENO-INDIAS I, TORRES M, MONTSERRAT JM, SÁNCHEZ-ALCOHOLADO L, CARDONA F, TINAHONES FJ ET AL. Intermittent hypoxia alters gut microbiota diversity in a mouse model of sleep apnoea.The European respiratory journal. 2015.

TORRES M., ROJAS M., CAMPILLO N., CARDENES N., MONTSERRAT J.M., NAVAJAS D. ET AL. Parabiotic model for differentiating local and systemic effects of continuous and intermittent hypoxia. Journal of Applied Physiology. 2015;118(1):42-47.

VIZOSO M., PUIG M., CARMONA F.J., MAQUEDA M., VELASQUEZ A., GÓMEZ A. ET AL. Aberrant DNA methylation in non-small cell lung cancer-associated fibroblasts. Carcinogenesis. 2015;36(12):1453-1463.

CASARES L, VINCENT R, ZALVIDEA D, CAMPILLO N, NAVAJAS D, ARROYO M ET AL. Hydraulic fracture during epithelial stretching.Nature materials. 2015;14(3):343-51.

KOSMALSKA A.J., CASARES L., ELOSEGUI-ARTOLA A., THOTTACHERRY J.J., MORENO-VICENTE R., GONZÁLEZ-TARRAGO V. ET AL. Physical principles of membrane remodelling during cell mechanoadaptation. Nature Communications. 2015;6.

Highlights

Obstructive Sleep Apnea (OSA) is a very prevalent disease characterized by patient exposure to intermittent hypoxic events. We have addressed the basic mechanisms involved in the consequences of this disease. We have established and validated a parabiotic mouse model, two animals sharing circulation by surgical union through the skin, and confirmed the hypothesis that when one of the parabionts breathes room air and the other one is subjected to hypoxic air, both mice share systemic circulation but remain normoxic and hypoxic, respectively. This novel model is useful to investigate the effects of local and systemic intermittent hypoxia. In another study in mice we proved for the first time that intermittent hypoxia modifies the microenvironment oxygenation and the microbiota in the gut. Evidence of altered fecal microbiota composition and diversity suggests that physiological interplays between host and gut microbiota could be deregulated in OSA.

Acute lung injury is a severe disease associated with disruption of the alveolar epithelial cell monolayer. The underlying mechanisms of alveolar barrier damage and repair remain poor known. The origin of fracture in epithelial cell sheets subject to stretch is commonly attributed to excess tension in the cells' cytoskeleton, in the plasma membrane, or in cell-cell contacts. We showed a new poroelastic mechanism involved in the disruption of epithelial cell monolayer subjected to stretch. We also showed that the 3D remodelling of the cell membrane during cell mechanoadaptation can be explained by a purely mechanical process generating different types of membrane invaginations that can repeatedly store and release large fractions of cell membrane. Once formed, cells reabsorb the invaginations through an active process with duration of the order of minutes.

Lung cancer is the leading cause of cancer-related deaths worldwide. Our current knowledge of the aberrant genomic DNA methylation in tumor-associated fibroblasts (TAFs) is very scarce. We therefore conducted genome-wide DNA methylation profiling on lung TAFs and paired control fibroblasts. Our findings shed light on the unique origin and molecular alterations underlying the aberrant phenotype of lung TAFs, and identify a stromal biomarker with potential clinical relevance.

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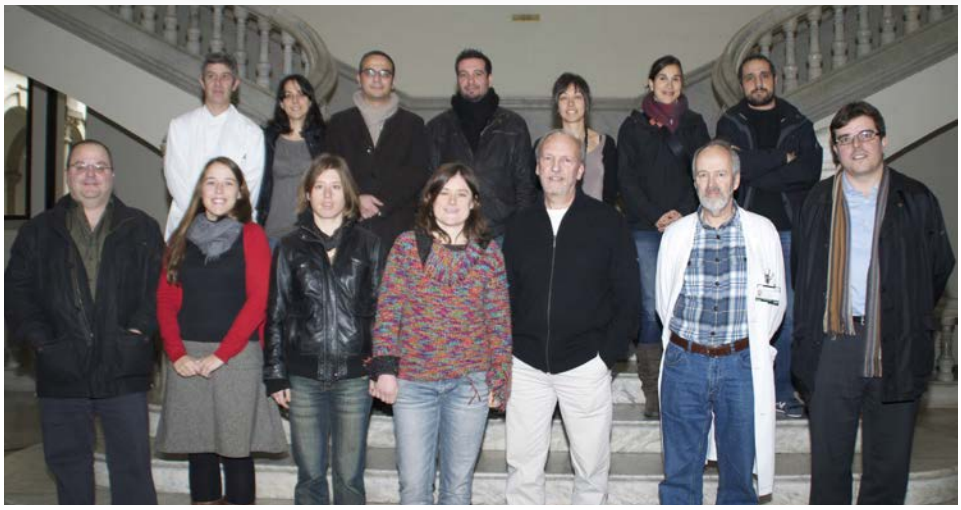
Biomedical Imaging Group

Programme: **Bioengineering & Medical Image**

Lead Researcher: **Pavía Segura, Javier**

Group members



STAFF MEMBERS: Tudela Fernández, Raúl.

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

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

Main lines of research

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

Most relevant scientific articles

GISPERT J.D., RAMI L., SÁNCHEZ-BENAVIDES G., FALCON C., TUCHOLKA A., ROJAS S. ET AL. Nonlinear cerebral atrophy patterns across the Alzheimer's disease continuum: Impact of APOE4 genotype. Neurobiology of Aging. 2015;36(10):2687-2701.

NINEROLA-BAIZAN A., ROJAS S., BONASTRE M., TUDELA R., LOMENA F., PAVIA J. ET AL. In vivo evaluation of the dopaminergic neurotransmission system using [123I] FP-CIT SPECT in 6-OHDA lesioned rats. Contrast Media and Molecular Imaging. 2015;10(1):67-73.

CORDOVA-PALOMERA A., TORNADOR C., FALCON C., BARGALLO N., NENADIC I., DECO G. ET AL. Altered amygdalar resting-state connectivity in depression is explained by both genes and environment. Human Brain Mapping. 2015;36(10):3761-3776.

SAMPEDRO F., VILAPLANA E., DE LEON M.J., ALCOLEA D., PEGUEROLES J., MONTAL V. ET AL. APOE-by-sex interactions on brain structure and metabolism in healthy elderly controls. Oncotarget. 2015;6(29):26663-26674.

GALLEGO J., NINEROLA-BAIZAN A., COT A., AGUIAR P., CRESPO C., FALCON C. ET AL. Validation of semi-quantitative methods for DAT SPECT: Influence of anatomical variability and partial volume effect. Physics in Medicine and Biology. 2015;60(15):5925-5938.

Highlights

PHD THESIS: :

- Aida Niñerola Baizán. Universitat de Barcelona. "Quantification of striatal dopamine transporter SPECT in animal models and clinical research".
- Miguel L. Rodríguez Castillo. Universitat Politècnica de Catalunya. "Automation of the Monte Carlo simulation of medical linear accelerators".
- Carles Gomà. Eidgenössische Technische Hochschule Zürich (ETH Zürich). "Radiation dosimetry of clinical proton beams".

NEW PROJECTS:

- Deutsche Forschungsgemeinschaft (DFG, Germany). Development of the PRIMO system for automatic Monte Carlo simulation of medical linacs and study of its applications in the clinical practice.

INTERNATIONAL COLLABORATIONS:

- Dr Aldo Badano from the Center for Devices and Radiological Health de la U.S. Food and Drug Administration. Our activities are focused on the Monte Carlo simulation of indirect x-ray detectors for medical imaging.
- Dr. Luca Cozzi from the Humanitas Cancer Center, Milano, Italia. Dr. Cozzi is scientific advisor for Varian. He acts as a link between one of our groups and the linear accelerator manufacturing company.
- Prof. Vasiliy Shvedunov from Lomonosov Moscow State University. We collaborate in the development of a microtron prototype with applications in intraoperative radiation therapy (IORT). The PENELOPE/penEasy Monte Carlo code is employed for the design of the beam modifiers.
- Dr Alberto Bravin from European Synchrotron Radiation Facility (ESRF, Grenoble, France). In the framework of the EU FP7 COST TD1205 action (https://www.syra3.eu) PENELOPE/penEasy is being assessed for dosimetric studies of a new radiotherapy technique with synchrotron radiation.

DATA BASES:

- A data base of 575 MRI studies has been collected from a cohort of middle-aged subjects, cognitively healthy and descendants of the first degree of Alzheimer's disease. The selection of this sample was made after genetic analysis of the entire cohort of 2743 subjects, allowing us to collect the largest number of subjects homozygous for e4 allele of the APOE gene, the greatest genetic risk factor of Alzheimer disease.

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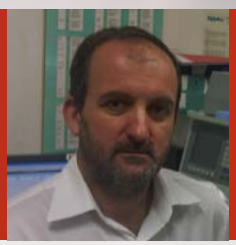
Micro and Nano Technologies, Biomaterials and Cells Research Group



Programme: Nanomedicine / Biomaterials & Advanced Therapies
Lead Researcher: Pedraz Muñoz, José Luis

Group members

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

ASSOCIATED MEMBERS: Acarregui Garalde, Argia | Esquisabel Alegría, Amaia | Hernández Martín, Rosa María | Igartua Olaechea, Manoli | Orive Arroyo, Gorka | Puras Ochoa, Gustavo | Sáenz del Burgo Martínez, Laura | Salvador Martínez, Aiala | Santos Vizcaíno, Edorta | Zárate Sesma, Jon.

CONTRIBUTORS: Agirre Díez, Mireia | Egusquiaguirre Martín, Susana Patricia | Gartziandia López de Goikoetxea, Oihane | Herrán Martínez, Enara | Moreno Sastre, María.

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 advan-

tages, 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

GAINZA G., BONAFONTE D.C., MORENO B., AGUIRRE J.J., GUTIERREZ F.B., VILLULLAS S. ET AL. The topical administration of rhEGF-loaded nanostructured lipid carriers (rhEGF-NLC) improves healing in a porcine full-thickness excisional wound model. Journal of Controlled Release. 2015;197:41-47.

MORENO-SASTRE M., PASTOR M., SALOMON C.J., ESQUISABEL A., PEDRAZ J.L. Pulmonary drug delivery: A review on nanocarriers for antibacterial chemotherapy. Journal of Antimicrobial Chemotherapy. 2015;70(11):2945-2955.

PURAS G, MARTÍNEZ-NAVARRETE G, MASHAL M, ZÁRATE J, AGIRRE M, OJEDA E ET AL. Protamine/DNA/Niosome Ternary Nonviral Vectors for Gene Delivery to the Retina: The Role of Protamine.Molecular pharmaceutics. 2015;12(10):3658-71.

SOTO-SÁNCHEZ C, MARTÍNEZ-NAVARRETE G, HUMPHREYS L, PURAS G, ZARATE J, PEDRAZ JL ET AL. Enduring high-efficiency in vivo transfection of neurons with non-viral magnetoparticles in the rat visual cortex for optogenetic applications.Nanomedicine : nanotechnology, biology, and medicine. 2015.

GAINZA G., VILLULLAS S., PEDRAZ J.L., HERNÁNDEZ R.M., IGARTUA M. Advances in drug delivery systems (DDSs) to release growth factors for wound healing and skin regeneration. Nanomedicine: Nanotechnology, Biology, and Medicine. 2015;11(6):1551-1573.

Highlights

- DRIVE EUROPEAN PROJECT: NanoBioCel group takes part of DRIVE consortium, which is a 4-year project to be carried out by 14 European partners. The project have received funding of 9 MILLION OF EUROS from the Horizon 2020, the biggest EU framework Programme for Research and Innovation. Its aim is to develop an bioartificial pancreas.
- KARUNA: A spin-off that has its origin in a TERFIQEC Spanish project, an INNPACTO program that had the aim to get results to the market from collaborations between companies and research groups. The mail objective of Karuna is approaching different diseases using cell therapy.
- Patent: ""Molécula de acido nucleído, proteína de fusión y método para modificar el material genético de una célula". It is an invention that uses molecular tools for modifying the genetic material of a cell.
- Scientific article awarded by Sociedad Española de Farmacia Industrial y Galénica: "A novel cationic niosome formulation for gene delivery to the retina". Developed jointly with researchers Eduardo Fernández y Ramon Eritja members of CIBER-BBN.

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Health Technology Group

Programme: Biomaterials & Advanced Therapies / Bioengineering & Medical Image

Lead Researcher: Peris Serra, José Luis

Group members

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

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

Main lines of research

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

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

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

FUNCTIONAL ASSESSMENT OF HUMAN MOVEMENTS.

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

ASESORAMIENTO TECNOLÓGICO

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

- The selection of biomaterials to be used in medical devices.

• All stages of product development and design:

- Detecting the needs of the patient and surgeon. - Defining the design specifications. - Selecting the manufacturing techniques and materials. - Developing the conceptual designs and details of the product. - Collaboration in defining the processes required for manufacturing an CE market approved medical device. - Consultation regarding the definition of any tests required to obtain CE marking for the product. - Collaboration with companies in preparing the documents required to obtain CE

marking of medical devices certification: defining essential requirements; carrying out risk analyses, and clinical justification of the design.

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

BIOMECHANICAL EVALUATION OF MEDICAL DEVICES.

TRAINING.

ICT APPLICATIONS.

Most relevant scientific articles

LÓPEZ-NAJERA D., RUBIO-ZARAGOZA M., SOPENA-JUNCOSA J.J., ALENTORN-GELI E., CUGAT-BERTOMEU R., FERNÁNDEZ-SARMIENTO J.A. ET AL. Effects of plasma rich in growth factors (PRGF) on biomechanical properties of Achilles tendon repair. Knee Surgery, Sports Traumatology, Arthroscopy. 2015.

BELDA-LOIS J.-M., SÁNCHEZ-SÁNCHEZ M.L. A new methodology for Functional Principal Component Analysis from scarce data. Application to stroke rehabilitation. Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS. 2015;2015-November:4602-4605.

LÓPEZ-PASCUAL J., CACERES M.L., DE ROSARIO H., PAGE A. The reliability of humerothoracic angles during arm elevation depends on the representation of rotations. Journal of Biomechanics. 2015.

Highlights

PROYECTOS:

- DuoTrainer. New robotic medical device for autonomous, home-based gait neurorehabilitation and weight-bearing leg exercise, aimed at adults with loss of standing and walking function. INSPIRO A/S, 44.000 €. 4 December 2015. PI: HELIOS DE ROSARIO MARTÍNEZ. Participants: BRUNO BAZUELO RUIZ, JOSÉ NAVARRO GARCÍA, IGNACIO BERMEJO BOSCH, LAURA MARTÍNEZ GÓMEZ, MARÍA JOSÉ VIVAS BROSETA, JAIME MIGUEL PRAT PASTOR, RAFAEL MENGUAL ORTOLÁ. CAREMIBRAIN.
- A brain-dedicated Positron Emission Tomography (PET) system to identify ß-amyloid biomarker in the brain for the early diagnosis of Alzheimer's disease. GENERAL EQUIPMENT FOR MEDICAL IMAGING, S. A. (ONCOVISION), 397.500 €. 3 December 2015 - 29 de Marzo de 2019. PI: JOSÉ LUIS PERIS SERRA. Participants: CARLOS MANUEL ATIENZA VICENTE, JUAN ALFONSO GÓMEZ HERRERO, Mª JESÚS SOLERA NAVARRO, JOSÉ NAVARRO GARCÍA, JAVIER MARIANO FERRÍS OÑATE, JOSÉ DAVID GARRIDO JAÉN, CARLOS CHIRIVELLA MORENO.
- A new RX diagnostic medical application enabling real dimension determinations. INFORMATION STORAGE, S.L., 2.130 €. 5 November 2015 - PI: JUAN FERNANDO GIMENEZ PLA. Participants: HELIOS DE ROSARIO MARTÍNEZ, MARÍA JESÚS SOLERA NAVARRO, CARLOS MANUEL ATIENZA VICENTE.
- i-LiveRest. Intelligent control system based on smart textiles to reduce pressure ulcer risk by real time measuring of tissue viability and intelligent trigger of prevention strategies adapted to user and context. QIMOVA AS, 37.500 €. 8 September 2015 -PI: RICARD BARBERÁ GUILLEM. Participants: RAUL MORON BALLESTER, CARLA ANDREA ARTACHO PÉREZ, JOSÉ LAPARRA HERNÁNDEZ, IGNACIO BERMEJO BOSCH, MARÍA AMPARO GUERRERO ALONSO, FRANCISCO JOSÉ MATEY GONZÁLEZ, FERNANDO MOLLA DOMENECH.

TESIS DIRIGIDAS:

- DIRECTOR: PAGE, Á. PhD: Juan LÓPEZ PASCUAL. TITLE: Kinematic characterization of the humeral elevation in the scapular plane. Definition of normal patterns and analysis of the pathological movement. UNIVERSITY: Universitat Politècnica de València. March 2015

Institution: Asociación Instituto de Biomecánica de Valencia · **Contact:** Instituto de Biomecánica de Valencia Camino de Vera s/n Edificio 9 C. 46022 Valencia · Tel.: 96 111 11 70 · E.mail: joseluis.peris@ibv.upv.es Website: http://tecnologia-sanitaria.ibv.org/

Center for Biomedical Technology – Bioengineering and Telemedicine group

Programme: Bioengineering & Medical Image
Lead Researcher: Del Pozo Guerrero, Francisco

Group members

STAFF MEMBERS: Cobo Sánchez De Rojas, Antonio | Pérez Gandía, Mª Carmen.

ASSOCIATED MEMBERS: Bajo Bretón, Ricardo | Bruña Fernández, Ricardo | Cáceres Taladriz, César | Caunet Delis, Leonides | De Toledo Heras, Paula | Gómez Aguilera, Enrique José | González Nieto, Daniel | Hernando Pérez, Mª Elena | López García, Mª Eugenia | Maestu Unturbe, Ceferino | Maestú Unturbe, Fernando | Ramos Gómez, Milagros | Serrano Olmedo, José Javier.

CONTRIBUTORS: Castellanos , Nazareth | Félix González, Nazario | García García, Fernando | Gutiérrez Díez, Ricardo | Martínez Sarriegui, Iñaki | Mina Rosales, Alejandra | Moratti , Stephan | Moreno Sánchez, Pedro Antonio | Niso Galán, Julia Guiomar | Rodríguez Herrero, Agustín | Sánchez González, Patricia | Sánchez López de Pablo, Cristina | Solana Sánchez, Javier.

Main lines of research

Oscillatory activity of the brain: Towards the understanding of the normal cognition and brain disorders; cerebral basis of cognitive function in healthy people and in patients with neurological and psychiatric diseases.

Advanced biomedical imaging technologies: Neuroimaging biomarkers in aging and dementia; simultaneous EEG-fMRI Recording; functional and structural connectivity.

Diabetes technologies to apply the available technologies to optimize follow-up and metabolic control of people suffering from diabetes.

Neurorehabilitation Engineering: to help restore, minimize and/or compensate the alterations, those typically appear on a person after suffering a Traumatic Brain Injury (TBI) or a stroke; Neurorehabilitation processes modeling: dysfunctional and hybrid bionics models; Smart monitoring of cognitive and physical rehabilitation.

Development of sensors and medical devices based on nanoparticles: hyperthermia induction in living tissues (optical and radiofrequency); biosensors based on nanoparticles for early diagnosis of bacterial diseases.

Development of biofunctionalized nanomaterials for biomedical applications: Design and manufacture of biocompatible and stable nanostructures for RMI contrast agents for in vivo early diagnosis of Alzheimer disease; Labeling of human neural precursor cells for in vivo cell tracking in cell replacement therapies against neurodegenerative diseases.

Computational systems biology & study of structure and function in cultured neuronal networks.

Exploring the physiopathological mechanisms of connexinopathies: Role of Connexin-36 in Epilepsy; Therapeutic approaches for stroke in preclinical models.

Interaction of brain functions with very low frequency and intensity pulsed electromagnetic fields; Pain Brain DTI-MRI Function in Transgenic mice; Pulsed Magnetic Field Stimulation to enhance Neurite Growth.

Bioinspired fibres for biomedical applications applied to biostructural prosthesis.

Microanatomical and neurochemical alterations of the cerebral cortex in Alzheimer's.

Biomedical Informatics: natural language processing, indexing and knowledge discovery; MEG data analysis. Big data analytics to predict biomarkers for early stages of Alzheimer and Parkinson.

Technology to empower healthy habits to manage habit changing.

Most relevant scientific articles

CANUET L., PUSIL S., LÓPEZ M.E., BAJO R., PINEDA-PARDO J.A., CUESTA P. ET AL. Network disruption and cerebrospinal fluid amyloid-beta and phospho-tau levels in mild cognitive impairment. Journal of Neuroscience. 2015;35(28):10325-10330.

GARCES P., PEREDA E., HERNÁNDEZ-TAMAMES J.A., DEL-POZO F., MAESTU F., ANGEL PINEDA-PARDO J. Multimodal description of whole brain connectivity: A comparison of resting state MEG, fMRI, and DWI. Human Brain Mapping. 2015.

MARTÍN-BURO M.C., GARCES P., MAESTU F. Test-retest reliability of resting-state magnetoencephalography power in sensor and source space. Human Brain Mapping. 2015.

GARCÍA-GARCÍA F., KUMARESWARAN K., HOVORKA R., HERNANDO M.E. Quantifying the Acute Changes in Glucose with Exercise in Type 1 Diabetes: A Systematic Review and Meta-Analysis. Sports Medicine. 2015;45(4):587-599.

RAMOS-GÓMEZ M., SEIZ E.G., MARTÍNEZ-SERRANO A. Optimization of the magnetic labeling of human neural stem cells and MRI visualization in the hemiparkinsonian rat brain. Journal of Nanobiotechnology. 2015;13(1).

Highlights

Early detection of Alzheimer Disease. In the last year we have consolidated 15 years of work on the analysis the brain functional networks by proposing a biomarker for cognitive decline in the early stages of dementia: to predict who of the MCI (mild cognitive impairment) patients will develop dementia. Along 2015 we were running an international multicenter study to transfer our finding to the market: 1) cloud service for secondary diagnosis; 2) objective test of pharmacological or non-pharmacological interventions.

EIT Health. UPM become core partner of the EIT-Health Program, coordinated by the Centre for Biomedical Technology (CTB). A program to contribute to increase the competitiveness of European industry, improve the quality of life of Europe's citizens and the sustainability of healthcare system.

HBP. Human Brain Project. Researchers of CTB has collaborate in this ten-year special flagship ERANET and Horizon 2020 to build a completely new ICT infrastructure for neuroscience and for brain-related research in medicine and computing.

Dual Ms on Clinical Science. During 2015 it was approved a dual Master degree by UPM and the University of Colorado Denver, based in CTB, a two year program designed to meet the demand for further education of clinical researchers in academia and industry.

Acreditation of CTB as a health center. The Laboratory for Cognitive and Computational Neuroscience of the CTB obtained in year 2015 the accreditation as health center by the Ministry of Health of the Community of Madrid.

Animal facility. An animal facility in the Center for Biomedical Technology (CTB) was built and approved this year for breeding and maintenance different species of rodents.

NEUROTEC. This biomedical engineering 4 year program (Ministry of Health of the CAM) for the development of diagnostic and therapeutic technologies for neurological pathologies, from the molecular to the systemic level, ended in 2015.

Institution: Universidad Politécnica de Madrid · **Contact:** ETSI Telecomunicación. Ciudad Universitaria, s/n. 28040 Madrid · Tel.: 91 336 46 32 · E.mail: francisco.delpozo@ctb.upm.es · Web: http://www.ctb.upm.es

Centre of Regenerative Medicine in Barcelona

Programme: **Biomaterials & Advanced Therapies**

Lead Researcher: **Raya Chamorro, Ángel**

Group members

STAFF MEMBERS: Ferrer Lorente, Raquel.

ASSOCIATED MEMBERS: Bedford Guaus, Sylvia | Pulecio Rojas, Julián Andrés.

Main lines of research

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

Most relevant scientific articles

MARTORELL L., CORRALES I., RAMIREZ L., PARRA R., RAYA A., BARQUINERO J. ET AL. Molecular characterization of ten F8 splicing mutations in RNA isolated from patient's leucocytes: Assessment of in silico prediction tools accuracy. Haemophilia. 2015;21(2):249-257.

NOTARI M., PULECIO J., RAYA A. Update on the pathogenic implications and clinical potential of microRNAs in cardiac disease. BioMed Research International. 2015;2015.

GALVEZ-MONTON C., FERNÁNDEZ-FIGUERAS M.T., MARTI M., SOLER-BOTIJA C., ROURA S., PEREA-GIL I. ET AL. Neoinnervation and neovascularization of acellular pericardial-derived scaffolds in myocardial infarcts. Stem Cell Research and Therapy. 2015;6(1).

CANALS I., SORIANO J., ORLANDI J.G., TORRENT R., RICHAUD-PATIN Y., JIMÉNEZ-DELGADO S. ET AL. Activity and high-order effective connectivity alterations in sanfilippo C patient-specific neuronal networks. Stem Cell Reports. 2015;5(4):546-557.

FERNÁNDEZ-SANTIAGO R., CARBALLO-CARBAJAL I., CASTELLANO G., TORRENT R., RICHAUD Y., SÁNCHEZ-DANES A. ET AL. Aberrant epigenome in iPSC-derived dopaminergic neurons from Parkinson's disease patients. EMBO Molecular Medicine. 2015.

Highlights

During 2015, the research activities of our group have centered on the development of biomedical applications of cell reprogramming. These activities have pursued the design of strategies of regenerative medicine in the context of cardiac disease, with the ultimate goal of generating tissue engineering constructs (myocardial patches and grafts) useful for treating end-stage heart failure. For this purpose, we have developed protocols for the directed differentiation of human pluripotent stem cells toward heart muscle cells, and for their 3D culture in hydrogels and/or porous scaffolds using continuous perfusion bioreactors. Within these culture systems, we have tested the positive effect of electrical and mechanical stimulation on the functional maturation of cardiomyocytes. In addition to this, we have developed a variety of human disease models based on patient-specific induced pluripotent stem (iPS) cells. Specifically, we have developed and further validated experimental models of neuronal dysfunction in Sanfilippo C disease, of pre-mRNA processing in hepatocytes derived from hemophilia patients, and of the epigenetic alterations present in dopaminergic neurons derived from Parkinson's disease patients. This last experimental model has also been the basis to search for molecular links between diabetes and neurodegenerative diseases, a large-scale project involving 12 research groups from 4 different CIBERs, funded as an Integrated Project of Excellence, and coordinated by our group.

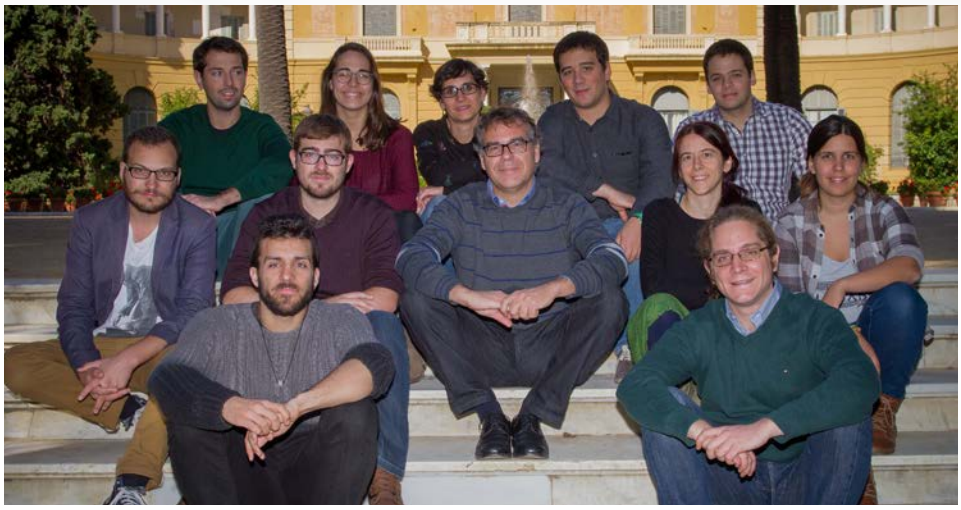
Institution: Centro de Medicina Regenerativa de Barcelona · **Contact:** Dr. Aiguader 88, 7ª planta. 08003 Barcelona · E.mail: director@cmrb.eu · Web: http://www.cmrb.eu

Small Biosystems Lab

Programme: **Nanomedicine**

Lead Researcher: **Ritort Farran, Félix**

Group members



STAFF MEMBERS: Pastor del Campo, Isabel.

ASSOCIATED MEMBERS: Palassini, Matteo.

CONTRIBUTORS: Alemany, Anna | Camuñas Soler, Joan | Mañosas Castejón, Maria | Ribezzi Crivellari, Marco.

Main lines of research

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

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

Our group is internationally recognized for having made fundamental advances in the understanding and characterization of the energetic of folding and assembly of nucleic acids, characterization of molecular motors that regulate DNA replication and fundamental theories describing the behavior of disordered systems out of equilibrium. Over the coming years we will continue working on these lines of research that have proved so profitable. However, the overture to begin a new line related to the fundamental problem of molecular evolution in order to better understand the physical principles that describe the increasing complexity and diversification of mutant molecular populations. The objectives set by the group are listed below:

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

Most relevant scientific articles

RIBEZZI-CRIVELLARI M., ALEMANY A., RITORT F. Universal axial fluctuations in optical tweezers. Optics Letters. 2015;40(5):800-803.

CAMUNAS-SOLER J., MANOSAS M., FRUTOS S., TULLA-PUCHE J., ALBERICIO F., RITORT F. Single-molecule kinetics and footprinting of DNA bis-intercalation: The paradigmatic case of Thiocoraline. Nucleic Acids Research. 2015;43(5):2767-2779.

DE LORENZO S., RIBEZZI-CRIVELLARI M., ARIAS-GONZÁLEZ J.R., SMITH S.B., RITORT F. A Temperature-Jump Optical Trap for Single-Molecule Manipulation. Biophysical Journal. 2015;108(12):2854-2864.

ALEMANY A., RIBEZZI-CRIVELLARI M., RITORT F. From free energy measurements to thermodynamic inference in nonequilibrium small systems. New Journal of Physics. 2015;17(7).

DIETERICH E., CAMUNAS-SOLER J., RIBEZZI-CRIVELLARI M., SEIFERT U., RITORT F. Single-molecule measurement of the effective temperature in non-equilibrium steady states. Nature Physics. 2015;11(11):971-977.

Highlights

Among the most important results of our group in 2015 should be noted that:

We have developed a single molecule footprinting technique molecule, which allows to identify the power and the binding site of ligands to DNA. We have shown that the force spectroscopy technique is usefull to determine the kinetics of binding of small molecules to DNA, for example in the case of anticancer peptide Thiocoraline. In addition, we have developed a set of methodologies and techniques that allow us to identify like this molecule binds to the double helix at specific positions using unzipping experiments. This technique is being used for studying the interaction of another molecules to DNA, as Netropsin or dendrimers. The results are the starting point for collaborations with PharmaMar or the Dendrimer Group for Biomedical Applications of CIBER-BBN.

We have demonstrated experimentally that it is possible to measure violations of fluctuation-dissipation theorem and extract the effective temperature in small non-equilibrium systems. This result is very important because it opens the possibility of understanding the theory of disordered systems using small molecule systems only.

We have improved a new instrument of optical tweezers with temperature controller to measure between 5 and 40 °C, which is essential for enthalpy and entropy unzipping measurements.

We have been working on expanding our experimental capabilities at the level of individual cells through the development of new experimental methods and data analysis techniques.

And finally, we have taken the first steps of a new line of research related to the fundamental problem of molecular evolution in order to better understand the physical principles that describe the growing complexity and diversity of mutant molecular populations.

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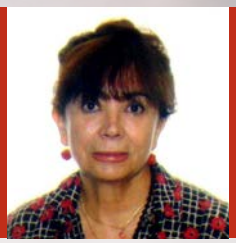
Biomedical Engineering Research Group

Programme: **Bioengineering & Medical Image**

Lead Researcher: **Roa Romero, Laura María**



Group members

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

ASSOCIATED MEMBERS: Gómez Cia, Tomás | Milan Martín, José Antonio | Palma Álvarez, Alfonso | Reina Tosina, Luis Javier | Román Martínez, Isabel | Salgueira Lazo, Mercedes.

CONTRIBUTORS: Barbarov Rostan, Gerardo Andrés | Callejón Leblic, María Amparo | Calvillo Arbizu, Jorge.

Main lines of research

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

Institution: Universidad de Sevilla · **Contact:** Escuela Sup. de Ingenieros · Avda. Los Descubrimientos, s/n. 41092 Sevilla · Tel.: 95 448 73 42 · E.mail: lroa@us.es · Web: http://gib.us.es/

BIOFORGE

Programme: **Biomaterials & Advanced Therapies**
Lead Researcher: **Rodríguez Cabello, José Carlos**

Group members

STAFF MEMBERS: Girotti, Alessandra | Montequi Merchán, Irene.

ASSOCIATED MEMBERS: Acosta Rodríguez, Sergio | Alonso Rodrigo, Matilde | Arias Vallejo, Francisco Javier | Báñez Sanz, José Manuel | Flora, Tatjana | López Martín, Isabel María | Orbanic, Doriana | Quintanilla Sierra, Luis | Reboto Rodríguez, Virginia | Santos García, Mercedes | Testera Gorgojo, Ana María.

CONTRIBUTORS: Fernández Colino, Alicia | García Lera, Rocio | González de Torre, Israel | González Obeso, Constancio | Ibáñez Fonseca, Arturo | Misbah Elzehiri, Mohamed Hamed | Pinedo Martín, Guillermo | Piña Lancho, María Jesús.

Main lines of research

- New "smart" materials.
- Hydrogels for tissue bioengineering.
- Injectable self-gelling and bioactive systems for biomedical applications.
- Bioactive and micro-patterned surfaces.
- Thermosensitive and 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

RODRIGUEZ-CABELLO J.C., ARIAS F.J., RODRIGO M.A., GIROTTI A.. Elastin-like polypeptides in drug delivery. Advanced Drug Delivery Reviews. 2015.

INOSTROZA-BRITO K.E., COLLIN E., SITON-MENDELSON O., SMITH K.H., MONGE-MARCET A., FERREIRA D.S. ET AL. Co-Assembly, spatiotemporal control and morphogenesis of a hybrid protein-peptide system. Nature Chemistry. 2015;7(11):897-904.

SÁNCHEZ-FERRERO A., MATA A., MATEOS-TIMONEDA M.A., RODRIGUEZ-CABELLO J.C., ALONSO M., PLANELL J. ET AL. Development of tailored and self-mineralizing citric acid-crosslinked hydrogels for in situ bone regeneration. Biomaterials. 2015;68:42-53.

DE TORRE I.G., WOLF F., SANTOS M., RONGEN L., ALONSO M., JOCKENHOEVEL S. ET AL. Elastin-like recombinamer-covered stents: Towards a fully biocompatible and non-thrombogenic device for cardiovascular diseases. Acta Biomaterialia. 2015;12(1):146-155.

FERNÁNDEZ-COLINO A., ARIAS F.J., ALONSO M., RODRIGUEZ-CABELLO J.C. Amphiphilic Elastin-Like Block Co-Recombinamers Containing Leucine Zippers: Cooperative Interplay between Both Domains Results in Injectable and Stable Hydrogels. Biomacromolecules. 2015;16(10):3389-3398.

Highlights

In 2015 BIOFORGE's funding came from 13 research projects and 2 networks with different funding sources. As for the Projects, BIOFORGE participated in 6 European projects funded by the European Commission (FP7-NMP-2010, FP7-Health-2011, FP7-ITN-2012, H2020-ITN-2014 and H2020-NMP-2014) and ERA-NET (ERA-IB); 4 national projects funded by the Spanish Ministry of Economy and Comepetitivity (3 of them belonging to the Programme Societal Challenges and one International Complementary Action); and 3 regional projects funded by the Ministries of Education and Health of the Regional Gonvernment of Castilla y León. As far as the Networks is concerned, BIOFORGE took part in 2 Biomaterial Networks funded by the Carlos III Health Institute (*CIBER-BBN and Regenerative Medicine and Cell Therapy Network of Castilla y León*).

In this period, 18 articles were published in international journals, 16 of them in indexed high impact journals. Furthermore, one national patent applications was filled in Italy (PZ2015A000004).

The group members attended many scientific meetings giving around 15 oral presentations and 4 invited plenary talks.

One PhD thesis with European mention was presented by the researcher Israel González, who received the highest qualification. Moreover, this thesis was awarded with the *European Prize Julia Polak European Doctorate Award 2015* and the *Extraordinary Doctoral Award 2015 of the University of Valladolid*.

Also in 2015, BIOFORGE received the Award for Health of Castilla y Leon issued by Sanitaria 2000 and Janssen in the category of Research Activity.

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

Institution: Universidad de Valladolid · **Contact:** Centro de Investigación Científica y Desarrollo Tecnológico Departamento de Física de la Materia Condensada, Campus Miguel Delibes, Pº de Belén, 1. 47011 Valladolid
E.mail: roca@bioforge.uva.es · Website: http://www.bioforge.uva.es

Tissue Bioengineering and Cell Therapy Group

Programme: **Biomaterials & Advanced Therapies**

Lead Researcher: **Ruiz Romero, Cristina**

Group members

STAFF MEMBERS: Fernández Burguera, Elena | Fernández Moreno, Mercedes | Filgueira Fernández, Purificación.

ASSOCIATED MEMBERS: De Toro Santos, Francisco Javier | Díaz Prado, Silvia María | Doménech García, Nieves | Fuentes Boquete, Isaac | López Peláez, Eduardo | Oreiro Villar, Natividad | Rendal Vázquez, María Esther | Silva Magalhaes, Joana Cristina.

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

Main lines of research

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

Institution: Servicio Gallego de Salud · **Contact:** Complejo Hospitalario Universitario A Coruña
Centro de Investigación Biomédica, Servicio de Reumatología. C/ As Xubias, 84. 15006 A Coruña
Tel.: 98 117 63 99 ext. 292494 · E.mail: cristina.ruiz.romero@sergas.es · Website: http://www.inibic.es

Nanomedicine Group

Programme: **Nanomedicine**

Lead Researcher: **Samitier Martí, Josep**

Group members

STAFF MEMBERS: Lagunas Targarona, Anna | Mir Llorente, Mónica.

ASSOCIATED MEMBERS: Altay, Gizem | Alvira Torre, Margarita | Caballero Vila, David | Martínez Fraiz, Elena | Montserrat Pulido, Nuria | Rigat Brugarolas, Luis.

CONTRIBUTORS: Funes Luque, Miriam | Hortigüela Lázaro, Verónica | Izquierdo García, David | Pardo, Wilmer Alfonso | Tahirbegi, Islam Bogachan | Zaffino, Rosa L.

Main lines of research

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

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

- Biosensors and Lab-on-a-chip for clinical diagnosis and food safety applications: Development of DNA sensors for the detection of cancer biomarkers./ Development of antibody-based sensors for the detection of pathogen microorganisms./ Development of olfactory sensors based on G-protein coupled receptors for the detection of volatiles. / Development of ion-selective electrodes (ISE) for nutrient analysis. / Development of sensors based on conducting polymers. / Development of microfluidic platforms for simple handling and detection. / Development of microfluidic platforms for bacteria counting and sorting.
- Materials for the study of cellular response: Design, production and characterization of micro/nanoenvironments made of different biocompatible materials for the study of cell proliferation, migration and differentiation. In particular, study of the effects of extracellular matrix. Which include:
  -Effects of nanoscale ligand distribution on cell adhesion and differentiation.
  -Biophysics of migration and differentiation onto biological matrices.
  -Study of interactions between magnetic nanoparticles and cells.

- Microfluidic systems and organ-on-chip devices: Development of a microfluidic system for blood/plasma filtering. / Development of a spleen model on a chip (splenon-on-a-chip). / Development of a microfluidic system for neurobiological studies.

Most relevant scientific articles

GALAN T., LAGUNAS A., MARTÍNEZ E., SAMITIER J. Fabrication of bioactive polypyrrole microelectrodes on insulating surfaces by surface-guided biocatalytical polymerization. RSC Advances. 2015;5(82):67082-67088.

REGINENSI D., CARULLA P., NOCENTINI S., SEIRA O., SERRA-PICAMAL X., TORRES-ESPIN A. ET AL. Increased migration of olfactory ensheathing cells secreting the Nogo receptor ectodomain over inhibitory substrates and lesioned spinal cord. Cellular and Molecular Life Sciences. 2015;72(14):2719-2737.

TELLER S., TAHIRBEGI I.B., MIR M., SAMITIER J., SORIANO J. Magnetite-Amyloid-β deteriorates activity and functional organization in an in vitro model for Alzheimer's disease. Scientific Reports. 2015;5.

TONG Z., SEGURA-FELIU M., SEIRA O., HOMS-CORBERA A., DEL RIO J.A., SAMITIER J. A microfluidic neuronal platform for neuron axotomy and controlled regenerative studies. RSC Advances. 2015;5(90):73457-73466.

TORRAS N., AGUSIL J.P., VAZQUEZ P., DUCH M., HERNÁNDEZ-PINTO A.M., SAMITIER J. ET AL. Suspended Planar-Array Chips for Molecular Multiplexing at the Microscale. Advanced Materials. 2015.

Highlights

The NANOMED-IBEC group has been involved in three intramural projects (OLIGOCODES, ChondroNanoNet and E-leukemia).

NANOMED-IBEC group concluded in 2015 the European project "Innovative Robotic Artefacts Inspired by Plant Roots for Soil Monitoring, PLANTOID" (FP7 293431) and the MINECO project OLIGOCODES (MAT2012-38573-C02).

The collaborative work with the Prof. del Río (from CIBERNED) on the fabrication of a microfluidic neuronal platform for neuron axotomy and controlled regenerative studies resulted in two publications.

The NANOMED-IBEC group have received funds from the competitive projects:

-"Glass-Laser Multiplexed Biosensor (GLAM)" (H2020-EU PHC-10-2015).

-"Suspensions of MicroNanoTools for applications in living cells (TEC2014-51940-C2-1-R).

"MIcrofluidic 3D compartmentalized Neuronal culture platform for neurological Diseases Studies (MINDS)" TEC-2015-70104-P.

"Nanoconductance of electron transfer proteins of the respiratory chain. Direct measurement at the single molecular level and therapeutic regulation in cancer stem cells" CTQ2015-66194-R.

NANOMED-IBEC constituted a joint unit with with Genomica S. A. from Zeltia group to develop a Point of Care diagnosis system , and received funds from CELLEX foundation to develop a system of biosensors for fetal surgery in close collaboration with clinician groups at Hospital Sant Joan de Déu-Hospital Clínic de Barcelona.

NANOMED-IBEC group have been widely present on the media during 2015:

http://www.elpuntavui.cat/societat/article/15-ciencia/924253-xips-miniaturitzats-per-detectar-malalties.html

http://www.ibecbarcelona.eu/josep-samitier-on-btv/

http://www.ibecbarcelona.eu/avanza-la-busqueda-de-medicinas-personalizadas-incluso-para-los-resfriados/

http://www.ibecbarcelona.eu/y-si-todos-tuvieramos-un-corazon-de-repuesto/

http://www.ibecbarcelona.eu/espana-entra-en-el-proyecto-europeo-eit-sobre-salud/

http://www.ibecbarcelona.eu/wp-content/uploads/2015/06/2015-06-08-IBEC-ElPeriodico-La-investigacion-tiene-futuro.pdf

http://www.ibecbarcelona.eu/wp-content/uploads/2015/05/2015-05-03-NMontserrat-ARA.pdf

http://www.ibecbarcelona.eu/saber-vivir-programme-dia-de-rinon/

http://www.ibecbarcelona.eu/wp-content/uploads/2015/02/montserrat_minirin%CC%83ones.pdf

Institution: Fundación Instituto de Bioingeniería de Cataluña · **Contact:** Edifici Administració.
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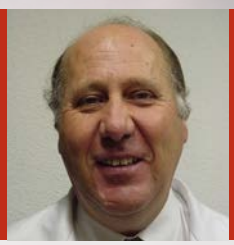
Website: http://www.ibecbarcelona.eu/nanobioengineering

Biomaterials Group



Programme: Biomaterials & Advanced Therapies / Nanomedicine

Lead Researcher: San Román del Barrio, Julio

Group members

STAFF MEMBERS: Castellanos Páez, Aida | Fernández Gutierrez, María del Mar | Parra Cáceres, Juan.

ASSOCIATED MEMBERS: Aguilar de Armas, Mª Rosa | Domingo Pascual, Concepción | González Gómez, Álvaro | Ramírez Jiménez, Rosa Ana | Rodríguez Crespo, Gema | Rodríguez Lorenzo, Luis | Vázquez Lasa, Blanca.

CONTRIBUTORS: Palao Suay, Raquel | Parra Ruiz, Francisco Jesús.

Main lines of research

- Preparation of selfcuring polymeric systems for surgery. The line is centered in the development of selfcuring polymer systems of low toxicity, high biocompatibility for application for the biomechanical stabilization of prosthesis and as controlled delivery systems of bioactive compounds (antibiotics, bactericide, anti-inflammatory agents, antithromobgenic).
- Polymer Drugs 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

REYES-ORTEGA F., CIFUENTES A., RODRIGUEZ G., AGUILAR M.R., GONZÁLEZ-GÓMEZ A., SOLIS R. ET AL. Bioactive bilayered dressing for compromised epidermal tissue regeneration with sequential activity of complementary agents. Acta Biomaterialia. 2015;23:103-115.

ROJO L., FERNÁNDEZ-GUTIERREZ M., DEB S., STEVENS M.M., SAN ROMAN J. Designing dapsone polymer conjugates for controlled drug delivery. Acta Biomaterialia. 2015;27:32-41.

PALAO-SUAY R., AGUILAR M.R., PARRA-RUIZ F.J., FERNÁNDEZ-GUTIERREZ M., PARRA J., SÁNCHEZ-RODRIGUEZ C. ET AL. Anticancer and antiangiogenic activity of surfactant-free nanoparticles based on self-assembled polymeric derivatives of vitamin E: Structure-activity relationship. Biomacromolecules. 2015;16(5):1566-1581.

SERVAT-MEDINA L., GONZÁLEZ-GÓMEZ A., REYES-ORTEGA F., SOUSA I.M.O., QUEIROZ N.C.A., ZAGO P.M.W. ET AL. Chitosan–tripolyphosphate nanoparticles as Arrabidaea chica standardized extract carrier: Synthesis, characterization, biocompatibility, and antiulcerogenic activity. International Journal of Nanomedicine. 2015;10:3897-3909.

ROJO L., RADLEY-SEARLE S., FERNÁNDEZ-GUTIERREZ M., RODRIGUEZ-LORENZO L.M., ABRADELO C., DEB S. ET AL. The synthesis and characterisation of strontium and calcium folates with potential osteogenic activity. Journal of Materials Chemistry B. 2015;3(13):2708-2713.

Highlights

Development and comercialization by the company iVASCULAR of a new generation of "Coronary Stents ", metallic stents coated with bioactive polymers that control and modulate the local reléase of an antiproliferative drug, Sirolimus. This biomedical device is known as Drug Eluted Stents DES, and has been comercialice by the company with the trade name ANGIOLITE that was enter in the biomedical market in January 2015.

Development of a injectable formulation for the treatment of osteochondritis and regeneration of joint cartilage. This Project has been developped in close cooperation with the pharmaceutical company INIBSA. The self-hardening formulation is under animal experimentation.

Development of a new formation of acrylic bone tissue for the local treatment of infections related with joint prosthesis. The patented system by the group is now aplying in a new model of animal experimentation using rabits as animals. and depending of the results thesystem will be comercialised by the company LVD BIOTECH that is the owner of the patent. All these activities have been developed by means of contracts of cooperation established between the companies and the Group of Biomaterials.

It has been obtained an auropean Project in the program ERA-NET (MAT) for the development of advanced bioimaterials from marine sources, biodegradable and that can be incorporated to hieararchical systems for advanced biomedical applications (self-curing systems, drug delivery systems, etc..). The Project with financial support fron the and national bodies, is developped in close cooperation with a research group of the Minho University , Portugal and the portuguese company STEMMATERS, and will be developped duirng a period of three years.

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Nanostructured Films and Particles

Programme: **Nanomedicine**

Lead Researcher: **Santamaría Ramiro, Jesús**

Group members

STAFF MEMBERS: Martínez Martínez, Gema | Mas Font, Nuria.

ASSOCIATED MEMBERS: Arruebo Gordo, Manuel | Balas Nieto, Francisco | Irusta Alderete, Silvia | Lobera González, María Pilar | Mallada Viana, Reyes | Moreno Vidorreta, Iván | Ortega Liébana, María del Carmen | Pina Iritia, María Pilar | Pradas Barriga, Irene | Sebastián Cabeza, Víctor.

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

Main lines of research

CATALYSIS AND CATALYTIC REACTORS: Synthesis of catalytic nanoparticle clusters (metallic, bimetallic, core/shell and metal oxides) as well as methods for their deposition on different substrates (carbon nanostructures, mesoporous silica, zeolites). The direct heating of the active centers by unconventional techniques (microwave heating by laser irradiation or by magnetic hyperthermia) is especially interesting for our group. This specific topic has received one of the prestigious ERC Advanced Grants.

MOLECULAR RECOGNITION - SENSORS: Design of nanostructured materials with specific interactions with specific molecules and micro-gas sensors for high sensitivity and selectivity.

NANOMEDICINE: Research on the biomedical applications of nanomaterials in cancer therapies (optical hyperthermia), gene therapy (nanoparticles as transfection vectors) and bactericidal applications (reservoirs for antimicrobial agents). Applications are tested in collaboration with other groups in this field: Dr N. Villaboa (HULP, Madrid - gene therapy and cell scaffolds), Dr Carles Arus (UAB - Medical Imaging), Dr MA de Gregorio (UZ - combination therapies in oncology) , Dr L. Luján (UZ - bactericidal applications in trauma). In this area, an ERC Advanced Grant has been recently awarded.

NANOCOMPOSITES: Development of polymer based composites with different types of nanomaterials with mechanical reinforcement applications, bactericidal plastics, magnetic and barrier films.

NANOSAFETY: Analysis of the impact of nanomaterials in workplaces through the development of

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

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

Most relevant scientific articles

VALLES G., BENSIAMAR F., CRESPO L., ARRUEBO M., VILABOA N., SALDANA L. Topographical cues regulate the crosstalk between MSCs and macrophages. Biomaterials. 2015;37:124-133.

USON L., SEBASTIAN V., MAYORAL A., HUESO J.L., EGUIZABAL A., ARRUEBO M. ET AL. Spontaneous formation of Au-Pt alloyed nanoparticles using pure nano-counterparts as starters: A ligand and size dependent process. Nanoscale. 2015;7(22):10152-10161.

LARREA A., SEBASTIAN V., IBARRA A., ARRUEBO M., SANTAMARIA J. Gas Slug Microfluidics: A Unique Tool for Ultrafast, Highly Controlled Growth of Iron Oxide Nanostructures. Chemistry of Materials. 2015;27(12):4254-4260.

ORTEGA-LIEBANA M.C., HUESO J.L., LARREA A., SEBASTIAN V., SANTAMARIA J. Feroxyhyte nanoflakes coupled to up-converting carbon nanodots: A highly active, magnetically recoverable, Fenton-like photocatalyst in the visible-NIR range. Chemical Communications. 2015;51(93):16625-16628.

MALUMBRES A., MARTÍNEZ G., HUESO J.L., GRACIA J., MALLADA R., IBARRA A. ET AL. Facile production of stable silicon nanoparticles: Laser chemistry coupled to in situ stabilization via room temperature hydrosilylation. Nanoscale. 2015;7(18):8566-8573.

Highlights

Throughout the year 2015, the NFP group has been focused on the research of methods to synthesize nanostructured materials (metal and metal-oxide nanoparticles, micro and mesoporous nanoparticles, hybrid nanoparticles, films nanostructured on different media and nanocomposites polymer matrix prepared from the above-mentioned materials) with controlled properties, the study of interface phenomena, the development of applications with technological interest based on these results and, finally, the development of engineering methods for the safe handling of nanomaterials and their manufacture at larger scale than the lab-bench production.

It is also interesting to note the intense activity of collaboration with other CIBER-BBN groups through intramural projects.

- ECO NANOPETSTEM (BBN15PI08)
- TARMAC-UZ (BBN15PI15)

Likewise, and through the Unit of Nanoparticle Synthesis of the NANBIOSIS Platform, which is coordinated within the group, research contacts with different groups in CIBER-BBN has been intensified.

The intense activity in the group work areas is reflected in numerous publications in the highest impact journals in the relevant areas. The vocation of this group through the applications in the industrial realm is reflected in the awarded research projects along this year, among which are:

- ADREM / Adaptable Reactors for Resource and Energy-Efficient Methane Valorisation (01-Oct-2015 to 30-Sep-2019) Funded by EUROPEAN UNION
- CTQ2014-52384-R: Based on Nanostructured Intelligent dressings containing fibers with natural biocides Pharmacokinetic Control his release (01 Jan 2015-31 Dec 2017) Funded by MINECO (50%) and ERDF (50%)

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Biomedical Imaging Technology Group

Programme: Bioengineering & Medical Image
Lead Researcher: Santos Lleó, Andrés

Group members

STAFF MEMBERS: Ortuño Fisac, Juan Enrique | Rojas Sánchez-Pantoja, Eva.

ASSOCIATED MEMBERS: Gil Casanova, Sara | Gómez Valverde, Juan José | Guerra Gutiérrez, Pedro | Kontaxakis Antoniadis, Georgios | Ledesma Carbayo, María Jesús | Rubio Guivernau, José Luis | Sportelli, Giancarlo | Zorraquino Gastón, Carlos.

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

Main lines of research

- Multimodal diagnosis.
- Cardiovascular imaging.
- High resolution preclinical imaging.
- Microscopy image analysis for modeling embryo development.
- Software utilities for image-guided medical diagnosis and treatment.

Most relevant scientific articles

GONZÁLEZ G., JIMÉNEZ-CARRETERO D., RODRIGUEZ-LÓPEZ S., KUMAMARU K.K., GEORGE E., ESTEPAR R.S.J. ET AL. Automated axial right ventricle to left ventricle diameter ratio computation in computed tomography pulmonary angiography. PLoS ONE. 2015;10(5).

DEL VILLAR C.P., BERMEJO J., RODRIGUEZ-P'CROSSED D., MARTÍNEZ-LEGAZPI P., BENITO Y., ANTORANZ J.C. ET AL. The role of elastic restoring forces in right-ventricular filling. Cardiovascular Research. 2015;107(1):45-55.

SIMOES R.V., ORTUNO J.E., BOKACHEVA L., CANDIOTA A.P., LEDESMA-CARBAYO M.J., DELGADO-GONI T. ET AL. Effect of acute hyperglycemia on moderately hypothermic GL261 mouse glioma monitored by T1-weighted DCE MRI. Magnetic Resonance Materials in Physics, Biology and Medicine. 2015;28(2):119-126.

DING H., FERNÁNDEZ-DE-MANUEL L., SCHAR M., SCHULERI K.H., HALPERIN H., HE L. ET AL. Three-dimensional whole-heart Three-Dimensional Whole-Heart T^2 Mapping at 3T mapping at 3T. Magnetic Resonance in Medicine. 2015;74(3):803-816.

PETITJEAN C., ZULUAGA M.A., BAI W., DACHER J.-N., GROSGEORGE D., CAUDRON J. ET AL. Right ventricle segmentation from cardiac MRI: A collation study. Medical Image Analysis. 2015;19(1):187-202.

Highlights

A new framework has been proposed for the analysis of multi-scale cell dynamics that enables to quantify automatically mechanical patterns from in-vivo images in a non-invasive way. It has been applied to obtain valuable insight about the organization and scales of the mechanical interactions during embryo development. Such a characterization will help to improve mechanical models and contribute to understand the complexity of embryogenesis. This work has led to a PhD thesis defended in 2015.

In the field of neuroimaging, an evaluation framework has been proposed to evaluate existing methodologies to correct magnetic susceptibility artifacts in diffusion MRI data, including whole-brain realistic phantoms. An image segmentation and registration method to enable processing in the native space of diffusion MRI data has been proposed. The work contributes to the understanding of the impact of distortions on brain connectivity analysis and it has led to a PhD thesis defended in 2015.

New methodological approaches for the analysis of pulmonary images have been developed. They include an automatic method for the separation of arterial and venous trees in CT lung images as a tool for the clinical study of cardiopulmonary diseases. It has been validated with synthetic phantoms and real images, and has led to a PhD thesis defended in 2015.

Two new research contracts have been signed with *Massachusetts Institute of Technology and Fundación madri+d para el Conocimiento*. One has the aim of developing a fast and cheap non-invasive neutrophil test for lymphoma patients and the other is to detect Parkinson's disease by analyzing typing patterns.

Our international patent, jointly developed with *Massachusetts Institute of Technology* and *Brigham and Women's Hospital*, on determining the prognosis of patients suffering from pulmonary embolism has been licensed to IMBIO LCC, a medical imaging software company located in Minneapolis (MN, USA).

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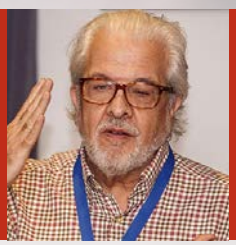
Nanomembrane Group

Programme: **Nanomedicine**

Lead Researcher: **Sanz Carrasco, Fausto**



Group members

STAFF MEMBERS: Camarero Palao, Nuria | Giannotti, Marina Inés.

ASSOCIATED MEMBERS: Díez Pérez, Ismael | Gorostiza Langa, Pau | Torrent Burgues, Joan.

CONTRIBUTORS: Cortijos Aragonés, Albert | López Martínez, Montserrat | Oliva Herrera, Mireia | Pozuelo Ruiz, Marta.

Main lines of research

Electrochemical STS of biomimetic membranes with redox systems. Measuring the energy levels of a protein under a variety of experimental conditions (in the presence of illumination or certain cofactors and partner proteins) will provide new insights into the detailed electron transfer mechanisms.

Mechanical stability at the molecular level. Nanomechanics of lipid bilayers and other biosystems. Understanding the effect of mechanical stress on biological membranes is of fundamental importance since cells are known to naturally perform their function under the effect of a complex combination of forces.

Development and application of light-activated nanoswitches to control the activity of protein complexes and cells. We will develop new optical switches (like the light-gated glutamate receptor LiGluR) in order to study the processes involved in neurosecretion, exocytosis and endocytosis.

Vectorization of therapeutically active molecules. We prepare and characterize therapeutic agent (drugs, peptides, proteins, genetic material...) release systems based on supramolecular conjugates which allow reaching the point of action in a directed and effective manner.

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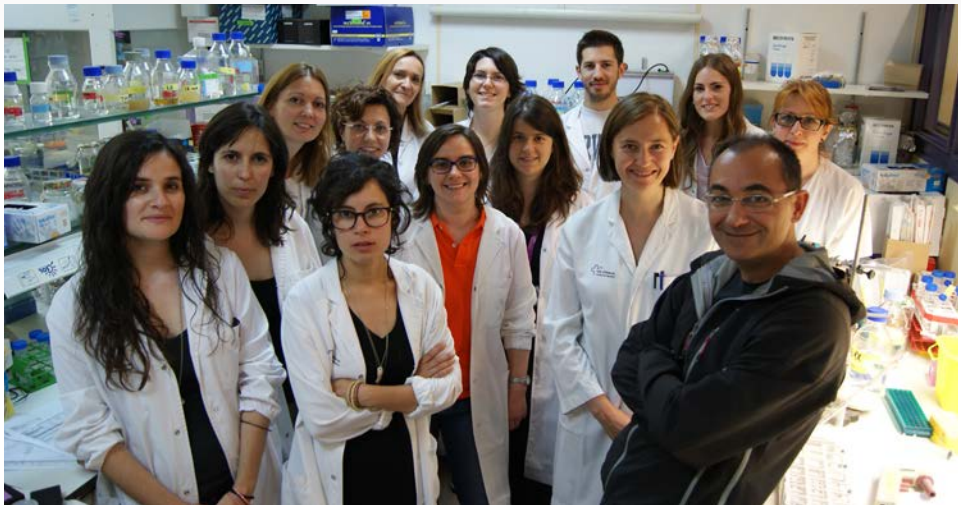
Drug Delivery and Targeting Group

Programme: **Nanomedicine**

Lead Researcher: **Schwartz Navarro, Simó**

Group members



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ASSOCIATED MEMBERS: Abasolo Olaortua, Ibane | Alijotas Reig, Jaume | Arango del Corro, Diego | Armengol Carrasco, Manuel | Baldrich Rubio, Eva | Espin Basany, Eloy | Fernández Amurgo, Yolanda | López Cano, Manuel | Sayos Ortega, Juan.

CONTRIBUTORS: Andretta, Elena | Bazzocco, Sarah | García Aranda, Natalia | García Latorre, Laura.

Main lines of research

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

These projects are conducted around three preferred work areas:

- Área 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).
- Área 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.
- Área 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 im-

aging 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

ANDRADE F., NEVES J.D., GENER P., SCHWARTZ S., FERREIRA D., OLIVA M. ET AL. Biological assessment of self-assembled polymeric micelles for pulmonary administration of insulin. Nanomedicine: Nanotechnology, Biology, and Medicine. 2015;11(7):1621-1631.

GENER P., GOUVEIA L.P., SABAT G.R., DE SOUSA RAFAEL D.F., FORT N.B., ARRANJA A. ET AL. Fluorescent CSC models evidence that targeted nanomedicines improve treatment sensitivity of breast and colon cancer stem cells. Nanomedicine: Nanotechnology, Biology, and Medicine. 2015;11(8):1883-1892.

BAZZOCCO S., DOPESO H., CARTON-GARCÍA F., MACAYA I., ANDRETTA E., CHIONH F. ET AL. Highly expressed genes in rapidly proliferating tumor cells as new targets for colorectal cancer treatment. Clinical Cancer Research. 2015;21(16):3695-3704.

CARTON-GARCÍA F., OVEREEM A.W., NIETO R., BAZZOCCO S., DOPESO H., MACAYA I. ET AL. Myo5b knockout mice as a model of microvillus inclusion disease. Scientific Reports. 2015;5.

MORAL-VICO J., BARALLAT J., ABAD L., OLIVE-MONLLAU R., MUNOZ-PASCUAL F.X., GALAN ORTEGA A. ET AL. Dual chronoamperometric detection of enzymatic biomarkers using magnetic beads and a low-cost flow cell. Biosensors and Bioelectronics. 2015;69:328-336.

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 new EuroNanoMed II 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 (DiamESTar, Targets4Cancer), and four additional projects, one of them from Marató TV3, Pentri: for active targeting against cancer stem cells), a RETOS project recently approved together with SMEs and focused into scale-up and preclinical validation of drug delivery systems, and an H2020 European project recently approved (Nocanther). Additional National grants were also obtained. Several in vitro and in vivo cancer models have been generated by the group for preclinical testing of nanomedicines, including the generation of specific cancer stem cell models. Two patents from the group are in National Fases. Dr Schwartz Jr is also member of the Nanomedicine Spanish Platform (NanomedSpain), the "European Platform for Nanomedicine" and the "European Fundation for Clinical Nanomedicine" (CLINAM). Dr Schwartz has also been appointed as Scientific Advisor by the Southern Denmark University of the excellence center NANOCAN for Nanomedicine andacts as an external evaluator of the Swedish Research Council and associate editor of Nanomedicine NMB an European J Nanomedicine. Further, Dr Schwartz's group published papers in top science journals in 2015.

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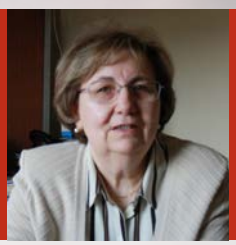
Colloidal and Interface Chemistry Group



Programme: **Nanomedicine**

Lead Researcher: **Solans Marsá, Concepción**

Group members

STAFF MEMBERS: Dols Pérez, Aurora | Monge Azemar, Marta.

ASSOCIATED MEMBERS: Beldengrün, Yoran | Esquena Moret, Jordi | Fornaguera Puigvert, Cristina | García Celma, Mª José | Lendimez Gris, María Carmen | Magaña Rodríguez, José Rodrigo | Miras Hernández, Jonathan | Néstor, Jeremie | Roig Roig, Ferran | Silvan, Baltazar | Sobrevías Bonells, Laura | Vílchez Maldonado, Susana.

CONTRIBUTORS: Homs San Millán, Maria.

Main lines of research

- Study of surfactant self-assembly processes in multicomponent systems and structural characterization of the self-assemblies.
- Study of nano-emulsion formation by condensation (low-energy) emulsification methods.
- Design and fabrication of advanced nanomaterials (nanoparticles, solid foams) using surfactant self-assemblies and colloidal dispersions as structure directing agents (templates).
- Development of multifunctional nanocarriers as delivery systems by nano-emulsion and micro-emulsion 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

FORNAGUERA C., GRIJALVO S., GALAN M., FUENTES-PANIAGUA E., DE LA MATA F.J., GÓMEZ R. ET AL. Novel non-viral gene delivery systems composed of carbosilane dendron functionalized nanoparticles prepared from nano-emulsions as non-viral carriers for antisense oligonucleotides. International Journal of Pharmaceutics. 2015;478(1):113-123.

VILANOVA N., SOLANS C. Vitamin A Palmitate-β-cyclodextrin inclusion complexes: Characterization, protection and emulsification properties. Food Chemistry. 2015;175:529-535.

FORNAGUERA C, CALDERÓ G, MITJANS M, VINARDELL MP, SOLANS C, VAUTHIER C. Interactions of PLGA nanoparticles with blood components: protein adsorption, coagulation, activation of the complement system and hemolysis studies.Nanoscale. 2015;7(14):6045-58.

FORNAGUERA C., DOLS-PÉREZ A., CALDERO G., GARCÍA-CELMA M.J., CAMARASA J., SOLANS C. PLGA nanoparticles prepared by nano-emulsion templating using low-energy methods as efficient nanocarriers for drug delivery across the blood-brain barrier. Journal of Controlled Release. 2015;211:134-143.

FORNAGUERA C., FEINER-GRACIA N., CALDERO G., GARCÍA-CELMA M.J., SOLANS C. Galantamine-loaded PLGA nanoparticles, from nano-emulsion templating, as novel advanced drug delivery systems to treat neurodegenerative diseases. Nanoscale. 2015;7(28):12076-12084.

Highlights

The research activities have been mainly performed in the frame of CIBER-BBN intramural project "Novel nanocarriers as delivery systems across the Blood-Brain barrier" (Nano3B). The main objective of the project was the design, characterization and functionalization of advanced multifunctional polymeric nanoparticles for the therapy of neurodegenerative diseases. Nanoparticles, with sizes below 100 nm, have been obtained by nano-emulsion templating using low-energy methods. This technology, developed in our group, allows nanoparticle size control and high drug entrapment efficiency using biocompatible components. Moreover, it can be performed under mild processing conditions, requires simple equipment and it is easily scalable. The nanoparticles have been functionalized with self-penetrating peptides and monoclonal antibodies for the specific blood-brain barrier (BBB) targeting and encapsulated with fluorescents agents and specific drugs to treat X-linked adrenoleukodystrophy (X-ALD) disease. In addition, in vitro and in vivo evaluation of the drug–loaded functionalized nanoparticles has been performed. The results have showed that the designed nanoparticles are appropriate for the intended application. The group has also performed research activities in the frame of the following projects: "Multifunctional nanotechnology for selective detection and treatment of cancer" (FP7-NMP-2010-LARGE-4; C-NMP/0878) finalized in June 2015, "Studies on amphiphile self-assembly processes and technologies for eco-friendly and biocompatible applications" (CTQ2011-29336-C03) and "Formation of Pickering emulsions by low-energy methods for the preparation of new porous nanostructured materials" (CTQ2011- 23842) both finalized in December 2015. The most important outcomes are reflected in 13 indexed publications, as well as in the presentation of 12 oral and 13 poster presentations in national and international conferences. Moreover, 3 PhD thesis and 4 Master thesis have been presented.

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Research Group in Intelligent Biomaterials

Programme: Biomaterials & Advanced Therapies / Nanomedicine
Lead Researcher: Vallet Regí, María

Group members

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ASSOCIATED MEMBERS: Arcos Navarrete, Daniel | Colilla Nieto, Montserrat | García Fontecha, Ana | Gómez Cerezo, Natividad | González Ortiz, Blanca | Izquierdo Barba, Isabel | Manzano García, Miguel | París Fernández de la Puente, Juan Luis | Salinas Sánchez, Antonio Jesús | Sánchez Salcedo, Sandra | Vila Juárez, Mercedes | Villaverde Cantizano, Gonzalo | Villegas Díaz, María Rocío.

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

Main lines of research

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

Most relevant scientific articles

IZQUIERDO-BARBA I., GARCÍA-MARTÍN J.M., ALVAREZ R., PALMERO A., ESTEBAN J., PÉREZ-JORGE C. ET AL. Nanocolumnar coatings with selective behavior towards osteoblast and Staphylococcus aureus proliferation. Acta Biomaterialia. 2015;15:20-28.

MARTÍNEZ A., FUENTES-PANIAGUA E., BAEZA A., SÁNCHEZ-NIEVES J., CICUENDEZ M., GÓMEZ R. ET AL. Mesoporous Silica Nanoparticles Decorated with Carbosilane Dendrons as New Non-viral Oligonucleotide Delivery Carriers. Chemistry - A European Journal. 2015;21(44):15651-15666.

PARIS J.L., CABANAS M.V., MANZANO M., VALLET-REGI M. Polymer-Grafted Mesoporous Silica Nanoparticles as Ultrasound-Responsive Drug Carriers. ACS Nano. 2015;9(11):11023-11033.

MARTÍNEZ-CARMONA M., BAEZA A., RODRIGUEZ-MILLA M.A., GARCÍA-CASTRO J., VALLET-REGI M. Mesoporous silica nanoparticles grafted with a light-responsive protein shell for highly cytotoxic antitumoral therapy. Journal of Materials Chemistry B. 2015;3(28):5746-5752.

VILLEGAS M.R., BAEZA A., VALLET-REGI M. Hybrid Collagenase Nanocapsules for Enhanced Nanocarrier Penetration in Tumoral Tissues. ACS Applied Materials and Interfaces. 2015;7(43):24075-24081.

Highlights

The most important achievements during 2015 include the design, optimization and implantation of 3D scaffolds based on bioceramics for bone tissue regeneration, and the development of nanotechnological strategies to design smart drug delivery systems for antitumor therapy and infection treatment (www.valletregigroup.esy.es). During 2015, GIBI group has developed diverse research lines in the frame of different national research projects including MAT2012-35556, MAT2013-43299-R and CSO2010-11384-E and European project within Research and Innovation Actions of Horizon 2020 program (Mozart 685872). Moreover, GIBI group has participated in different Intramural Projects (Nanoantilathiv, 3d-Timpte and Spring), translational CIBER-ECO project (SMART4NB) and private Domingo Martínez foundation project. GIBI group is member of the Research Institute of "Hospital 12 de Octubre (i+12)" and European Networking for prevention and treatment of osteoporotic fractures (www.agening.net). GIBI group has also published 20 original research articles indexed in JCR, 1 PCT-patent, 4 book chapters, 1 complete book entitled "Nanoceramics in Clinical Use: From Materials to Applications" (2nd Edition) of RSC Nanoscience & Nanotechnology Editorial. In addition, 10 invited conferences in international research forums have also highlighted. GIBI group collaborates with many clinic institutions as Hospital Miguel Servet, Zaragoza, La Paz Hospital, Madrid, Alcalá de Henares University Hospital, Jimenez Diaz Foundation, Hospital del Mar Barcelona, University Hospital of Getafe, University Children's Hospital Niño Jesus, Research Institute of Hospital 12 de Octubre (I+12). Furthermore, Prof. María Vallet-Regí has coordinated in the Ramón Areces Foundation, the symposium on "The cancer as a result of aging: potential solutions" celebrated on 3rd of November in Madrid. Moreover, the group has received the award IDEA2 (2015) with "Nanodrone: Nanomedicines directed to Neuroblastoma" proyect. Finally, Prof. María Vallet-Regí has received the degree of Doctor Honoris Causa by Jaume I University and also she has been selected as a member of Spanish Team of Science 2015 by the Quo Magazine.

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Molecular Nanoscience and Organic Materials Group

Programme: Nanomedicine / Biomaterials & Advanced Therapies
Lead Researcher: Veciana Miró, Jaume

Group members

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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.
- Nanomedicine.
- Biomaterials.
- Materials processing.
- Molecular magnetism.

Most relevant scientific articles

FRISENDA R., GAUDENZI R., FRANCO C., MAS-TORRENT M., ROVIRA C., VECIANA J. ET AL. Kondo effect in a neutral and stable all organic radical single molecule break junction. Nano Letters. 2015;15(5):3109-3114.

MUGNAINI V., CALZOLARI A., OVSYANNIKOV R., VOLLMER A., GONIDEC M., ALCON I. ET AL. Looking inside the perchlorinated trityl radical/metal spinterface through spectroscopy. Journal of Physical Chemistry Letters. 2015;6(11):2101-2106.

CORDOBA A., MONJO M., HIERRO-OLIVA M., GONZÁLEZ-MARTÍN M.L., RAMIS J.M. Bioinspired Quercitrin Nanocoatings: A Fluorescence-Based Method for Their Surface Quantification, and Their Effect on Stem Cell Adhesion and Differentiation to the Osteoblastic Lineage. ACS Applied Materials and Interfaces. 2015;7(30):16857-16864.

DEL POZO F.G., FABIANO S., PFATTNER R., GEORGAKOPOULOS S., GALINDO S., LIU X. ET AL. Single Crystal-Like Performance in Solution-Coated Thin-Film Organic Field-Effect Transistors. Advanced Functional Materials. 2015.

MARCHANTE E., CRIVILLERS N., BUHL M., VECIANA J., MAS-TORRENT M. An Electrically Driven and Readable Molecular Monolayer Switch Based on a Solid Electrolyte. Angewandte Chemie - International Edition. 2015.

Highlights

- 15 scientific publications in JCR indexed journals with an average impact factor of 6.548.
- 3 international extensions of three patents.
- 21 invited lectures given in international conferences.
- Participation on the activities of EU FP7 and H2020 projects: a) "Nanochemistry of molecular materials for 2-photon functional applications (Nano2Fun)", b) "Cost-effective sensors, interoperable with international existing ocean observing systems, to meet EU policies requirements (Common Sense)", c) "Electrical spin manipulation in electroACtive MOLecules (ACMOL)", d) "Self Assembled Monolayer Tunnel Junctions Engineering with Eutectic Gallium Indium Tips (SAM-Tune GAIN)", e) "Multifunctional surfaces structured with ELECTROactiveand MAGneticmolecules for electronic and spintronIC devices (ELECTROMAGIC)", f) "Organic sensor based electronic-skin with integrated logic (OSES-Int-Log)", and g) "Integrated self-assembled SWITCHable systems and materials: towards responsive organic electronics – a multi-site innovative training action".
- Participation in the TERARMET consortium (RETOS COLABORACIÓN) to carry out the project "Desarrollo de terapias para el tratamiento de enfermedades raras metabólicas congénitas", coordinated by the company PRAXIS PHARMACEUTICALS.
- Approval of the RETOS COLABORACIÓN project UNDERLIPDS, coordinated by the company PHARMAMAR.
- Approval of the H2020-INFRAIA project NFFA (Nanoscience Foundries and Fine Analysis). Participation in the JRA2 (WP7).
- Implementation of scientific activities of ERC Starting Grant project "e-GAMES".
- Implementation of scientific activities of ERC PoC Project "Large Area Organic Devices with Bar-assisted Meniscus Shearing Technology (LAB-TECH)".
- Participation in the 7th FP granted European project "BEnznidazol and triazol Research group for Nanomedicine and Innovation on Chagas disease (BERENICE)", coordinated by the Vall d'Hebron Research Institute.
- Execution of scientific activities of CIBER-BBN intramural projects: NANO-OPHTHAL, ORDECA, NANOPROTHER, DYNAMIC-VASC, ULTRASEN-4BIO-2MD, NANOLYSO.
- Coordination of the CIBER-BBN Transfer Project: "Functionalized nanoliposomes for the development of therapies for intracellular-based diseases. Application to Fabry disease and homozygous familial hypercholesterolemia (LIPOCELL)" in collaboration with the company BIOPRAXIS RESEARCH AIE.
- Implementation of scientific activities of the EXPLORA project "Engineering Cell Vessels on Surfaces using Dynamic Molecular Bio-Interfaces".
- Implementation of scientific activities of Be-Well project (MINECO).
- Implementation of activities as Scientific Direction of the Large Scientifical and Technical Facility NANBIOSIS.

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Research Group in Bone Physiopathology and Biomaterials

Programme: Biomaterials & Advanced Therapies

Lead Researcher: Vilaboa Díaz, Nuria

Group members

STAFF MEMBERS: Boré Medina, Alba | Martín Saavedra, Francisco Manuel.

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

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

CIFUENTES S.C., GAVILAN R., LIEBLICH M., BENAVENTE R., GONZÁLEZ-CARRASCO J.L. In vitro degradation of biodegradable polylactic acid/magnesium composites: Relevance of Mg particle shape. Acta Biomaterialia. 2015.

BLOOM D.C., FELLER J., MCANANY P., VILABOA N., VOELLMY R. Replication-competent controlled herpes simplex virus. Journal of Virology. 2015;89(20):10668-10679.

VOELLMY R., BLOOM D.C., VILABOA N. A novel approach for addressing diseases not yielding to effective vaccination? Immunization by replication-competent controlled virus. Expert Review of Vaccines. 2015;14(5):637-651.

FRUTOS E., GONZÁLEZ-CARRASCO J.L. Dynamic nanomechanical properties of novel Si-rich intermetallic coatings growth on a medical 316 LVM steel by hot dipping in a hypereutectic Al-25Si alloy. Journal of the Mechanical Behavior of Biomedical Materials. 2015;46:93-103.

VALLES G., BENSIAMAR F., CRESPO L., ARRUEBO M., VILABOA N., SALDANA L. Topographical cues regulate the crosstalk between MSCs and macrophages. Biomaterials. 2015;37:124-133.

Highlights

The group of Bone Physiopathology and Biomaterials has performed a thorough characterization of several modifications of polymers, stainless steel and ferritic alloys, including the study of their degradability, nanomechanical properties and biocompatibility. The group has progressed in the development of gene switches for the spatial and temporal regulation of therapeutic transgenes. The switches have been adapted to drive the expression of viral proteins for generating replication- competent controlled herpes simplex virus as well as of osteogenic and angiogenic growth factors. These molecular tools are being targeted for use in several biomedical applications such as vaccination, oncolytic therapy or regenerative medicine. Furthermore, we examined whether surface topographical features can regulate the paracrine interactions that mesenchymal stem cells establish with the mononuclear phagocyte system. The clinical scientists of the group have continued their participation in clinical trials for therapeutic interventions in bone-related diseases. The group funded its activities by means of grants from MINECO, ISCIII and research contracts with the industry.

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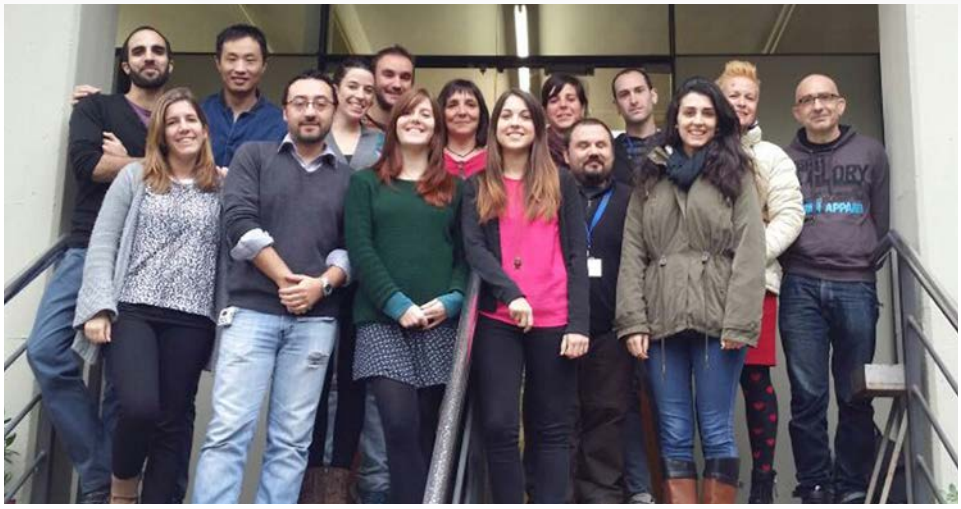
Nanobiotechnology

Programme: **Nanomedicine**

Lead Researcher: **Villaverde Corrales, Antonio**

Group members



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

Main lines of research

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

Most relevant scientific articles

RUEDA F., CESPEDES M.V., CONCHILLO-SOLE O., SÁNCHEZ-CHARDI A., SERAS-FRANZOSO J., CUBARSI R. ET AL. Bottom-Up Instructive Quality Control in the Biofabrication of Smart Protein Materials. Advanced Materials. 2015.

UNZUETA U., CESPEDES M.V., VAZQUEZ E., FERRER-MIRALLES N., MANGUES R., VILLAVERDE A. Towards protein-based viral mimetics for cancer therapies. Trends in Biotechnology. 2015;33(5):253-258.

PELUFFO H., UNZUETA U., NEGRO-DEMONTEL M.L., XU Z., VAQUEZ E., FERRER-MIRALLES N. ET AL. BBB-targeting, protein-based nanomedicines for drug and nucleic acid delivery to the CNS. Biotechnology Advances. 2015;33(2):277-287.

CORCHERO J.L., VAZQUEZ E., GARCÍA-FRUITOS E., FERRER-MIRALLES N., VILLAVERDE A. Recombinant protein materials for bioengineering and nanomedicine. Nanomedicine. 2015;9(18):2817-2828.

RODRIGUEZ-CARMONA E., MENDOZA R., RUIZ-CANOVAS E., FERRER-MIRALLES N., ABASOLO I., SCHWARTZ S. ET AL. A novel bio-functional material based on mammalian cell aggresomes. Applied Microbiology and Biotechnology. 2015;99(17):7079-7088.

Highlights

The group has developed projects aimed at generating new drugs and functional materials for treating rare diseases, inflammatory conditions such as mastitis, and breast and colorectal cancer. Through various projects funded by public and private entities (INIA, EC, MINECO; FIS, MARATO DE TV3), we have developed molecular principles dedicated to the engineering of molecular interactions between proteins that allow the generation of nanostructured functional materials, as therapeutics per se or as carriers of conventional and innovative drugs.

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