IBMC

ANNUAL REPORT 2013

UNIVERSITAS Miguel Hernández de Elche

INSTITUTE OF MOLECULAR AND CELL BIOLOGY

UNIVERSITY "MIGUEL HERNÁNDEZ"

IBMC

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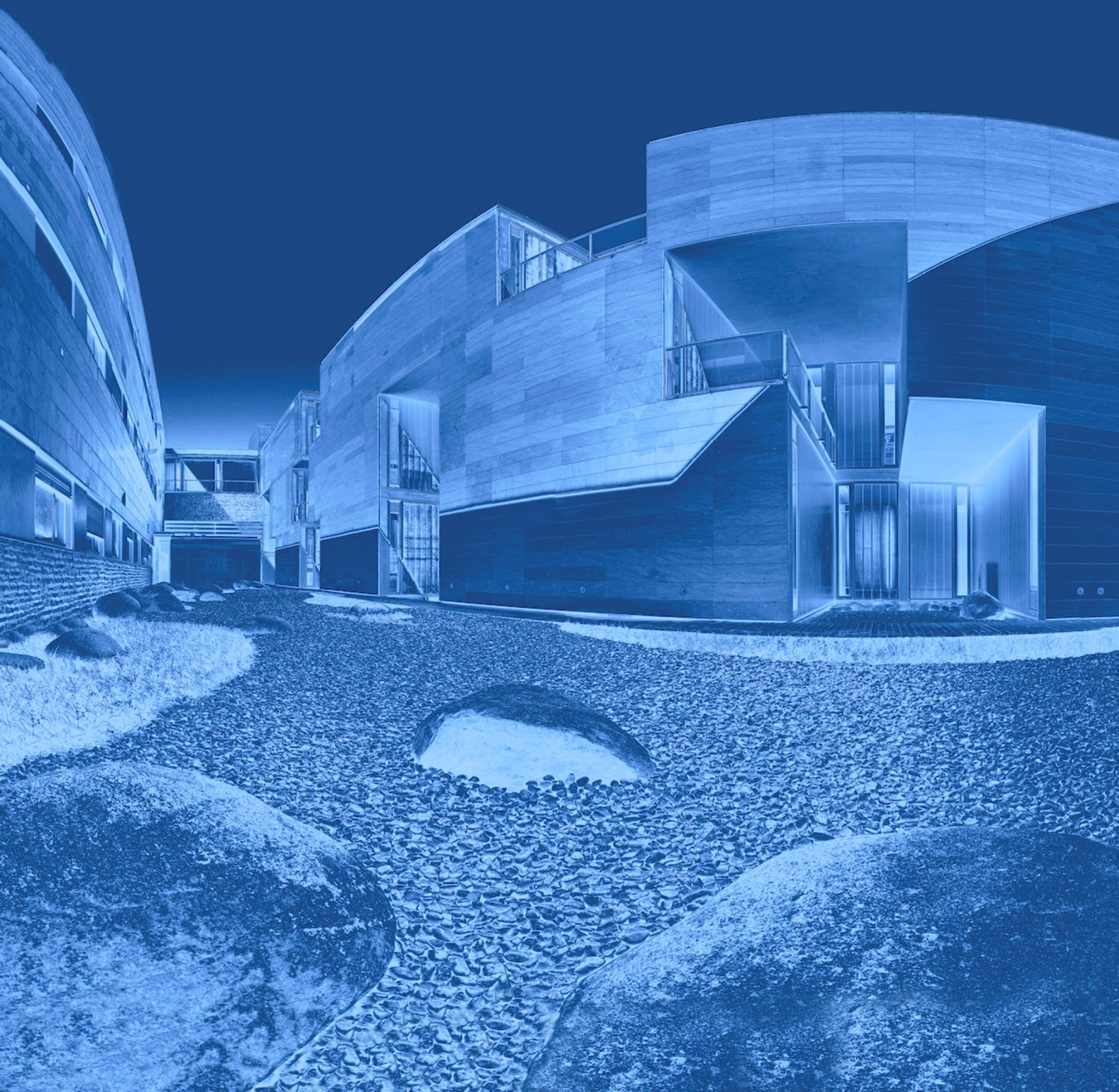
Institute of Molecular and Cell Biology



INSTITUTE OF MOLECULAR AND CELL BIOLOGY

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IBMC Annual Report 2013

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DIRECTOR'S FOREWORD

The Institute of Molecular and Cell Biology (IBMC) is one of the University Research Institutes at the University *Miguel Hernandez de Elche*. The IBMC is located in the University Campus in Elche, occupying a 4,000 sq. m. of laboratory in the Torregaitán Building. The Institute was created in 2002 from a transformation of the Center of Molecular and Cell Biology, thanks to the initiative and enthusiasm of its inspirator and first Director Prof. José Manuel González-Ros, who had the vision of creating a multidisciplinary research Institute in the University as a wise strategy to carry competitive and transferable research in the fields of Biomedicine and Biotechnology. This devotion to translational research has been a pivotal hallmark of the IBMC since its creation. As a result, in the past 16 years the IBMC has excelled in its scientific production as well as in the exploitation of the results generated by their groups. Furthermore, the interest of transferring the scientific results to society has thrust the creation of spin-off companies and Joint ventures with private enterprises and local Hospitals. This seminal vision has been kept invariable and can be fully appreciated in the Annual Report 2013 that describes all our achievements in research, exploitation, training and dissemination activities. All these accomplisments are in line with the objectives set in our Plan of Action.

Research teams have been very active in securing funding from both governmental and private sources, publishing papers that are widely cited, training young scientists with the highest scientific standards as recognized by the Excellence Mention of our Doctorate program by the Ministry of Education, and to disseminate our activities and achievements to society. Notwithstanding, a major success of the Institute has been the commercialization of innovative products generated from the research projects in the fields of nutraceuticals, cosmeceuticals and biotechnology; and having a lead compound close to enter clinical development in humans. To reinforce our translational activities, two technological platforms were launched. This success has been possible thanks to our philosophy of potentiating collaborations and sharing all the infrastructures, and to the contribution of our administrative and technical personnel facilitating the activities of our research teams.

Although we have walked a long and fruitful way, there is still plenty to achieve for increasing the IBMC international exposure and scientific distinction. In this regard, our Strategic Plan of Action for the next 5 years (2013-2017), strengthens the original vision, and establishes the central mission to consolidate a multidisciplinary program of translational excellence in the areas of biotechnology and health. In the first year we have strictly followed this plan and achieved up to 40% of the planned objectives. We will continue with our comitment to become a reference Institute in the arena of transferable knowledge.

Sincerely yours,

Antonio Ferrer

Prof. Antonio Ferrer-Montiel
IBMC Director

1. STRUCTURE AND GENERAL DESCRIPTION

1. STRUCTURE AND GENERAL DESCRIPTION

EXECUTIVE SUMMARY

The IBMC's **mission** is to promote a **multidisciplinary program of translational excellence** at a molecular and cell level, directed at the **identification, validation and development** of **bioactive molecules,** with an application in the areas of biotechnology and health, serving as a channel for bringing the interest of **basic research** in these areas closer to the **productive and service sectors** of our **society**.

The IBMC **vision** is to generate an **Institute of excellence** on a national level focused on a **unique research project** and with a commitment to **technological transfer** to the private sector and **clinical translation** of knowledge. Since its creation, the IBMC has maintained a high-standard research program, which has been transferred far above that of many national Research Institutes, which makes it a **reference** in innovation for the productive and clinical world. In order to foster and consolidate these actions, two technological platforms have been created: a) ***the Biological Screening Platform (BSP)*** whose mission is the development, validation and use of biological assays for screening libraries of synthetic and natural chemicals in order to identify compounds with biological activity; and, b) ***the Skin Research Platform (SRP)***, a public-private initiative whose mission is to develop molecular and cell research in all aspects related to human and animal skin, including physiopathology, therapy and biotechnology.

The IBMC has established an unparalleled research and educational program, which uses the **multidisciplinarity** and **complementarity** of its groups and exploits their **synergies** as a strategy for attaining **Excellence** and for increasing **Competitiveness and Productivity and for performing Research Frontier.** To accomplish it, in the last 2 years, research has been organized around **two complementary areas of research** namely, (i) ***molecular and cell design and (ii) molecular diagnosis and therapy*****,** for which the groups' abilities and experience have been organized in relation to supplementary areas of bioactive molecular development, therefore reducing scientific dispersion and grouping their activities to undertake singular and ambitious projects. Furthermore, by making the most of the technological platforms, in the next five-year period, the IBMC is intended to become a reference centre in the discovery of pharmacological and biotechnological tools **for the study and treatment** of **cutaneous pathologies and conditions,** with a clear translational and transference potential, and with the following future approaches:

1) **To consolidate** a multidisciplinary platform for basic research and their applications, that promotes the excellence in both basic scientific production and in technological transference, which in turn would permit laying the foundations for new business initiatives.
2) **To strengthen** research in relation to the discovery and development of bioactive molecules, which allows exploiting the complementarities and synergies of the

pluridisciplinary team, creating an original and unprecedented project on a national level. These actions would facilitate the implementation of a Research Institute integrated in the area of "drug discovery" focused on performing frontier research.

3) **To generate** a stimulating environment in which science, with the highest international level, is supported by the existence of an organization with sufficient material and human resources, including not only the scientific staff itself but also, technical and administration staff.
4) **To promote** a translational research platform in conjunction with the University and Hospitals which facilitates the translation of our researchers' scientific achievements to a clinical level as well as meeting the clinical demand of basic science.
5) **To stimulate** the activities of the Research Platforms as an exclusive project aimed to be the basis of a future research program which will include the current capacities of the Institute, and a market-oriented R&D.
6) **To internationalize** the activities so as to become a world reference in translational research in the development of bioactive compounds.
7) **To implement** an international Doctorate Program of excellence for educating young researchers in a university/business/hospital environment characteristic of this Institute.
8) **To disseminate and diffuse** scientific advances in such a way that these are promoted to society through reach-out activities, in order to get closer to the different entities of social environment.

In order to achieve these objectives, apart from focusing on the scientific goals, **agreements** with Public Research Organizations (**PROs**) will be pursued to: *1) complement and improving coverage of the scientific objectives of the proposed project; 2) execute a coordinated research and development; 3) attracting investment from public and private funds; 4) reinforce weak areas or those which require an impetus for their consolidation through the incorporation of researchers belonging to these entities,* thereby creating an **unprecedented research project** which sets the bases for the generation of a **unique Research Institute** on a national and international level, centered on the discovery of **bioactive molecules** with a high **pharmacological, cosmetic** and/or **nutraceutical** potential. There are no Institutes, or research centers with a scientific project, which has these characteristics. The **Spanish National Research Council (CSIC)** is undoubtedly the first option in the search for such alliances. This institution covers areas that are relevant to the IBMC and provides institutional channels for stable collaboration. The proposed **strategy** for implementing this project would be the creation of a **Joint Centre.** This new Centre would be supported on the **complementarity** of the two Institutions and would take advantage of the current infrastructure of the **IBMC**. The **profitability** of the strategy is guaranteed by the exploitation of the synergies and by the **uniqueness** of the action**.**

GENERAL INFORMATION

The IBMC was constituted as a University Research Institute after having passed the evaluations set out in the regulations in force, by virtue of Decreto 134/2002, de 27 de agosto, del Gobierno Valenciano. The IBMC was developed from a pre-existing nucleus - the Centre for Molecular and Cell Biology - which at the time had been created by agreement of the UMH Management Commission on May 21st, 1998, as a consequence of the university's concerted vocation to promote the multidisciplinary and synergic grouping of its researchers.

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The IBMC initially focused on a multidisciplinary approach on a molecular and cell level in the areas of biotechnology and health. In the last two years it has been oriented towards promoting a **pluridisciplinary** program of **translational excellence** in relation to the **discovery, validation and development** of **bioactive molecules** with biotechnological and therapeutic applications, serving as a channel for bringing the interests of **basic research** closer to the **productive and service sectors** of our **society.** From its creation, the Institute has reached a scientific maturity endorsed by the number and quality of its scientific publications in international journals, and by the volume of economic resources obtained from competitive sources. The Institute has also carried out **intense translational and technological transfer activity,** which has led to the registration of more than **29 patents**, or to the **creation of several "spin-off" companies**, besides maintaining an excellent relationship with business and production sectors. These activities are developed through agreements, such as the Cooperation Agreement between the UMH and the "Consellería de Sanidad" (Department of Health) to promote scientific collaborations and to facilitate staff mobility between the IBMC and the University of Hospital of Elche and its Foundation; or agreements for the creation of so-**called University-Business Joint Units**, first with the **Lipotec group** in 2000, in the biotechnological and chemical-pharmaceutical area, and later with the **multi-national JBT**, in the agro-alimentary area.

The IBMC is located at the **Torregaitán Building** on the UMH's Elche Campus UMH, which is fully occupied by Institute staff and has recently been extended to **4.000 m²**.

As a University Research Institute, the IBMC is governed by the regulations established in articles 12, 31 and 43 of the UMH Statute, as well as by articles 10 and 26 of the LOU (Organic Law for Universities). The Internal Regulations were drawn up once the corresponding University Framework Regulation was passed. The Institute is currently waiting for their approval by the Governing Board of the UMH.

The Institute's **Staff structure** includes the following positions:

a) **Researchers**, in accordance with the terms indicated in articles 12.5.a and 12.5.b of the UMH Legal Statute.

b) **Associated Researchers**, as defined in the Framework Agreement with the Foundation of the University Hospital of Elche.

c) **Collaborators**, pre and post doctorate staff undergoing training, who are integrated in the different work teams.

d) **Administration and Technical Staff** (PAS) belonging to the University staff structure or contracted under projects or agreements.

The highest collegiate body is the **Institute Council,** made up of all the PhD members of the Institute as well as representatives of the Institute's administration staff (PAS) and doctorate students. The governing positions are **Director, Deputy director and Secretary**, who in conjunction with the Institute's **research coordinator** and the **outgoing Director** (**Figure 1, Annex II**), make up the so-called **Board of Directors**, which in turn may or may not incorporate advisors "*ad hoc*" to deal with specific matters. The Director and the Board of Directors are assisted by an international external Scientific Advisory Board (**SAB**) (**Figure 1**), integrated by: **Dr. Praveen Anand**, neurologist at Hammersmith Hospital and a lecturer at Imperial College London (UK); **Prof. Pilar Goya**, Research Professor at the Institute of Medicinal Chemistry, CISC, Madrid; **Prof. José Pio Beltrán**, Research Professor at the Institute of Molecular and Cell Biology of Plants, CSIC, Valencia; **Dr. Luis Ruiz**, CEO of Janus Developments and **Prof. Anne Ulrich** from the Karlsruhe Institute of Technology (KIT), Institute of Biological Interfaces (IBG-2), Karlsruhe, Germany.

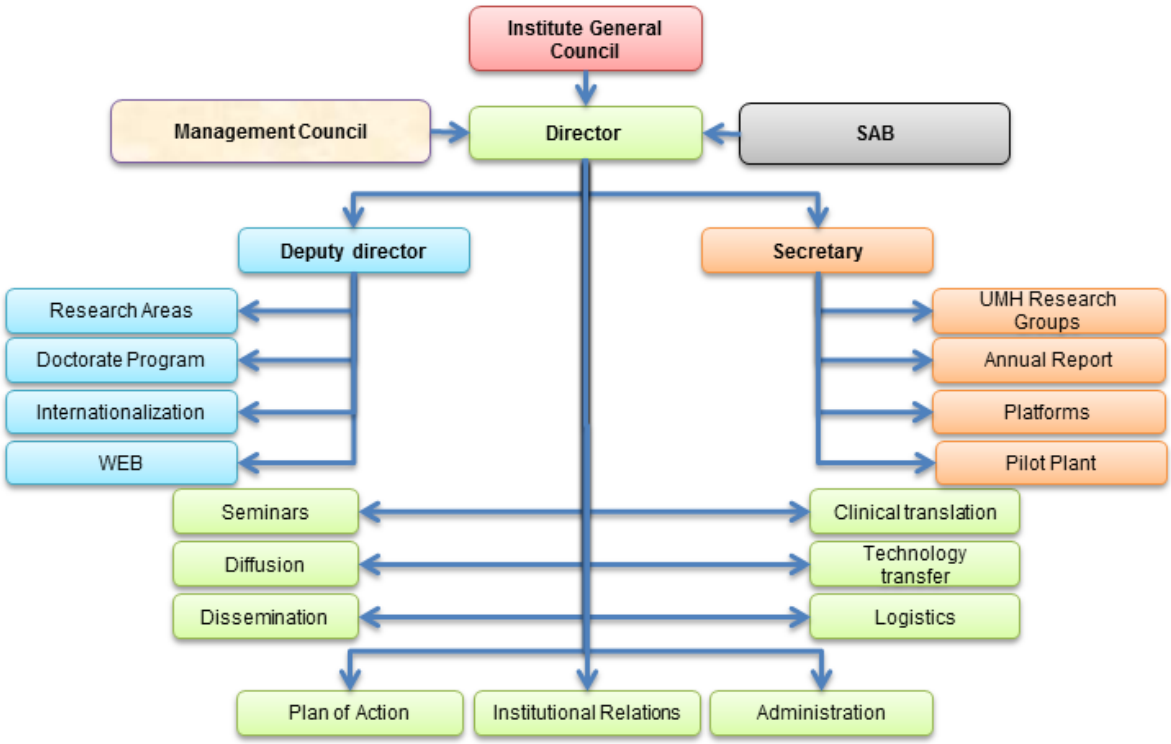

Figure 1. IBMC Functional Organigram.

Scientifically, the IBMC research activities in the area of the discovery of bioactive molecules has been organized into two complementary lines of research:

- **Molecular and Cell Design**
- **Molecular Diagnosis and Therapy**

The educational activities provided by the IBMC will revolve around the Official Doctorate Program for Molecular and Cell Biology, distinguished with a **Mention of Excellence** by the Ministry of Education (**ref. MEE2011-0637**).

THE IBMC IN FIGURES

The numerical data about the IBMC for the last four-year period are given below illustrating the current organization of human resources, activities and efforts made to obtain financial resources and the scientific and translational productivity carried out by its members. These numbers have positioned the IBMC at an excellent level of national and international competitiveness.

HUMAN RESOURCES

The IBMC's staff is made up of 78% researchers (senior, post- and pre-doctorate), 16% technical support staff, and 6% administration staff (Figure 2). Since its foundation as a Research Center and later as an Institute, the IBMC has always been very careful about maintaining gender parity among its staff, currently having 59% female staff members and 41% male.

Board of Directors:

Antonio Ferrer Montiel
Director

Amparo Estepa Pérez
Deputy Director

Vicente Micol Molina
Secretary

Reyes Mateo Martínez
Director of Research Areas

José Manuel González Ros
Outgoing Director

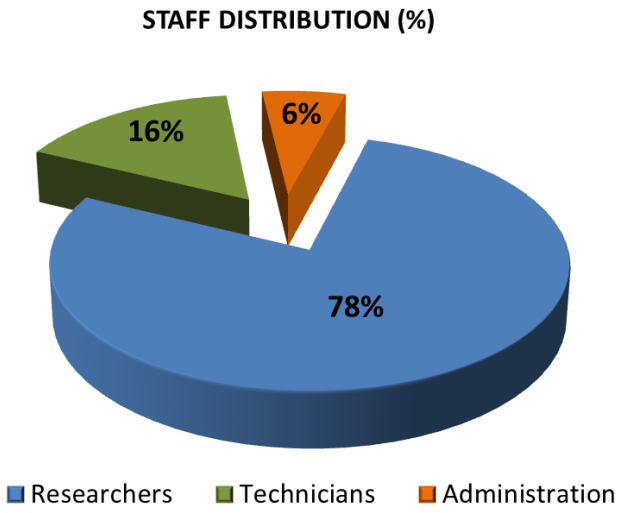

Figure 2. IBMC Staff distribution.

The team in charge of the administration services at the IBMC is made up of two administration technicians, supported by an auxiliary from the Department of Biochemistry and Molecular Biology, and supported by an auxiliary contracted under the CONSOLIDER-INGENIO 2010 project (CSD2008-00005). This is a team of staff with wide experience in managing research projects and doctorate programs and an excellent capacity for organization and prioritization of tasks, as well as being accustomed to working as a team.

Furthermore, this team maintains a high level of commitment and involvement in the development of the IBMC Project, which enormously facilitates the work of the Institute's management.

The Institute technical facilities are supervised by mid-level technical staff. The tissue culture unit, chromatographic analysis and purification unit, nucleic acid processing unit, image processing and flow cytometry unit, instrumental analysis unit, NMR unit, high throughput screening unit and protein expression and purification expression unit are all attended by six Specialist Technicians, supported by two technicians under contract through a project.

IBMC scientists also benefit from other facilities that the UMH provides through its Research Technical Services available in the Elche campus itself or in San Juan (animal facility, isotopes unit, electronic microscopy, confocal microscopy, etc.) or infrastructures available in the Institute of Neurosciences (UMH-CSIC) and in the Bioengineering Institute.

Administration services:

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IBMC Secretary
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Raquel Jorquera
SICI Consolider Secretary
Phone: +34 96 522 2185

Technicians:

Elena López Alonso
Mª Teresa Garzón Cabrerizo
Eva Martínez Martínez

Ángeles Gómez Martínez
Antonio Manuel Zafra Pinto
Elisa Pérez García
José Miguel Ramos Baddouh

ECONOMIC RESOURCES

The economic data shown below (Table I) are those reflected in the research reports published annually by the Vice-chancellor's Office for Research and Innovation, which are available on the OTRI website. These data only refer to projects and contracts, that are managed by the UMH and, therefore, do not include other projects awarded to IBMC researchers belonging to the Hospital of Elche, which are managed by the Foundation itself and which the UMH has no control over.

Table I. Annual Evolution and sources of IBMC funding per source

	SOURCES OF IBMC FUNDING (€)				
	2010	**2011**	**2012**	**2013**	**TOTAL**
National P.	736.217	669.656	769.538	949.434	**3.124.845**
European P.	---	66.373	33.300	---	**99.673**
Autonomous Reg. P.	136.100	82.600	62.429	150.000	**431.129**
Foundations	186.937	---	---	---	**186.937**
Contracts	352.626	465.759	361.000	321.878	**1.501.263**
IBMC-Research Expenses	56.781	19.636	16.816	28.000	**121.233**
UMH – IBMC (cap.II)	65.637	43.372	34.258	32.076	**175.343**
TOTAL	**1.534.298**	**1.347.396**	**1.277.341**	**1.481.388**	**5.640.423**

It can be appreciated that during the last four years period, the IBMC has raised resources to an average of approximately **1.41 M€** per year, mainly from the Ministry of Science's National Plan for R+D+i (55%) and contracts with companies (27%). These numbers indicate the high level of competitiveness of IBMC projects, as well as its capacity to attract private funding (Fig. 3).

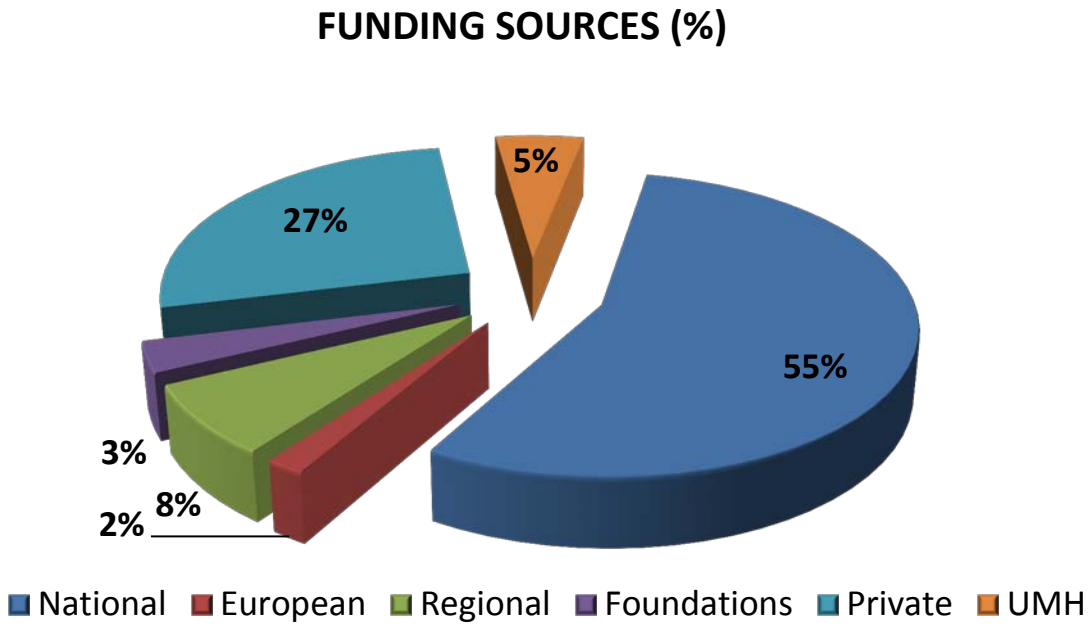


Figure 3. Distribution of IBMC funding sources

SCIENTIFIC PERFORMANCE

A detailed description of the scientific publications by the different research groups Institute during the 2013 period is included later in this report. The analysis of the IBMC competitive position during the 2010-2013 period has been estimated through current bibliometric databases using the publications and the number of citations through the ISI Web of Knowledge (www.accesowok.fecyt.es), and using the Web of Science database.

In line with the IBMC's high level of competitiveness in raising economic resources is its scientific and translational performance. As seen in Table II, throughout the last four years period, IBMC researchers continued to publish a growing number of publications. Besides the number of articles, constant growth in the percentage of articles within the top quartile of the area (Q1), within the last four years period should be highlighted. This value almost reached 80% in 2013. The average impact factor throughout the period remains at around 3.4.

Furthermore, the impact of the results produced by the IBMC groups has been increasing as indicated by the number of citations, which, in the last few years and after the consolidation of the groups, shows a growth consistent with its excellent competitive position. Note that this growth occurs without undermining the strong commitment to transfer of results to the industry, which requires more time for publishing as results have to be protected first.

Table II. Annual evolution of several bibliometric parameters related to the articles published by the IBMC.

	2010	2011	2012	2013	TOTAL
Nº of publications	**78**	**89**	**85**	**109**	**361**
Q1 Publications	38	50	52	87	**227**
Total Impact	255	284	297	396	**1232**
Average Impact	3.6	3.5	3.2	3.5	**3.45**
Citations	1669	1734	1786	2290	**7479**

TRANSLATIONAL AND TECHNOLOGICAL TRANSFER ACTIVITIES

A unique activity by the IBMC is its commitment to technological transfer to the private sector, as well as in the translation of laboratory knowledge to clinical practice. The IBMC has maintained a highly active transfer activity since its creation, which is much higher than that of many national Research Institutes, making it a reference for the translation of basic science to the productive and clinical world. Table III summarizes the translational activities carried out since its creation. Due to the unique nature of these activities, we have included the whole period so that the quantity and diversity of the breakthroughs achieved can be appreciated.

Table III. Transfer and translation activities and results

A. TECHNOLOGICAL TRANSFER (1998-2013)		
A.1. COLLABORATION ACTIVITIES WITH PRIVATE ENTERPRISES		
	Number	**Financing**
1. PETRI/TRACE Projects	3	212.780 €
2. R+D Contracts	75	5.130.465 €
3. Provision of services	22	67.780 €
A.2. PATENTS		
1. Applied for	39	
2. Extended via PCT	18	
3. Published with WO n.	15	
4. Granted	10	
5. Licensed	12	
6. Exploitation	12	
7. Commercialized products	LyTag resin, LyTag2Phase, Argireline, Chromabright, Bodyfensin, Leuphasyl, Cartixan-4, PLX, Hypoxdermin, NutroxSun, Melatime, Thermostressin, Diffuporine, Adifyline, Silusyne.	

A.3. CREATION OF SPIN-OFF COMPANIES			
Company	**Holding %**	**CIF**	**Year**
DiverDrugs	5.38 %	B-61905725	1999
Nutracitrus	7.50 %	B-73263154	2003
Mitra Sol Technologies	73 %	B-54704127	2013

A.4. PARTICIPATION IN COMPANY SCIENTIFIC ADVISORY COMMITTEES	
Company	**Period**
Diverdrugs	1999-present
Lipotec	1998-present
GP Pharm	2006-present
Nutracitrus	2003-present
LipoPharm	2007-present
Bioarray	2008-present
BCN Peptides	2008-present
Monteloeder	2001-present
New Developments in Nutraceuticals	2004-2011
Quimicas del Vinalopo	2004-present
Endemic Biotech	2006-present
Angelini ACRAF	2013-present
PRIMADERM	2013-present
Cátedra Dermocosmética	2010-present

A.5. JOINT UNITS IBMC-UMH-COMPANIES	
Company	**Period**
Lipotec/Diverdrugs	2000-present
JBT	2001-present

B. TRANSLATIONAL ACTIVITIES (1998-2013)		
	Number	**Period**
1. Agreements with hospitals: Elche General Hospital Alicante General Hospital Elche Hospital Foundation	3 1 1 1	 2001-present 2003-present 2009-present
2. Hospital staff collaboration projects	14	1998-present
3. Hospital staff joint publications	16	1998-present
4. Joint seminars/workshops	1	2008
5. Doctorate programs	1	1998-present
6. Scientific networks	1	2007-2010
7. HTS Platform	1	1999-present
8. Skin Research Platform	1	2010-present

PERFORMANCE IN EDUCATION

As mentioned above, training activities by the IBMC revolve around the Doctorate Program in Molecular and Cell Biology. The corresponding data given below are included in the Reports by the Vice-chancellor's Office for Research and Innovation at the University Miguel Hernández.

Main achievements of the doctorate program (2007-2013) (Table IV). The performance of the Doctorate Program is above the general average for graduate programs as demonstrated by its distinction with the **Mention of Excellence** by the Ministry of Education. This mention has been given to only about 100 programs out the total number of programs presented by Spanish Universities (BOE nº 254 20 October 2012). Likewise, within the University Miguel Hernández, the Institute holds a predominant position out of the only two doctorate programs that have received this recognition of excellence. The dedication and enthusiasm of the IBMC researchers who have participated in the Doctorate Program have contributed to endowing it with a symbol of identity and ensuring the enrolment of young people who receive an education of excellence in molecular and cell biology, biotechnology and biomedicine. Furthermore, a differential fact of IBMC training is education in technology transfer and clinical translation of results, with the participation of entrepreneurs and clinicians who provide highly valued sessions. The seminar program, which complements students' education, is a pivotal part of the program. This means that students receive an integral education and that graduates are professionally trained.

Table IV. Doctorate program performance (2011-2013 Biennial).

Average performance (2011-2013)	
Thesis defended	12
Nº of students enrolled	20
Nº of Professors on the program	15
Thesis/ Professors average	0.8
Thesis/year average	6
Doctorate Excellence Awards	2
Nº publications deriving directly from thesis	60%
Publications/thesis average	3

THE IBMC SCIENTIFIC PROGRAM

The IBMC has established a unique research and training program, which exploits **multidisciplinarity,** making the most of the **complementarities** of the groups and using **synergies** as a strategy for attaining **excellence** and increasing **competitiveness and productivity.** To accomplish this aim, in the last two years, research has been organized into **two complementary areas of research,** namely, (i) ***molecular and cell design and*** (ii) ***molecular diagnosis and therapy.*** These research lines, in turn, are organized into sub-areas, which rationally combine the groups' abilities and skills in the supplementary fields that contribute to the development of bioactive molecules (Figure 4), reducing scientific dispersion by grouping activities in order to carry out unique and ambitious research projects. Consequently, in the next five-year period, the IBMC aspires to become a center of reference in the **discovery of pharmacological and biotechnological tools,** with a clear translational and transfer potential. The intense and sustain work in this line is the central objective for the next five year period, and to so agreements with PROs will be pursued which will permit reinforcing deficient areas or those that require an impetus for their consolidation, and thereby generating a unique and unprecedented project on a national and international level.

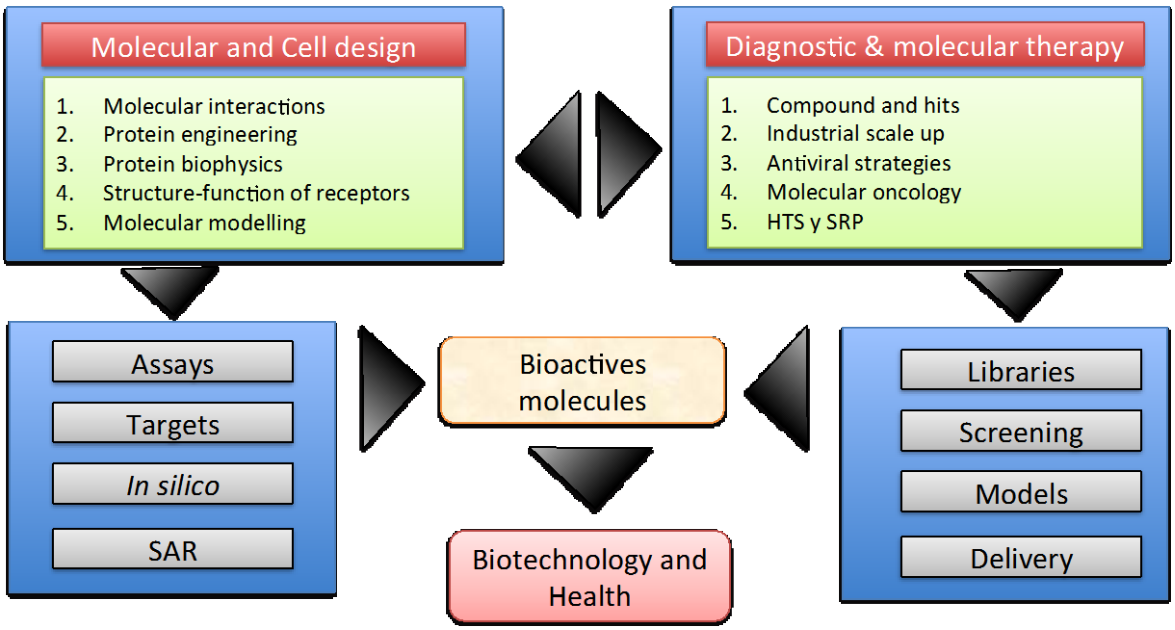
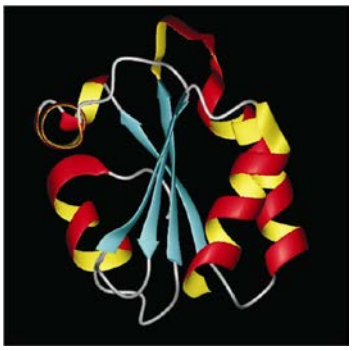


Figure 4. Organization of IBMC research areas

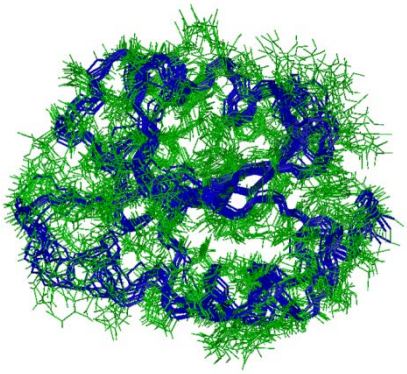
In scientific terms, the targets of these research areas of the IBMC are developed as follows:

A. Molecular and Cellular Design



Research within the line of Molecular and Cellular Design aims at advancing knowledge of relationships between structure and function in proteins, in order to be able to modify them rationally and specifically. The underlying goal is the transformation of the activity of these proteins with bio and chemo-technological purposes, or the use of the information to design targeted ligands to modulate the receptor activity acting as sensors.

The line of investigation has 9 researchers (7 consolidated and 2 more in the process of consolidation) organized in five research groups, although not in all of them there is a sufficient critical mass to successfully achieve the scientific objectives pursued. The different scientific backgrounds of the researchers who develop this research line allows a reasonably and pluridisciplinary (though improved) approach to analyze problems, offering an opportunity for the development of common interests and benefiting from synergies that naturally appear in this context. This multidisciplinary approach of issues enables a broad focusing on scientific topics, ranging from a perspective of basic science to investigations with clear translational vocation.

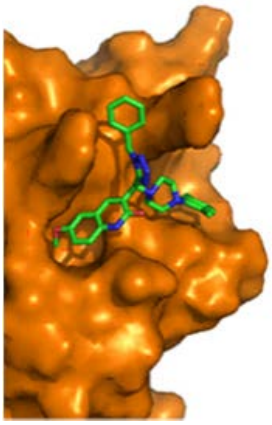


Both the composition of the different research groups that make up this line of research as its multidisciplinarity and flexibility to raise specific scientific goals fosters a high competitiveness, both in the uptake of competitive sources and scientific production, in the training of research personnel and in the technological transfer of research results. In this sense, strong links with research groups both national as international have been notably established, which have materialized, for example, in leadership or participation in projects coordinated with other institutions both within the different National Plans of Research, including projects CONSOLIDER, and funded by the European Union and recently granted.

Molecular and Cellular Design line is organized into two sub-lines, each comprising several research groups with common research interests. The first in centered around **Molecular Recognition and Protein Biophysics and Engineering**, while the second focuses his research on **Structure-Function Relationships in Membrane Proteins**.

B. Diagnosis and Molecular Therapy

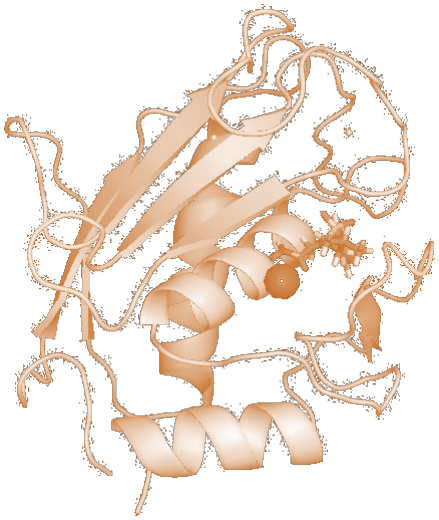
The Diagnosis and Molecular Therapy line seeks the identification and validation of molecular markers in human and animal pathologies of high prevalence, as well as the



development of diagnostic methods and therapeutic or preventive strategies. This line consists of a multidisciplinary team of researchers covering from molecular aspects to the semi-industrial production of biological actives. Such multidisciplinarity is sustained by the contribution of 12 researchers (10 consolidated and 2 more in the process of consolidation) organized in six research groups, which provides a balanced composition and favors a high competitiveness both in scientific contributions, as in the abstraction of resources, training of research personnel and generating transferable and exploitable technologies.

Milestones achieved in this line of research have had and have a high scientific impact, as shown by scientific publications in magazines of recognized international prestige, as well as the generation of unique technologies that are protected by patents extended worldwide and have been licensed to interested companies. Also, it should be noted as a strong point of this line the high level of national and international collaborations with public bodies and private research, contributing to increase the impact of activities and its internationalization. In addition, the interrelationship of the sub-lines that make up this line of research has fostered identifying synergies and common interests between groups that have driven collaborations that accelerate the achievement of results and technologies.

Clearly, the activities of this line have a high potential for clinical translation materialized in close collaboration with the General Hospital and the University of Elche, as well as biotechnology transfer and exploitation resulting in continuous and consolidated collaborations with biotech, food, cosmetics and pharmaceutical companies.



2. MOLECULAR AND CELLULAR DESIGN

2. MOLECULAR AND CELLULAR DESIGN

Molecular Recognition and Protein Biophysics and Engineering

Group name:

PROTEIN BIOTECHNOLOGY

We develop basic research on the structure and folding of proteins by the acquisition of structural and thermodynamic data. Many of our results are oriented towards technological transfer, more precisely those dealing with the design of new antibiotics and the setup of novel systems of purification and immobilization of recombinant proteins. Our studies are centered basically in three lines:

- Design, selection and evaluation of new antimicrobials against *Streptococcus pneumoniae* (pneumococcus) based on small molecules or in multivalent nanoparticles.

- The C-LytA affinity tag, that serves as a model to study the folding and engineering of repeat proteins and constitutes an efficient affinity tag for the single-step chromatographic purification and immobilization of recombinant proteins from nano- to macrosurfaces, including enzymatic electrodes.

- Bioplastics. Natural, biodegradable plastics of bacterial origin that may constitute an alternative to the use of petroleum derivatives. We study the structure and function of several proteins involved in the synthesis, stability and degradation of these bioplastics, and the immobilization of proteins on these polymers.

Laboratory expertise includes:

- Thermodynamic analysis of protein stability.

- Spectroscopy (absorption, fluorescence, circular dichroism).

- Protein engineering.

- Nanobiotechnology.

STAFF

Jesús Miguel Sanz Morales

Beatriz Maestro

Ph.D STUDENTS

Daniel Bello Gil

Jennifer Fonseca Pupo (Visiting scientist)

PUBLICATIONS

1. Maestro, B., Galán, B., Alfonso, C., Rivas, G., Prieto, M.A., Sanz, J.M. A New Family of Intrinsically Disordered Proteins: Structural Characterization of the Major Phasin PhaF from Pseudomonas putida KT2440. **PLoS One 8**, e56904. 2013.
2. Ribes, S., Riegelmann, J., Redlich, S., Maestro, B., de Waal, B., Meijer, E.W., Sanz, J.M., Nau, R. Multivalent choline dendrimers increase phagocytosis of Streptococcus pneumoniae R6 by microglial cells. **Chemotherapy 59**, 138-142. 2013.
3. Esquembre, R, Sanz, J.M., Wall, G., Mateo, C.R., del Monte, F., Ferrer, M.L. Thermal Unfolding and Refolding of Lysozyme in Deep Eutectic Solvents and Their Aqueous Dilutions. **Phys. Chem. Chem. Phys**. **15**, 11248-11256. 2013.

Group name:

PROTEIN STRUCTURE AND THERMODYNAMICS OF MOLECULAR RECOGNITION

Our group is involved in the study, by using calorimetric and spectroscopic techniques, of macromolecular interactions. To that end, the group has the expertise in DSC, ITC, fluorescence and circular dichroism. Furthermore, the group has the knowledge to solve structures by using state-of-the-art techniques. Some, but note exclusively, of the biomolecules currently under study in the group are: (i) those involved in the phosphorylation tranfer in micro-organisms; and (ii) those implicated in the aseembly of the capsid of HIV

STAFF

Javier Gómez-Pérez

José Luis Neira

POSTDOCTORAL FELLOWS

David Aguado Llera

Ph.D STUDENTS

Rosa Doménech

PUBLICATIONS

1. Sánchez-Morán, I., Muñoz-Barroso, I., Kostetsky, E.Y., Zhadan, G., Gómez, J., Shnyrov, V.L., Villar, E. Thermal stability of matrix protein from Newcastle disease virus. **Int. J. Biomol. 61**, 390-395, 2013.
2. Aguado-Llera, D., Tamidi, T., Doménech, R. , Pantoja-Uceda, D., Gironella, M., Santoro, J., Velázquez-Campoy, A., Neira, J.L., Iovanna, J.L. Deciphering the binding between NUPR1 and MSL1 and their dna-repairing activity. **PLoS One 8**, e78101. 2013.
3. Doménech, R. , Hernández-Cifre, J.G., Bacarizo, J., Díez-Peña, A.I., Martínez-Rodríguez, S., Cavasotto, C. N., García de la Torre, J., Cámara-Artigas, A., Velázquez-Campoy, A., Neira, J. L. The histidine-phosphocarrier protein of the phosphoenolpyruvate: sugar phosphotransferase system of *Bacillus Sphaericus* self-associates. **PLoS One 8**, e69307. 2013.
4. Vega, S., Neira, J.L., Marcuello, C., Lostao, A., Abian, O., Velázquez-Campoy, A. NS3 protease from hepatitis c virus: biophysical studies on an intrinsically disordered protein domain. **Int. J. Mol. Sci. 14**, 13282-13306. 2013.
5. Neira, J. L. NMR as a tool to identify and charcterize protein folding intermediates. **Arch. Biochem. Biophys. 531**, 90-99, 2013.

6. Neira, J.L., Sandí, M.J., Bacarizo, J., Archange, C., Cámara-Artigas, A., Iovanna, J.L. An N-terminally truncated mutant of human chemokine CXCL14 has biological activity. **Protein Pept. Lett. 20**, 955-967. 2013.
7. Neira, J. L. Protein folding and stability: a Prague cemetery. **Arch. Biochem. Biophys. 531**, 1-3. 2013.
8. Spínola-Amilibia, M., Rivera, J., Ortiz-Lombardía, M., Romero, A., Neira, J.L., Bravo, J. BRMS151-98 and BRMS151-84 are crystal oligomeric coiled coils with different oligomerization states, which behave as disordered protein fragments in solution. **J. Mol. Biol. 425,** 2145-2163. 2013.

Book chapters

1. Neira, J. L. Fluorescence, circular dichroism and mass spectrometry as tools in structure of virus. In Structure and Physics of Viruses. Mateu, M.G. Ed. Springer, 2013. ISBN 978-94-007-6551-1.
2. Neira, J. L. NMR as a tool for structure of virus. In Structure and Physics of Viruses. Mateu, M.G. Ed. Springer, 2013. ISBN 978-94-007-6551-1.

Books

1. Carbajo, R. J. & Neira, J. L. NMR for chemists and biologists. Springer, 2013. ISBN 978-94-007-6975-5

Group name:

FLUORESCENT NANOMATERIALS APPLIED TO BIOLOGICAL SYSTEMS

Our group is interested in the development of new fluorescent materials with applications in biological systems. On one hand, we design and develop fluorescent biosensors with high sensitivity, based on the entrapment of organic molecules and biomolecules in inorganic matrices, and characterize these hybrid materials at a molecular level in order to improve their applications. On the other hand, we work in the design, synthesis and characterization of novel fluorescent conjugated polyfluorenes, to be used as nanoparticles and nanofibers in applications such as bioimaging, drug delivery, clinical diagnosis and sensing devices for biomolecules. Other group activities include the characterization of macromolecular interactions, especially in non-conventional systems, such as ionic liquids as well as the synthesis of conjugated polymers to be applied in photonics and optoelectronics devices.

STAFF

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TECHNICIANS

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PUBLICATIONS

1. Martinez-Tomé, M.J., Esquembre, R., Mallavia R., Mateo, C. R. Formation and characterization of stable fluorescent complexes between neutral conjugated polymers and cyclodextrins. **J. Fluoresc. 23**, 171-180. 2013.

2. Vázquez-Guilló, R., Calero, A., Valente, A.J.M., Burrows, H.D., Mateo, C.R., Mallavia, R. Novel electrospun luminescent nanofibers from cationic polyfluorene/cellulose acetate blend. **Cellulose 20**, 169-177. 2013.

3. Kahveci, Z., Martinez-Tomé, M.J., Esquembre, R., Mallavia R., Mateo, C. R. Use of the Conjugated Polyelectrolyte Poly{9,9-bis(6′-N,N,N-trimethylammoniumhexyl9-fluorene-phenylene} (HTMA-PFP) as a Fluorescent Membrana Marker.

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4. Mallavia R., Martinez-Tomé, M.J., Vázquez-Guilló, R., Estepa, A., Mateo, C. R. Stabilization of neutral Polyfluorenein aqueous solution through their interaction with phospholipids and sol-gel encapsulation. **ACS App. Mater. Interfaces 5**, 2952-2958. 2013.

5. Esquembre, R, Sanz, J.M., Wall, G., del Monte, F., Mateo, C.R., Ferrer, M.L. Thermal Unfolding and Refolding of Lysozyme in Deep Eutectic Solvents and Their Aqueous Dilutions. **Phys. Chem. Chem. Phys**. **15**, 11248-11256. 2013.

Structure-Function Relationships in Membrane Proteins

Group name:

STRUCTURE-FUNCTION RELATIONSHIP OF ION CHANNELS

Potassium channels are considered very important components of all living organisms because they mediate a myriad of key biological processes, but also because they are actual or potential drug targets. They play critical roles in a variety of physiological processes, including the regulation of heart rate, muscle contraction, neurotransmitter release, neuronal excitability, insulin secretion, epithelial electrolyte transport, cell volume regulation, cell proliferation and others. Also, there is no question to date that K^+ channels are involved in human diseases such as cardiac disease and arritmia, epilepsy, diabetes, hypertension, neurodegeneration and probably many others.

By further understanding K^+ channels structure and function, we will not only learn new lessons on the biology of these important membrane proteins, but also facilitate their therapeutic exploitation. According to such expectations, our group is interested in understanding the mechanisms of modulation of K^+ channels, particularly those related with pioneering reports from our group, such as the recently described clustering and folding of channel proteins, or their interaction with membrane lipids and ions. We will attempt to apply the findings from above to develop new approaches for drug discovery, both in terms of identifying potentially useful, new therapeutic targets and by designing "structure-based" drug candidates.

STAFF

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Mª Luisa Molina Gallego

Estefanía Montoya Díaz

PUBLICATIONS

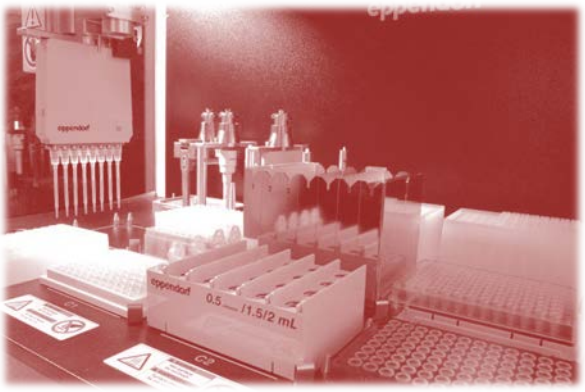
1. Poveda, J.A., Giudici, A.M., Renart, L., Molina, M.L, Montoya, E., Fernández, A.M., Fernández-Ballester, G., Encinar, J.A., González-Ros, J.M. Lipid modulation of ion channels through specific binding sites. **Biochim. Biophys. Acta 1838**, 1560-1567. 2013.

2. Ibarguren, M., López, D.J., Encinar, J.A., González-Ros, J.M., Busquets X. Escribá, P.V. Partitioning of Liquid-ordered / Liquid-disordered Membrane Microdomains Induced by the Fluidifying Effect of 2-Hydroxylated Fatty Acid Derivatives. **Biochim. Biophys. Acta 1828**, 2553-2563. 2013.

3. Martinez-López, A., Encinar, J.A., Medina-Gali, R.M., Balseiro, P., García-Valtanen, P., Figueras, A., Novoa, B., Estepa A. pH-dependent solution structure and activity of the host-defense peptide myticin C (Myt C) from the mussel Mytilus galloprovincialis. **Mar. Drugs 2013 11,** 2328-2346. 2013.

4. Giudici, A.M., Molina, M.L., Ayala, J.L., Montoya, E., Renart, M.L., Fernández, A.M., Encinar, J.A., Ferrer-Montiel, A, Poveda J.A., González-Ros, J.M. Detergent-labile, supramolecular assemblies of KcsA: Relative abundance and interactions involved. **Biochim. Biophys. Acta 1828**, 193-200. 2013.

5. Pérez-Faginas, P., Aranda, M.T., García-López, M.T., Infantes, L., Fernández, A.M., González-Ros, J.M., Ferrer-Montiel, A., González-Muñiz R. Highly functionalized 1,2-diamino compounds through reductive amination of amino acid-derived ß-keto esters. **PLoS One 8**, e53231. 2013.



3. MOLECULAR DIAGNOSIS AND THERAPY

3. MOLECULAR DIAGNOSIS AND THERAPY

Bioactive Molecules

Group name:

NATURAL BIOACTIVE COMPOUNDS

The relationship between the biological activity of natural dietary compounds and its effects on chronic human diseases is under intense debate. The research target of our group is to characterize the wide biological activity of natural bioactive compounds using cellular and animal models and to understand the mechanism underlying their health effects. Our group is focused on:

- The capacity of polyphenols to ameliorate metabolic disturbances (oxidative stress and insulin resistance) in cellular models and hyperlipidemic mice.
- Bioguided screening of antimicrobial herbal extracts and compounds for applications in cosmetics, hygiene or medical devices.
- The cytotoxic/cytostatic and apoptotic effects of polyphenols in cancer cellular models using global OMICs. Nano-encapsulation of potential anticarcinogenic compounds.
- Characterization of food and herbal materials by chromatography coupled to mass spectrometry. Semi-industrial scale production of herbal extracts deriving from plants or vegetal by-products.
- Optimization of juice extraction processes and integral exploitation of by-products.

STAFF

Vicente Micol Molina, Group Leader

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Nuria Martí Bruñá

Manuel Valero Roche

Enrique Barrajón Catalán

POSTDOCTORAL FELLOWS

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Ph.D STUDENTS

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Salud Vegara Gómez

Laura Tomás Menor

Almudena Pérez López

Verónica Ruiz Torres

TECHNICIANS

Mª Teresa Garzón Cabrerizo

PUBLICATIONS

1. Tomás-Menor, L., Morales-Soto, A., Barrajón-Catalán, E., Roldán-Segura, C., Segura-Carretero, Micol V. Correlation between the antibacterial activity and the composition of extracts derived from various Spanish Cistus species. **Food Chem. Toxicol. 55C**, 313-322. 2013.

2. Quirantes-Piné, R., Zurek, G., Barrajón-Catalán, E., Bäßmann, C., Micol, V., Segura-Carretero, A., Fernández-Gutiérrez, A. A metabolite-profiling approach to assess the uptake and metabolism of phenolic compounds from olive leaves in SKBR3 cells by HPLC-ESI-QTOF-MS. **J. Pharm. Biomed. Anal. 72,** 121-126. 2013.

3. Quirantes-Piné, R., Verardo, V., Arráez-Román, D., Fernández-Arroyo, S., Micol, V., Caboni, M.F., Segura-Carretero, A., Fernández-Gutiérrez, A. Evaluation of different extraction approaches for the determination of phenolic compounds and their metabolites in plasma by nanoLC-ESI-TOF-MS. **Anal. Bioanal. Chem**. **404**, 3081-90. 2013.

4. Quirantes Piné, R., Herranz-López, M., Funes, L., Borrás-Linares, I., Micol V., Segura-Carretero, Fernández-Gutiérrez, A. Phenylpropanoids and their metabolites are the major compounds responsible for blood-cell protection against oxidative stress after administration of *Lippia citriodora* in rats. **Phytomedicine 20**, 1112-18. 2013.

5. Ahmad-Qasem, M. H, Cánovas, J., Barrajón-Catalán, E., Micol V, Cárcel, J.A., García-Pérez, J.V. Kinetic and compositional study of phenolic extraction from olive leaves (var. Serrana) by using power ultrasound. **Inn. Food Sci. Emerg. Technol. 17**, 120-29. 2013.

6. Hussam Ahmad-Qasem, M., Barrajón-Catalán, E., Micol, V., Mulet, A., García-Pérez, J.V. Influence of freezing and dehydration of olive leaves (var. Serrana) on extract composition and antioxidant potential. **Food. Res. Int. 50**, 189-196. 2013.

7. Hussam Ahmad-Qasem, M., Barrajón-Catalán, E., Micol, V., Mulet, A., García-Pérez, J.V. Influence of air temperature on drying kinetics and antioxidant potential of olive pomace. **J. Food Eng. 119**, 516-524. 2013.

8. Falco, A., Barrajón-Catalán, E., Menéndez-Gutiérrez, M.P., Coll, J., Micol, V., Estepa, A., Melittin-loaded immunoliposomes against viral surface proteins, a new approach to antiviral therapy. **Antiviral Res. 97**, 218-21. 2013.

9. Joven, J., Rull, A., Rodríguez-Gallego, E., Camps, J., Riera-Borrull, M., Hernández-Aguilera, A., Martin-Paredero, V., Segura-Carretero, A., Micol, V., Alonso-Villaverde, C., Menéndez, J.A.; for the Bioactive food component platform. Multifunctional Targets of Dietary Polyphenols in Disease: A Case for the Chemokine Network and Energy Metabolism. **Food Chem. Toxicol. 51C**, 267-279. 2013.

10. Menendez. J.A, Joven, J., Aragonès, G., Barrajón-Catalán, E., Beltrán-Debón, R., Borrás-Linares, I., Camps, J., Corominas-Faja, B., Cufí, S., Fernández-Arroyo, S., García-Heredia, A., Hernández-Aguilera, A., Herranz-López, M., Jiménez-Sánchez, C., López-Bonet, E., Lozano-Sánchez, J., Luciano-Mateo, F., Martin-Castillo, B., Martín-Paredero, V., Pérez-Sánchez, A., Oliveras-Ferraros, C., Riera-Borrull, M., Rodríguez-Gallego, E., Quirantes-Piné, R., Rull, A., Tomás-Menor, L., Vazquez-Martín, A., Alonso-Villaverde, C., Micol, V., Segura-Carretero, A. Xenohormetic and anti-aging activity of secoiridoid polyphenols present in extra virgin olive oil: A new family of gerosuppressant agents. **Cell Cycle 12**, 555-78. 2013.

11. Cufí, S., Bonavia, R., Vazquez-Martin, A., Corominas-Faja, B., Oliveras-Ferraros, C., Cuyàs, E., Martín-Castillo, B., Barrajón-Catalán, E., Visa, J., Segura-Carretero, A., Bosch-Barrera, J., Joven, J., Micol, V., Menendez, J.A. Silibinin meglumine, a water-soluble form of milk thistle silymarin, is an orally active anti-cancer agent that impedes the epithelial-to-mesenchymal transition (EMT) in EGFR-mutant non-small-cell lung carcinoma cells. **Food Chem. Toxicol. 60**. 360-8. 2013.

12. Vazquez-Martin, A., Cufí, S., Oliveras-Ferraros, C., Torres-Garcia, V.Z., Corominas-Faja, B., Cuyàs, E., Bonavia, R., Visa, J., Martin-Castillo, B., Barrajón-Catalán, E., Micol, V., Bosch-Barrera, J., Menéndez, J.A. IGF-1R/epithelial-to-mesenchymal transition (EMT) crosstalk suppresses the erlotinib-sensitizing effect of EGFR exon 19 deletion mutations. **Nature Sci. Rep. 3,** 2560. 2013.

13. Vazquez-Martin, A., Cufí, S., Oliveras-Ferraros, C., Torres-Garcia, V.Z., Corominas-Faja, B., Cuyàs, E., Bonavia, R., Visa, J., Martin-Castillo, B., Barrajón-Catalán, E., Micol, V., Bosch-Barrera, J., Menendez, J,A. Silibinin suppresses EMT-driven erlotinib resistance by reversing the high *miR-21*/low *miR-200c* signature *in vivo.* **Nature Sci. Rep. 3**, 2459. 2013.

14. Corominas-Faja, B., Oliveras-Ferraros, C., Cuyàs, E., Segura-Carretero, A., Joven, J., Martin-Castillo, B., Barrajón-Catalán, E., Micol, V., Bosch-Barrera, J., Menendez, J.A. Stem cell-like ALDH^{bright} cellular states in EGFR-mutant non-small cell lung cancer: A novel mechanism of acquired resistance to erlotinib targetable with the natural polyphenol silibinin. **Cell Cycle 12**, 3390-404**.** 2013.

15. Catania, A., Barrajón-Catalán, E., Nicolosi, S., Cicirata, F., Micol V. Immunoliposome encapsulation increases cytotoxic activity and selectivity of curcumin and resveratrol against HER2 overexpressing human breast cancer cells. **Breast Cancer Res. Treat. 141**, 55-65. 2013.

16. García-Hernández, V.M., Gallar, M., Sánchez-Soriano, J., Micol, V., Roche, E., García-García, E. Effect of omega-3 dietary supplements with different oxidation levels in the lipidic profile of women: a randomized controlled trial. **Int. J. Food Sci. Nutr. 64**, 993-1000. 2013.

17. Andreu-Sevilla, A.J., Mena, P., Martí, N., García-Viguera, C., Carbonell-Barrachina, A.A. Volatile composition and descriptive sensory analysis of pomegranate juice and wine. **Food Res. Int. 54,** 246-254. 2013.

18. Giner, M.J., Hizarci, Õ., Marti, N., Saura, D., Valero, M. Novel approaches to reduce brown pigment formation and color changes in thermal pasteurized tomato juice. Eur. **Food Res. Technol. 236**, 507-515. 2013.

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20. Mena, P., Marti, N., Saura, D., Valero, M. Approaches to understanding the contribution of anthocyanins to the antioxidant capacity of pasteurizad pomegranate juices. **Food Chem. 141,** 1630-1636. 2013.

21. Vegara, S., Martí, N., Lorente, J., Coll, L., Streitenbergerc, S., Valero, M., Saura, D. Chemical guide parameters for Punica granatum cv. 'Mollar' fruit juices processed at industrial scale. **Food Chem. 147,** 203-208. 2013.

22. Mena, P., Marti, N., Saura, D., Valero, M. Effect of pasteurization process and storage on color and shelf-life of pomegranate juice. **LWT-Food Sci. Technol. 54,** 592-596. 2013.

PATENTS

Inventores: Laura Tomás, Enrique Barrajón, Juan Carlos Rodríguez, María Aznar, Nuria Martí, Domingo Saura, Vicente Micol
Titulo: Combinación sinérgica de polifenoles con actividad antibiótica eficaz frente a cepas bacterianas resistentes a antibióticos
Titular: Mitra Sol Technologies, S.L. - UMH
Registros: P2013-01181 (11/12/2013)

Inventores: Domingo Saura, Nuria Martí, Nieves Muñoz, Vicente Micol, Lorena Funes, Salud Vegara, Galina Ignatieva, Enrique Barrajón, Manuel Valero, Pedro Mena, Rafael Martínez, Mª Remedios Berenguer, Eva González.
Titulo: Aplicación industrial de la tecnología de expansión súbita en la obtención de zumo de caqui turbio.
Titular: Mitra Sol Technologies, S.L. - UMH
Registros: P2013-01182 (11/12/2013)

Inventores: Domingo Saura, Nuria Martí, Vicente Micol, Lorena Funes, Salud Vegara, Galina Ignatieva, Enrique Barrajón, Manuel Valero, Pedro Mena, Rafael Martínez, Mª Remedios Berenguer, Miguel Moliner.
Titulo: Método de producción de pectina modificada de cítricos
Titular: Mitra Sol Technologies, S.L. - UMH
Registros: P2013-01183 (11/12/2013)

Inventores: Galina Ignatieva, Domingo Saura, Nuria Martí, Vicente Micol, Salud Vegara, Enrique Barrajón, Manuel Valero, Pedro Mena, Rafael Martínez, Mª Remedios Berenguer, Miguel Moliner.
Titulo: Método de fabricación de pectina acromática normalizada

Titular: Mitra Sol Technologies, S.L. - UMH
Registros: P2013-01184 (11/12/2013)

Inventores: Nieves Muñoz, Nuria Martí, Domingo Saura, Vicente Micol, Lorena Funes, Salud Vegara, Enrique Barrajón, Manuel Valero, Pedro Mena, Rafael Martínez, Mª Remedios Berenguer.
Titulo: Tratamiento de zumos de frutas con resinas adsorbente para reducir el nivel de pesticidas
Titular: Mitra Sol Technologies, S.L. - UMH
Registros: P2013-01185 (11/12/2013)

Inventores: Nieves Muñoz, Nuria Martí, Domingo Saura, Vicente Micol, Lorena Funes, Salud Vegara, Enrique Barrajón, Manuel Valero, Pedro Mena, Rafael Martínez, Mª Remedios Berenguer.
Titulo: Tratamiento de cítricos con ultrasonido para reducir el nivel de pesticidas con recirculación del agua de lavado.
Titular: Mitra Sol Technologies, S.L. - UMH
Registros: P2013-01186 (11/12/2013)

Inventores: Nuria Martí, Domingo Saura, Pedro Mena, Vicente Micol, Manuel Valero, Rafael Martínez, Salud Vegara, Lorena Funes, Enrique Barrajón, Cristina García.
Titulo: Combinación sinérgica de flavonoides y Vit C
Titular: Mitra Sol Technologies, S.L. - UMH
Registros: ES2013-00578 (05/06/2013)

Inventores: Nuria Martí, Domingo Saura, Vicente Micol, Salud Vegara, Enrique Barrajón, Manuel Valero, Rafael Martínez, Mª Remedios Berenguer, Eulalio Bernat.
Titulo: Equipo de expansión instantánea a vacío y ultrasonidos.
Titular: Mitra Sol Tecnologies, S.L. - UMH
Registros: PCT/ES2013/000191 (08/08/2013)

Group name:

DRUG DESIGN ON THERMOTRPs AND PAIN SIGNALLING

Our group is interested in understanding the cellular and molecular basis underlying pain transduction in the peripheral nervous system, and to use this knowledge to design and validate novel therapeutic strategies for pain control. Our research is hypothesis-based and combines cellular and molecular approaches, using from animal models to purified proteins. Identification of the signalplexes involved in sensory and pain transduction allows us to identify new druggable targets that enter our drug discovery program for hit identification. To refine lead development, we are also interested in unveiling the protein structure of the selected targets, mostly thermoreceptor channels (thermoTRPs). This information is essential for accelerating the identification and development of lead compounds. Complementarily, we also characterize the biophysics of channel activity to further understand how ion channels work in terms of their underlying protein structure and the antagonists modulate their activity.

STAFF

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POSTDOCTORAL FELLOWS

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Sakthikumar Mathivanan
Christoph Wolf Jakob
Susana Quirce

TECHNICIANS

Efren Lucas Mañogil
Gema Osuna Tenorio
Antonio Manuel Zafra Pinto

PUBLICATIONS

1. Devesa, I., Fernández-Ballester, G., Ferrer-Montiel, A. Targeting protein-protein interactions to rescue ΔF508-CFTR: a novel corrector approach to treat cystic fibrosis. **EMBO Mol. Med. 5**, 1462-4. 2013.

2. Martínez-Mármol, R. Pérez-Verdaguer, M., Roig, S.R., Vallejo-Gracia, A., Gotsi, P., Serrano-Albarrás, A., Bahamonde, M.I., Ferrer-Montiel, A., Fernández-Ballester, G., Comes, N., Felipe, A. A non-canonical di-acidic signal at the C-terminal of Kv1.3 determines anterograde trafficking and surface expression. **J. Cell Sci. 126**, 5681-5691. 2013.

3. Poveda, J.A., Giudici, A.M., Renart, M.L., Molina, M.L., Montoya, E., Fernandez, A.M., Fernandez-Ballester, G., Encinar, J.A., Gonzalez-Ros, J.M. Lipid modulation of ion channels through specific binding sites. **Biochim. Biophys Acta 1838**, 1560-1567 2013.

4. Giudici, A.M., Molina, M.L., Ayal, J.L., Montoya, E., Renart, M.L., Fernández, A.M., Encinar, J.A., Ferrer-Montiel, A.V., Poveda, J.A., Gonzalez-Ros, J.M. Detergent-labile, supramolecular assemblies of KcsA: Relative abundance and interactions involved. **Biochim. Biophys Acta 1828**, 193-200. 2013

5. Camprubi-Robles, M., Mair, N., Andratsch, M., Benetti, C., Beroukas, D., Rukwied, R., Langeslag, M., Proia, R.L., Schmelz, M., Ferrer-Montiel, A.V., Haberberger, R.V., Kress, M. Sphingosine-1-phosphate induced nociceptr excitation and ongoing pain behaviour in mice and humans is largely mediated by S1P3 receptor. **J. Neurosci. 33**, 2582-2592. 2013.

6. Belghiti, M., Estéves-Herrera, J., Giménez-Garzo, C., González-Usano, I., Ferrer-Montiel, A., Felipo, V., Planells-Cases R. Potentiation of TRPV1 receptor activity contributes to pruritogenesis and thermal hypersensitivity in a rat model of chronic liver failure. **J. Biol. Chem. 288**, 9675-9685. 2013.

7. Pérez-Faginas, P., Aranda, M.T., García-López, M.T., Infantes, L., Fernández-Carvajal, A., González-Ros, J.M., Ferrer-Montiel, A., González-Muñiz, R. Highly functionalized β,γ–diamino compounds through reductive amination of amino acid-derived β–keto esters. **PLoS One 8**, e53231. 2013.

8. Bavassano, C., Marvaldi, L., Langeslag, M., Sarg, B., Lidner, H., Klimaschewski, L., Kress, M., Ferrer-Montiel, A. Knaus, H-G. Identification of voltage-gated K+ channel beta subunit 2 (Kvβ2) as a novel interaction partner of the pain transducer Transient Receptor Potential vanilloid 1 channel (TRPV1). **Biochim. Biophys Acta - Cell Research 1833**, 3166-3175. 2013.

9. Babakinejad, B., Jönsson, P., López-Córdoba, A., Actis, P., Nova, P., Takahashi, Y., Shevchuk, A., Anand, U., Anand, P., Drews, A., Ferrer-Montiel, A., Klenerman, D., and Korchev, Y.E. Modelling and Experimentally Verifying Voltage- and Pressure-Driven Delivery of Molecules from a Nanopipette. **Anal. Chem. 85**, 9333-9342. 2013.

PATENTS

Inventores: Ferrer Montiel, Antonio; Fernandez Ballester, Gregorio; Garcia Anton, Jose Maria; Carreno Serraima, Cristina; Alminana Domenech, Nuria; Delgado Gonzalez, Raquel
Titulo: Compounds which inhibit neuronal exocytosis.
Titular: Lipotec, S.A. (EP2013/057656; EP2013/057658; EP2013/057674)
Registros: WO2013153196 (A1) — 2013-10-17 // WO2013153192 (A1) — 2013-10-17 // WO2013153191 (A1) — 2013-10-17 // EP2649984 (A1) — 2013-10-16

Antiviral Strategies

Group name:

ANTIVIRAL STRATEGIES

The group of Virology at the IBMC was established fourteen years ago. The group members have proven expertise over 20 years in the field of viral diseases of fish in aquaculture. The group's interest is focused on the study of viruses, fish immune response related to virus infections and antiviral strategies for disease prevention and treatment:

- Study of the early steps of rhabdovirus infections.
- Design of new antivirals using combinatorial chemistry or molecules related to the innate immune response such as AMPs (antimicrobial peptides).
- Development of environmentally friendly DNA vaccines. Characterization of the immune response induced by DNA vaccines using genomic and proteomic approaches (microarrays) to determine the molecular bases of protection conferred by these vaccines.

STAFF

Amparo Estepa Pérez

Luis Pérez García-Estañ

POSTDOCTORAL FELLOWS

Mº Del Mar Ortega-Villaizan

Ph.D STUDENTS

Alicia Martinez-López

Pablo García-Valtanen

Regla María Medina Gali

TECHNICIANS

Beatriz Bonmatí

PUBLICATIONS

1. Boltaña, S., Rey, S., Roher, N., Vargas, R., Huerta, M., Huntingford, F.A., Goetz, F.W., Moore, J., Garcia-Valtanen, P., Estepa, A., Mackenzie, S. Behavioural fever is a synergic signal amplifying the innate immune response. **Proc. Biol. Sci. 280**, 20131381. 2013
2. Encinas, P., Garcia-Valtanen, P., Chinchilla, B., Gomez-Casado, E., Estepa, A., Coll, J. Identification of multipath genes differentially expressed in pathway-targeted

microarrays in zebrafish infected and surviving spring viremia carp virus (SVCV) suggest preventive drug candidates. **PLoS One 8**, e73553. 2103.

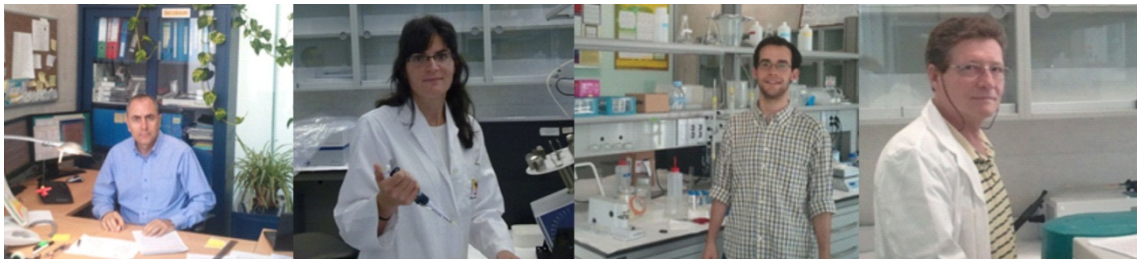
3. Martinez-Lopez, A., Encinas, P., García-Valtanen, P., Gomez-Casado, E., Coll, J.M., Estepa, A. Improving the safety of viral DNA vaccines: development of vectors containing both 5 and 3 homologous regulatory sequences. **Appl. Microbiol. Biotechnol. 97,** 3007-16. 2103.
4. Chinchilla, B., Encinas, P., Estepa, A., Coll, J., Gomez-Casado, E. Optimization of fixed-permeabilized cell monolayers for high throughput micro-neutralizing antibody assays: application to the zebrafish/viral hemorrhagic septicemia virus (vhsv) model. **J. Virol. Methods 193,** 627-632. 2103.
5. Jurado, M.T., García-Valtanen, P., Estepa, A., Perez, L. Antiviral activity produced by an IPNV-carrier EPC cell culture confers resistance to VHSV infection. **Vet. Microbiol. 166**, 412-418. 2013.
6. Chinchilla, B., Gomez-Casado, E., Encinas, P., Falco, A., Estepa, A., Coll, J. In Vitro Neutralization of Viral Hemorrhagic Septicemia Virus by plasma from innunized zebrafish. **Zebrafish 10,** 43-51. 2013.
7. Martinez-Lopez, A., García-Valtanen, P., Ortega-Villaizan, M.M., Chico, V., Medina-Gali, R.M., Perez, L., Coll, J., Estepa, A. Increasing Versatility of the DNA Vaccines through Modification of the Subcellular Location of Plasmid-Encoded Antigen Expression in the In Vivo Transfected Cells. **PLoS One 8**, e77426. 2013.
8. Falco, A., Barrajón-Catalán, E., Menéndez-Gutiérrez, M.P., Coll, J., Micol, V., Estepa, A., Melittin-loaded immunoliposomes against viral surface proteins, a new approach to antiviral therapy. **Antiviral Res. 97**, 218-21. 2013.
9. Mallavia R., Martinez-Tomé, M.J., Vázquez-Guilló, R., Estepa, A., Mateo, C. R. Stabilization of neutral Polyfluorenein aqueous solution through their interaction with phospholipids and sol-gel encapsulation. **ACS App. Mater. Interfaces 5**, 2952-2958. 2013.
10. Martinez-Lopez A, Encinar JA, Medina-Gali RM, Balseiro P, Garcia-Valtanen P, Figueras A, Novoa B, Estepa A. pH-dependent solution structure and activity of the host-defense peptide myticin C (Myt C) from the mussel Mytilus galloprovincialis. **Mar. Drugs**. 11, 2328-2346. 2013.

PATENTS

Inventores:	Amparo Estepa y Alicia Martinez Lopez
Título:	Vacuna DNA recombinante frente al virus de la septicemia hemorrágica vírica
Titular:	UMH (100%)
Nº de solicitud:	201331272. (23/08/2013)

Group name:

ENVELOPED VIRUSES. BIOMEMBRANES, PROTEINS AND DESIGN ON NOVEL ANTIVIRALS



Our research group aims the understanding of the structure and interaction of peptides derived from the structural and non-structural proteins from enveloped viruses, such as Hepatitis C (HCV) and Dengue (DENV) viruses in order to screen virus protein-derived peptide libraries in order to identify their membranotropic determinants, characterize their membrane interaction in structural terms, study the structure of the membranotropic segments, compare the HCV and DENV data and obtain a detailed presentation of the interaction, modulation and structure of these peptide segments with membranes. For our experimental approach we use infrared spectroscopy, steady-state and time-resolved fluorescence, differential scanning calorimetry, atomic force microscopy, solid-state nuclear magnetic resonance and molecular dynamics which provide us with an exhaustive information of the structure of the proteins and peptides, their location, arrangement and dynamics in the membrane, the specific interaction with the different lipids of the membrane and modulation of lipid polymorphism. All the information gathered should provide valuable insights to find therapeutic targets which will give place to new leading compounds useful for improved anti-viral combined therapies.

STAFF

José Villalaín Boullón

Ph.D STUDENTS

María Francisca Palomares Jerez

Henrique Nemesio Castro

TECHNICIANS

Miguel Ramos Baddouh

PUBLICATIONS

1. Nemésio, H., Palomares-Jerez, M.F., Villalaín, J. Hydrophobic segment of dengue virus C protein. Interaction with model membranes. **Mol. Membr. Biol. 30**, 273-87. 2013
2. Palomares-Jerez MF, Nemesio H, Franquelim HG, Castanho MA, Villalaín J. N-terminal AH2 segment of protein NS4B from hepatitis C virus. Binding to and interaction with model biomembranes. **Biochim. Biophys. Acta. 1828**, 1938-52. 2013

Molecular and Cellular Oncology

Group name:

MOLECULAR AND CELLULAR ONCOLOGY

Our group is focused on the emergence of chemoresistance to anti-cancer drugs by studying molecular changes associated with the acquisition and development of chemoresistance, examining the interlinkages between chemoresistance, apoptosis and differentiation in tumor cells. This problem is addressed from different complementary approaches:

- Search for alternative therapeutic strategies through the study of the mechanisms that regulate the expression of proteins associated to the chemoresistance phenotype both at the transcriptional and post-transcriptional level. This approach includes studies on the use of inhibitors of signal transduction pathways initiated by HER receptors, IGFR and PDGFR in glioblastoma, pancreatic exocrine carcinoma and colorectal carcinoma.
- A second line of work includes the characterization of the action mechanisms of histone deacetylases inhibitors in cancer cell lines and primary cultures obtained from tumors excised of cancer patients.
- The third research line is dedicated to explore the anticancer activity of drugs and natural products in parental tumor cells and chemoresistant tumor cells.

A complementary aspect of this group focuses on the extensive use of Genomics and Proteomics to determine markers of susceptibility and/or resistance allowing individualized treatment of patients with cancer. This research has a high translational potential and has facilitated the establishment of close relationships with private companies involved in the financial support of these studies.

STAFF

José Antonio Ferragut Rodríguez

Miguel Saceda Sánchez

Mª Isabel Martínez-Lacaci Fortuny

Mª Pilar García Morales

POSTDOCTORAL FELLOWS

Trinidad Mata Balaguer

Ph.D STUDENTS

Estefanía Carrasco García
Silvina Grasso Cicala
Lourdes Rocamora Reverte
Leticia Mayor López
Elena Tristante Barrenechea

TECHNICIANS

Ángeles Gómez Martínez

PUBLICATIONS

1. Valdés, A., García-Cañas, V., Rocamora-Reverte, L., Gómez-Martínez, A., Ferragut, J.A., Cifuentes, A. Effects of Rosemary polyphenols on human cáncer cells: transcriptomic profiling and functional enrichment analysis. **Genes Nutr. 8**, 43-60. 2013.

4. Other activities

PhD THESES (2011-2013)

"Cooperation between potassium channels and gap junctions: interaction between Kv1.1 channel and pannexin1. **Veronica Carmen Corsaro"**. Supervisors: Federico Cicirata and Asia Fernandez, 24 February 2012.

"Enhancement of efficacy and selectivity of chemopreventive compounds in human breast cancer cells by using immunoliposomes". **Angela Catania**. Supervisors: Federico Cicirata and Vicente Micol, 24 February 2012.

"Inhibición de receptores celulares de tipo tirosina quinasa como estrategia terapéutica contra el Glioblastoma Multiforme". **Estefanía Carrasco García**. Supervisors: Isabel Martínez Lacaci and Miguel Saceda, 5 October 2012.

"Estudios de interacciones macromoleculares en el diseño de antivirales y antibióticos". **Rosa Mª Domenech Mata**. Supervisors: José Luis Neira, 16 November 2012.

"Estudio del efecto de los inhibidores de la bomba de protones sobre la capacidad bactericida celular en pacientes cirróticos con ascitis". **Irma García Martínez**. Supervisors: Rubén Francés Guarinos and José Francisco Such Ronda, 13 December 2012.

"Caracterización biofísica de las regiones membranotrópicas de las proteínas no estructurales NS5A y NS4B del virus de la Hepatitis C". **Francisca Palomares Jerez**, Supervisor: José Villalaín, 14 December 2012.

"New phytopharmaceutical anti-breast cancer formulations: immunoliposomes containing extra virgin olive oil polyphenols". **Silvia Nicolosi**. Supervisors: Federico Cicirata and Vicente Micol, 2 February 2013

"Development of systems for protein immobilization. Biotechnological applications". **Daniel Bello-Gil**. Supervisor: Jesús M. Sanz, 21 June 2013.

"Valor pronóstico de los niveles de expresión del ARNm de osteopontina en inmunofenotipos de cáncer de mama". **Fernando Ortiz Martínez**. Supervisor: Gloria Peiró Cabrera, 22 February 2013.

"Efecto de agentes diferenciadores y compuestos de origen natural y sintético sobre líneas tumorales de origen humano". **Lourdes Rocamora Reverte**. Supervisor: Jose A. Ferragut, 22 February 2013.

"Obtención y análisis de nuevos alimentos, ricos en fitoquímicos bioactivos, a partir de la granada (púnica granatum L.)". **Pedro Miguel Mena Parreño**. Supervisor: Nuria Martí and Cristina García Viguera, 6 junio 2013.

"TRPV1 structure-function study: role of the TRP domain in TRPV1 allosteric gating". **Lucia Gregorio Teruel**. Supervisor: Antonio Ferrer, 17 December 2013.

SCIENCE COMMUNICATION

Organization of meetings

Elche, Spain, July 12, 2013
JORNADA SOBRE MECANISMOS DE FINANCIACIÓN DE TRANSFERENCIA DE TECNOLOGÍA
- **Jesús M. Sanz.** Chairman and coordinator

Palma de Mallorca, Spain, October, 2013
4th ITALIAN-SPANISH-PORTUGUESE WORSHOP IN BIOPHYSICS AND MOLECULAR BIOLOGY OF ION CHANNELS AND TRANSPORTERS.
- **A. Ferrer.** Co-organizer

Vigo, Spain, September 14, 2013
INTERNATIONAL CONFERENCE ON FISH INMUNOLOGY.
- **Estepa.** Member of Scientific Committee and co-organizer

Invited talks and courses

Cuenca, España. February 11-13, 2013.
RECI IV: New horizons in ion channel research.
- **A. Fernández-Carvajal**. "High-throughput screening assays for the identification of compounds targeting ion channels". Ponencia Invitada.

Barcelona, Spain, April 2013.
Almirall Pharma.
- **A. Ferrer**. "*Modulation of thermoTRP channels*".

Pamplona, Spain, May 2013.
CIMA.
- **A. Ferrer**. "*Novel Paradigms modulating ion channel signalling*".

Bilbao, Spain, June 2013.
UBF Retreat
- **A. Ferrer**. "*A TR(i)P to pain transduction*".

Turin, Italia, October 2013.
Congreso Nazionalle de la Società Italiana di Farmacologia.
- **A. Ferrer**. "*Thermo-TRP inhibition: novel strategies to treat pain and more*".

Science dissemination: outreach activities

II Jornada "Ciencia con Tapas". Taberna el Granero (Elche, Alicante), March 21, 2013.
- **A. Ferrer, V. Micol, E. Guillén.** "Productos naturales y nutracéuticos: mitos y verdades ".

II Jornada Científica difusión actividades del IBMC. Edificio Altabix, Universidad Miguel Hernández de Elche (Alicante), July 19, 2013
- **V. Micol, J.A. Poveda, C.R. Mateo, N. Martí, J. Gómez, M.J. Martínez-Tomé, A. Ferrer.**

Bodegas Casa Sicilia, September 18, 2013
Actividad para la difusión científica del IBMC.
- **N. Martí.** "Ciencia entre vinos. Conoce los vinos de Alicante y sus particularidades".

Centro Cultural Virgen de Carmen, Torrevieja, Alicante, Spain, November 19, 2013
II Ciclo de Divulgación Científica. Semana de la Ciencia (MICINN). A. C. Ars Creatio.

- **V. Micol.** "Polifenoles de extractos vegetales: ¿fármacos naturales polifuncionales?"

III Jornada "Ciencia con Tapas". Taberna el Granero (Elche, Alicante), November 20, 2013.

- **A. Ferrer, E. Roche, A. Aracil.** "Medicina y Nutrición Deportiva: mitos y verdades ".

Free Communications

Total number of communications to congresses (oral or poster presentations):

- National: 16 (1 oral contribution)
- International: 47 (26 oral contributions)

GOVERNMENTAL PROJECTS AND FUNDING

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. "El canal de potasio KCSA: Un banco de pruebas para avanzar en el conocimiento de la estructura y función de canales iónicos y en el descubrimiento de nuevos fármacos." (BFU2011-25920; 2012-2014). IP: **J.M. González-Ros**.

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. "Inhibición de la agregación de proteínas por polielectrolitos de alta densidad de carga" (CTQ2011-24393, 2012-2014). IP: **J. Gómez.**

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. "Polielectrolitos conjugados multifuncionales y nanoestructurados como plataformas terapéuticas" (MAT2011-23007, 2012-2014). IP: **R. Mallavia.**

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. "Improvement of VHSV DNA vaccines and transference of knowledge to other fish species and viruses" (AGL2011-29857-C03-03; 2012-2014). IP: **A. Estepa.**

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. "Foodomics evaluation of dietary polyphenols against colon cancer using in-vitro and in-vivo model" (AGL2011-29857-C03-03; 2012-2014). IP: **V. Micol.**

Proyectos de Investigación Fundamental no Orientada 2012. Ministerio de Economía y Proyectos del Plan Nacional de I+D+i. ceptor sensitization" (BFU2012-39092-C02-01; 2013-2015). IP: **A. Ferrer**.

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2012. Ministerio de Economía y competitividad. "Vesiculas de origen vegetal (bróculi) para la protección y vehiculización de compuestos bioactivos en bebidas y formulaciones dermatologicas de granada" (AGL2012-40157-C02-02; 2013-2015). IP: **N. Martí.**

Proyectos del Plan Nacional de I+D+i. Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. "Desarrollo de nuevas aplicaciones de los modulos de unión a colina para la purificación e inmovilización de proteínas" (Ref: BFU2010-17824; 2011-2014). IP: **J. Sanz**

Proyectos Consolider del Plan Nacional 2012-2014. Ministerio de Educación y Ciencia. "The Spanish Ion Channel Initiative". IP: **J.M. González-Ros**.

Acciones Complementarias. Ministerio de Economía y Competitividad. "Red Nacional de Canales Iónicos (RECI)" (BFU2010-09945-E; 2010-2013). IP: **A. Ferrer**.

Subprograma CIBER. Instituto de Salud Carlos III (ISCIII). Spanish Ministry of Health. Fisiopatología de la Obesidad y la Nutrición, CIBERobn, Spain (CIBER: CB12/03/30038) Coordinator: J.A. Tur. Research Group Bioactive Compounds, University Miguel Hernández, Spain. IP: **V. Micol.**

Proyectos competitivos de subvención pública. 2013. Conselleria de Educacion, Formacion y Empleo de la GV. “Equipamiento para unidad de genómica y cultivos celulares.” IP: **A. Ferrer**.

Proyectos competitivos de subvención pública 2012-2013. Conselleria de Educación de la GV. “Plataforma de investigación en piel - SKIN RESEARCH PLATFORM (SRP).”. (01/01/2012-31/12/2013). IP: **A. Ferrer**.

Generalitat Valenciana. Programa PROMETEO para grupos de investigación de excelencia. “Fisiopatología Neurosensorial: mecanismos e intervención terapéutica” (PROMETEO/2010/046, 2010-2013). IP: **A. Ferrer**.

Generalitat Valenciana. Programa PROMETEO para grupos de investigación de excelencia. “Aumento de la actividad biológica y biodisponibilidad celular de polifenoles bioactivos mediante la utilización de nanopartículas” (PROMETEO/2012/007, 2012-2015). IP: **V. Micol.**

Generalitat Valenciana. Programa PROMETEO para grupos de investigación de excelencia. “Interacción proteína-polielectrolito: diseño racional de nuevas herramientas en la optimización de procesos biotecnológicos” (PROMETEO/2013/018, 2013-2016). IP: **J. Gómez.**

Ayuda complementaria al Proyecto de Investigación del Plan Nacional de I+D+i “Foodomics evaluation of dietary polyphenols against colon cancer using in-vitro and in-vivo models”. Consellería de Educación (GV). ACOMP/2013/093. (01/01/2013-31/12/2013). IP: **V. Micol.**

Proyecto Motriz de la Junta de Andalucía “Desarrollo de nuevas estrategias de desreplicación basadas en la correlacion entre datos espectrométricos y bioactividad para la identificación de compuestos bioactivos en extractos vegetales” (P09-CTS-4564) (03/02/2010-31/12/2013). IP: **V. Micol.**

Ayuda a la transferencia de Tecnología. Proyectos competitivos de subvención pública. Universidad Miguel Hernández (03/10/2013 - 31/12/2013). IP: **V. Micol.**

Programa de Proyectos I+D+i. Centro para el desarrollo Tecnológico Industrial (CDTI). Ministerio de Economía y Competitividad. "Investigación y Desarrollo de extractos botánicos ricos en polisacáridos para su uso como emolientes y demulcentes no grasos en productos de cosmética" (Ref: IDI-20120888). IP: **V. Micol.**

Programa de Proyectos I+D+i. Centro para el desarrollo Tecnológico Industrial (CDTI). Ministerio de Economía y Competitividad. "Obtención de un ingrediente funcional para el tratamiento y la prevención de la esteatosis hepática (hígado graso) con aplicaciones en los sectores alimentarios, nutracéutico y farmacéutico” (Ref: IDI-20120741). IP: **V. Micol.**

Generalitat Valenciana. Ayudas FEDER Enero 2013 para la adquisición o renovación de equipamiento científico-técnico para grupos de investigación e investigadores principales de proyectos de investigación (UMH). IP: **V. Micol.**

Programa Nacional de Cooperación Público-Privada. Subprograma de PROYECTOS INNPACTO. “New generation of bioactive dermatologic compounds produced in plant biofactories” (NANODERMOPLANT; Ref: IPT-2012-0608-010000) (10/10/2012-31/12/2014). IP: **A. Estepa.**

Instituto de Salud Carlos III. Búsqueda de marcadores de quimiorresistencia en lesiones invasivas de cáncer de colon y recto. IP: I. **Martínez-Lacaci.** (FIS PI10/01123; 2011-2014).

Instituto de Salud Carlos III. "Desarrollo de inhibidores de PTK6 como posibles nuevos agentes terapéuticos en cáncer. Evaluación de su potencialidad en modelos celulares de tumores de mama, páncreas y colon" (FIS PI12/02025; 2012-2015). IP: **M. Saceda.**

PRIVATE FUNDING

Contracts

Contrato para la realización del Proyecto titulado "Investigación y Desarrollo de extractos botánicos ricos en polisacáridos para su uso como emolientes y demulcentes no grasos en productos de cosmética". Funded by QUIMICAS DEL VINALOPO, SL (21/02/2013-28/02/2014). IP: **V. Micol.**

Contrato de apoyo tecnológico para la realización del proyecto titulado "Obtención de un ingrediente funcional para el tratamiento y la prevención de la esteatosis hepática (hígado graso) con aplicaciones en los sectores alimentarios, nutracéutico y farmacéutico". Funded by MONTELOEDER, SL (25/01/2013 – 31/03/2014). IP: **V. Micol.**

Contrato para empresas EBT de Licencia de Know-how para la obtención de compuestos con actividad biológica a partir de subproductos de la industria enológica. Funded by MITRA SOL TECHNOLOGIES, SL. (27/03/2013 – 26/03/2033). IP: **N. Martí.**

Contrato para la realización del trabajo "Control de calidad en el proceso de elaboración de vinos tranquilos y espumosos CASA SICILIA SL" (24/01/2013-31/12/2013). I.P. **N. Martí.**

Contrato para la realización del proyecto titulado "*In vitro* and *in vivo* characterization of the oncolytic and antimicrobial activities of the recombinant peptides identified in the *Rhopalurus junceus* scorpion venom". Funded by: LABIOFAM S.A. (La Habana, Cuba). (01/09/2012-31/10/2013). IP: **A. Estepa.**

Contrato para la realización del proyecto titulado "La actividad biologica del veneno del escorpión *Rhopalurus junceus*. Funded by LABIOFAM S.A. (La Habana, Cuba) (01/06/2013-31/12/2014). IP: **A. Estepa.**

Contrato para la realización del proyecto titulado "Identificación y Desarrollo De Productos Cosméticos". Funded by Diverdrugs, S.L.: DIVERDRUGS2.12D. Ref: ICDQ37. **IP: A. Ferrer**

Technical services and assistance

Contrato "Realización de actividades de asesoramiento para explotación y la comercialización de estimuladores de la expresión de defensinas. LIPOTEC (2009-2013). **A. Ferrer.**

Contrato "Realización de actividades de asesoramiento para la explotación y comercialización de compuestos reguladores de la pigmentación. LIPOTEC (2009-2013). **A. Ferrer.**

Contrato "Realización de actividades de asesoramiento para la explotación y comercialización de compuestos inhibidores de la colagenasa. LIPOTEC (2009-2013). **A. Ferrer.**

Contrato "Realización de actividades de asesoramiento para la explotación y comercialización de las encefalinas. LIPOTEC (2009-2013). **A. Ferrer.**

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