IBMC

TRIENNIAL REPORT 2010-2012

UNIVERSITAS Miguel Hernández de Elche

INSTITUTE OF MOLECULAR AND CELL BIOLOGY

UNIVERSITY "MIGUEL HERNÁNDEZ"

IBMC

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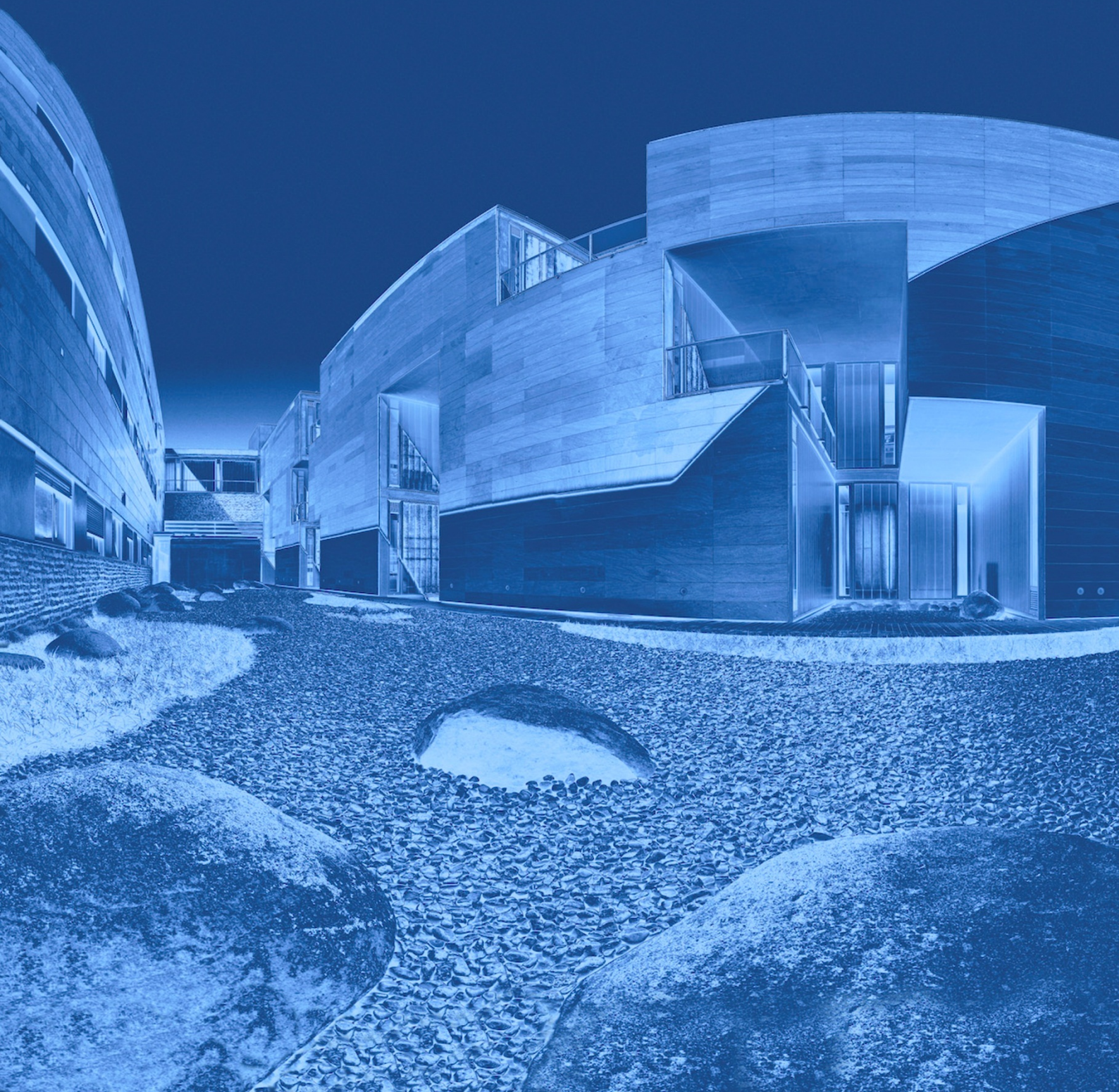
Institute of Molecular and Cell Biology



INSTITUTE OF MOLECULAR AND CELL BIOLOGY

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IBMC Triennial Report 2010-2012

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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 15 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 of Prof. González-Ros has been kept invariable and can be fully appreciated in the present triennial memory (2010-2012) that reports all our achievements in research, exploitation, training and dissemination activities.

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 have been created. 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, a Strategic Plan of Action has been approved by the Institute Council that establishes the objectives and milestones for the next 5 years (2013-2017), strengthening the original vision, and establishing as a central mission to consolidate our multidisciplinary program of translational excellence in the areas of biotechnology and health, serving as a channel for taking the interest in these areas closer to the productive sectors of our society. Undoubtedly, it is our commitment 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 which 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 article 12.5 a and b of the UMH 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.

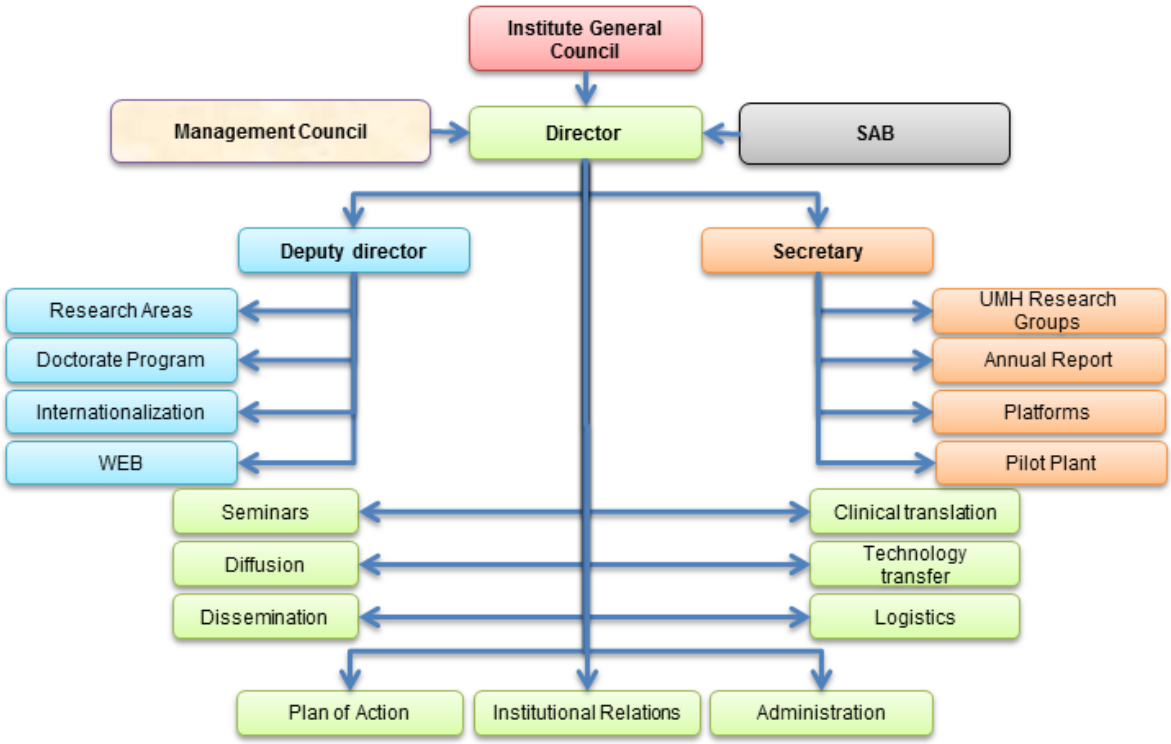

Figure 1. IBMC Functional Organigram.

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 three-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

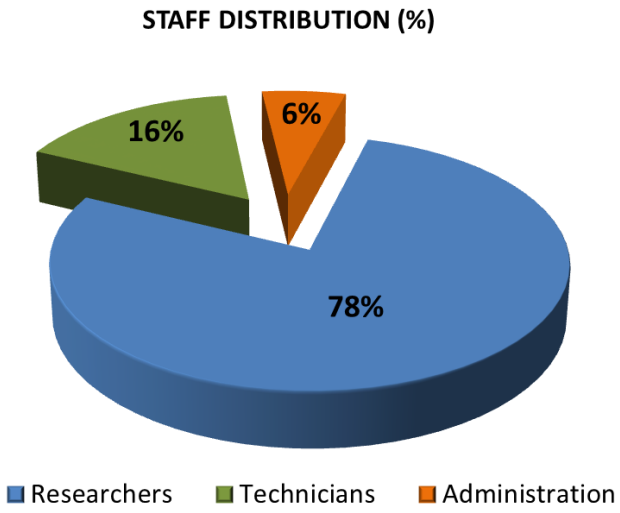

Figure 2. IBMC Staff distribution.

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 facilities and instruments are supervised by mid-level technical staff. The culture unit, analysis and chromatographic fractioning 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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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**	**TOTAL**
National P.	736.217	669.656	769.538	**2.175.411**
European P.	--	66.373	33.300	**99.673**
Autonomous Reg. P.	136.100	82.600	62.429	**281.129**
Foundations	186.937	--	--	**186.937**
Contracts	352.626	465.759	361.000	**1.179.385**
IBMC-Research Expenses	56.781	19.636	16.816	**93.233**
UMH – IBMC (cap.II)	65.637	43.372	34.258	**143.267**
TOTAL	**1.534.298**	**1.347.396**	**1.277.341**	**4.159.035**

It can be appreciated that during the last three years period, the IBMC has raised resources to an average of approximately **1.4 M€** per annum, mainly from the Ministry of Science's National Plan for R+D+i (**65%)** and contracts with companies (**23%**). These numbers indicate the high level of competitiveness of IBMC projects, as well as its capacity to attract private funding (Fig. 3).

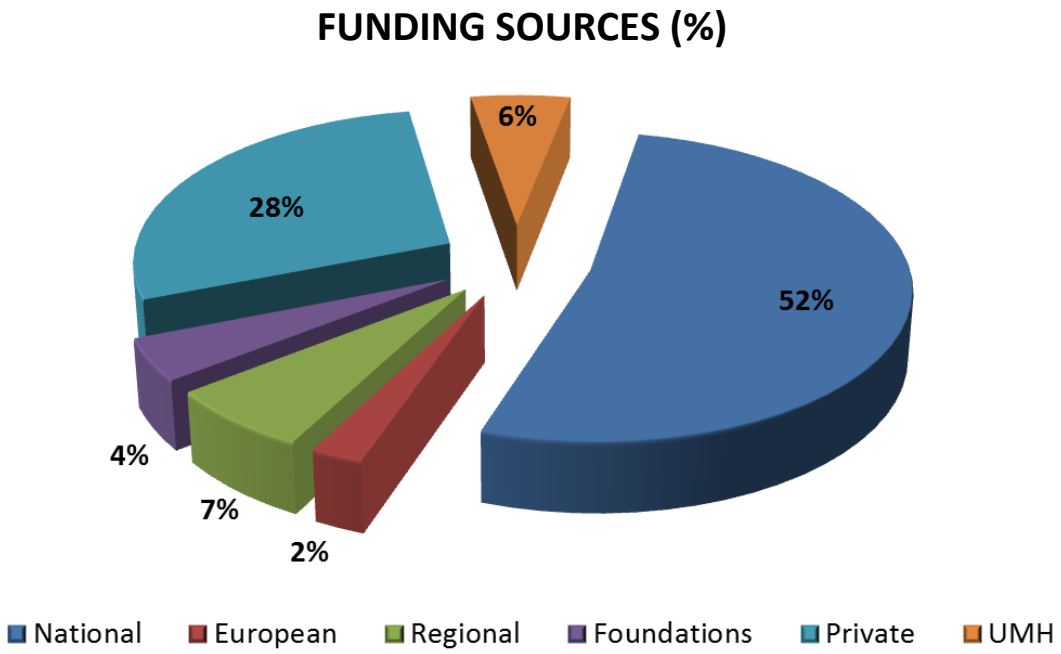


Figure 3. Distribution of IBMC funding sources

SCIENTIFIC PERFORMANCE

A detailed description of the scientific publications by the different research groups Institute during the 2010-2012 period is included later in this report. The analysis of the IBMC competitive position during the 2010-2012 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 three years period, IBMC researchers continued to publish a growing number of publications. Besides the number of articles, constant growth in the average impact index compared to last period should be highlighted, which 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 the arithmetic mean of the units of impact of articles published by the IBMC.

	2010	2011	2012	TOTAL
Nº of publications	**78**	**89**	**85**	**252**
Q1 Publications	38	50	52	**140**
Total Impact	255	284	297	**836**
Average Impact	3.6	3.5	3.2	**3.4**
Citations	1669	1734	1786	**5189**

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 (1998-2012)		
A.1. COLLABORATION ACTIVITIES WITH PRIVATE ENTERPRISES		
	Number	**Financing**
1. PETRI/TRACE Projects	3	212.780 €
2. R+D Contracts	65	4.808.587 €
3. Provision of services	22	67.780 €
A.2. PATENTS		
1. Applied for	29	
2. Extended via PCT	17	
3. Published with WO number	15	
4. Granted	10	
5. Licensed	12	
6. Exploitation	12	
7. Commercialized products	LyTag resin, LyTag2Phase, Argireline, Chromabright, Bodyfensin, Leuphasyl, Cartixan-4, Plx, Hypoxdermin, 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

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

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

B. TRANSLATIONAL ACTIVITIES (1998-2012)		
	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 (2007-2011) (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 (2010-2012).

Average performance (2010-2012)	
Thesis defended	9
Nº of students enrolled	19
Nº of Professors on the program	15
Thesis/ Professors average	0.6
Thesis/year average	3
Doctorate Excellence Awards	2
Nº publications deriving directly from thesis	38
Publications/thesis average	4.2

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.

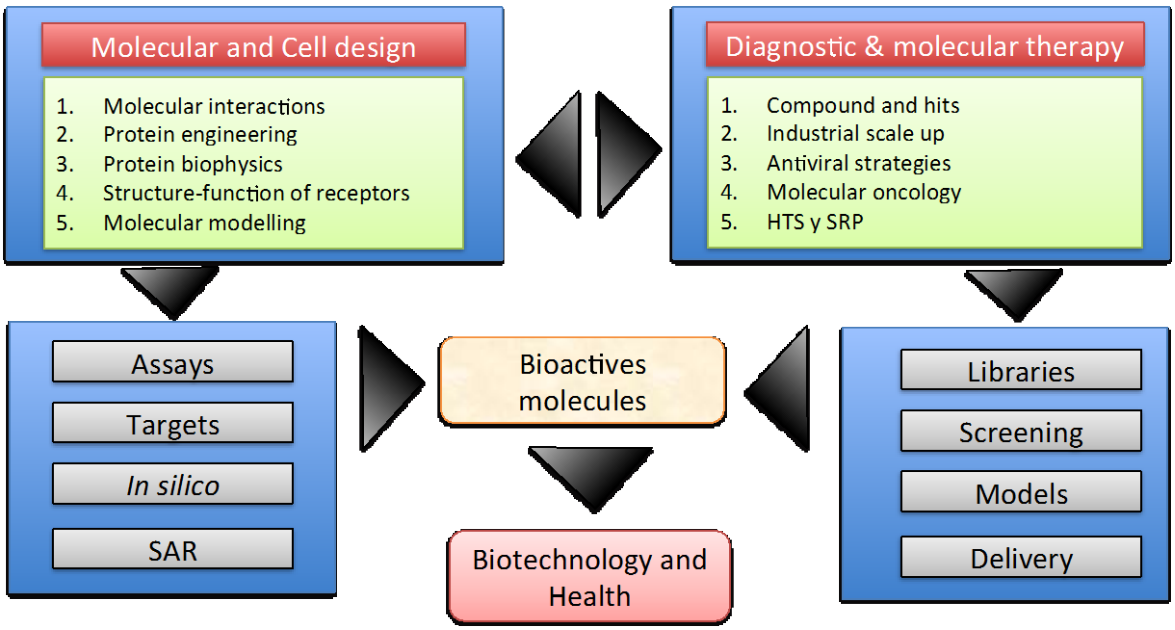
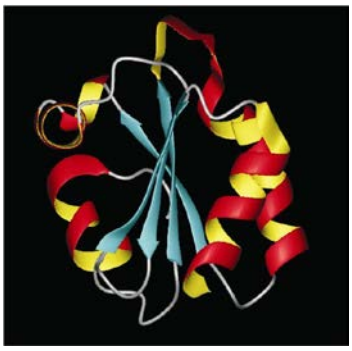


Figure 4. Organization of IBMC research areas

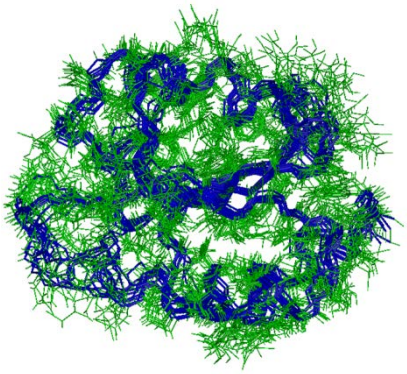
In scientific terms, the targets of these research areas of the IBMC are developed as follows:

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.

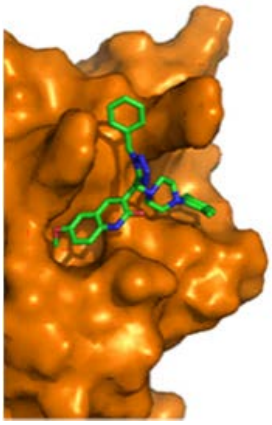


Both the composition of the different research groups that make up this line of research as its multidisciplinarity and flexibility to raise specific scientific goals fosters a high competitiveness, both in the uptake of competitive sources and scientific production, in the training of research personnel 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

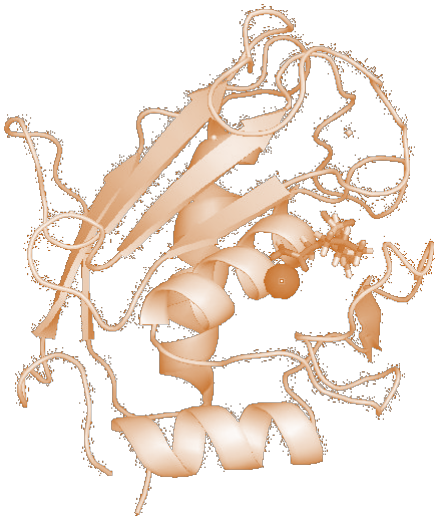
The Diagnosis and Molecular Therapy line seeks the identification and validation of molecular markers in human and animal pathologies of high prevalence, as well as the



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 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).

- Stopped-flow folding kinetics.

- Protein engineering.

- Nanobiotechnology.

STAFF

Jesús Miguel Sanz Morales

Ph.D STUDENTS

Daniel Bello Gil

Jennifer Fonseca Pupo (Visiting scientist)

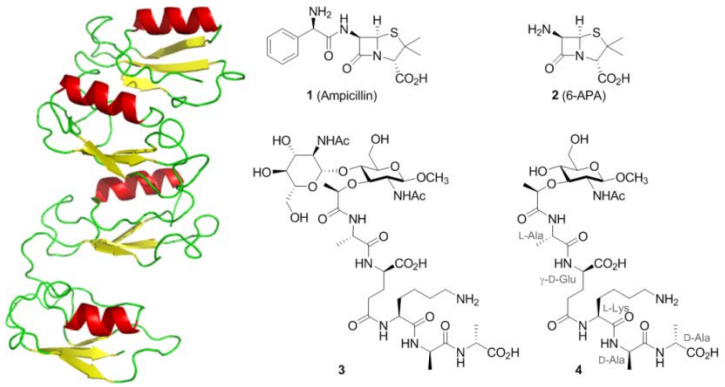
PUBLICATIONS

1. de Eugenio, L., Galán, B., Escapa, I.F., Maestro, B., Sanz, J.M., Garcia, J.L. and Prieto, M.A. The PhaD regulator controls the simultaneous expression of the pha genes involved in polyhydroxyalkanoate metabolism and turnover in Pseudomonas putida KT2442. **Environ. Microbiol. 12,** 1591-1603. 2010.
2. Maestro, B., Santiveri, C.M., Jimenez, M.A. and Sanz, J.M. Structural autonomy of a β-hairpin peptide derived from the pneumococcal choline-binding protein LytA. **Protein Eng. Des. Sel. 24**, 113-122. 2011.
3. Galán, B., Dijanksi, N., Maestro, B., De Eugenio, L.I., Escapa, I.F., Sanz, J.M., García, J.L and Prieto, M.A. Nucleoid-associated PhaF phasin drives intracellular location and segregation of polyhydroxyalkanoate granules in Pseudomonas putida KT2442. **Mol. Microbiol. 79**, 402- 418. 2011.
4. Maestro, B., Nováková, L., Hesek, D., Lee, M., Leyva, E., Mobashery, S, Sanz, J.M.* (Corresponding author) and Branny, P. Recognition of peptidoglycan and beta-lactam antibiotics by the extracellular domain of the Ser/Thr protein kinase StkP from Streptococcus pneumoniae. **FEBS Lett. 585**, 357- 363. 2011.
5. Hernández-Rocamora, V.M., Reulen, S.A.W., De Waal, B., Meijer, E.W., Sanz, J.M. and Merkx, M. Choline dendrimers as generic scaffolds for the non-covalent synthesis of multivalent protein assemblies. **Chem. Commun. 47**, 5997- 5999. 2011.
6. Rojas-Altuve, A., Carrasco-Lopez, C., Hernandez-Rocamora, V.M., Sanz, J.M. and Hermoso, J.A. Crystallization and preliminary X-ray diffraction studies of the transcriptional repressor PaaX, the main regulator of the phenylacetic acid degradation pathway in Escherichia coli W. **Acta Cryst. F.** 67, 1278-1280. 2011.

RESEARCH HIGHLIGHTS

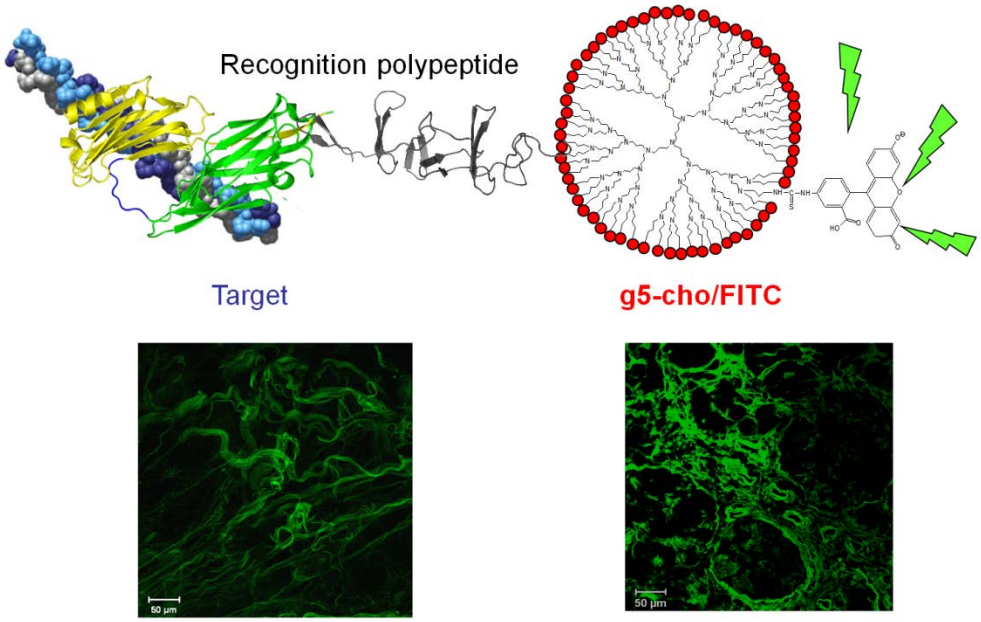
Recognition of peptidoglycan and beta-lactam antibiotics by the extracellular domain of the Ser/Thr protein kinase StkP from Streptococcus pneumoniae. Maestro, B., Nováková, L., Hesek, D., Lee, M., Leyva, E., Mobashery, S, Sanz, J.M.* (Corresponding author) and Branny, P. FEBS Lett. 585, 357- 363. 2011.

The eukaryotic-type StkP kinase is involved in the regulation of synthesis of many genes in Streptococcus pneumoniae. Here we describe, for the first time, that StkP is able to recognize small peptidoglycan fragments and beta-lactam molecules, leading to the hypothesis that nascent cell wall activates this kinase, and points to this protein as a novel target for the development of new beta-lactamic antibiotics.



Choline dendrimers as generic scaffolds for the non-covalent synthesis of multivalent protein assemblies. Hernández-Rocamora, V.M., Reulen, S.A.W., De Waal, B., Meijer, E.W., Sanz, J.M. and Merkx, M. . Chem. Commun. 47, 5997- 5999. 2011.

Multivalent display of choline molecules on the surface of fluorescently-labeled dendrimeric nanoparticles was used for the specific, strong immobilization of a collagen-binding protein fused to the C-LytA affinity tag. The outcome was the selective fluorescent labeling of collagen tissue preparations, which serves as a proof-of-principle for other similar detection procedures.



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. Pellicer, S, Bes, M.T., González, A., Neira, J.L., Peleato, M. L. and Fillat, M.F. High-recovery one-step purification of the DNA-binding protein Fur by mild guanidinium chloride treatment. Process. **Biochemistry 45**, 292-296. 2010.
2. Traverso, J., López-Jaramillo, F. J., Serrato, A. J., Ortega-Muñoz, M., Aguado-Llera, D., Sahrawy, M., Santoyo-González, F., Neira, J.L. and Chueca, A. Evidence of non-functional redundancy between two pea h-type thioredoxins by specificity and stability studies. **J. Plant Physiol. 167**, 423-429. 2010.
3. Neira, J.L. and Carbajo, R. J. The Bronze Age of science in Spain. **EMBO reports 11,** 12-3. 2010.
4. López-Redondo, M.L., Contreras, A., Marina, A. and Neira, J.L. The regulatory factor SipA is a highly stable beta-II class protein with a SH3 fold. **FEBS letters 584**, 989-994. 2010.
5. Aguado-Llera, D., Goormaghtigh, E., de Geest, n., Quan, X.-J., Prieto, A., Hassan, B., Gomez, J., Neira, J.L. The basic helix-loop-helix region of human neurogenin 1 is a monomeric natively unfolded protein which forms a “fuzzy” complex upon DNA binding. **Biochemistry 49,** 1577-1589. 2010.

6. Neira, J.L., Contreras, L.M., Ruiz de los Paños, O., Sánchez-Hidalgo, M., Martínez-Bueno, M., Maqueda, M., and Rico, M. Structural characterization of the natively unfolded enterocin EJ97. **Prot. Eng. Des. Sel. 23,** 507-518. 2010.

7. Romero-Beviar, M., Martínez-Rodríguez, S., Prieto, J., Goormaghtigh, E., Ariz, U., Martínez-Chantar, M. L., Gómez, J. and Neira, J.L. The N-terminal domain of the enzyme I is a monomeric well-folded protein with a low conformational stability and residual structure in the unfolded state. **Prot. Eng. Des. Sel. 23**, 729-742. 2010.

8. Domenech, R., Abian, O., Bocanegra, R., Correa, J., Sousa-Herves, A., Riguera, R., Mateu, M., Fernandez-Megia, E., Velazquez-Campoy, A., and Neira, J.L. Dendrimers as potential inhibitors of the dimerization of the capsid protein of hiv-1. **Biomacromolecules 11**, 2069-2078. 2010.

9. Bravo, J., and Neira, J.L. Folding and unfolding of proteins involved in pancreatic cancer: a layman's guide. **Sci. World J. 10,** 1612-1633. 2010.

10. Iovanna, J., and Neira, J.L. Pancreatic cancer: molecular, biochemical, chemopreventive and therapeutical aspects. **Sci. World J. 10**, 1967-1970. 2010.

11. Cebrián, R., Maqueda, M., Neira, J.L., Valdivia, E., Martínez-Bueno, M. and Montalbán-López, M. Insights into the funcionality of the putative residues involved in enterocin AS-48 maturation. **Appl. Environ. Microbiol 76**, 7268-7276. 2010.

12. Aguado-Llera, D., Oyenarte, I., Martínez-Cruz, L.A. and Neira. J.L. The CBS domain protein MJ0729 of Methanocaldococcus jannaschii binds DNA. **FEBS Letters 584**, 4485-4489. 2010.

13. Abian, O., Vega, S., Neira, J.L. and Velázquez-Campoy, A. Conformational stability of hepatitis c virus NS3 protease. **Biophys. J. 99** 3811- 3820. 2010.

14. Martínez-Cruz, L.A., Encinar, J.A., Sevilla, P., Oyenarte, I., Gómez-García, I., Aguado-Llera, D., García-Blanco, F., Gómez, J. and Neira, J.L. Nucleotide-induced conformational transitions in the CBS domain protein MJ0729 of Methanocaldococcus jannaschii. **Prot. Eng. Des. Sel. 24**, 161-169. 2011.

15. Aguado-Llera, D., Martínez-Gómez, A. I., Prieto, J., Marenchino, M., Traverso, J. Gómez, J., Chueca, A. and Neira, J.L. The conformational stability and biophysical properties of the eukaryotic thioredoxins of *pisum sativum* are not family-conserved. **PLOS One**, e17068. 2011.

16. Soriano-Maldonado, P., Martínez-Gómez, A.I., Andújar-Sánchez, M., Neira, J.L., Clemente-Jiménez, J.M., las Heras-Vázquez, F.J., Rodríguez-Vico, F. and Martínez-Rodríguez, S. Biochemical and mutational studies of the Bacillus cereus CECT 5050T formamidase support the existence of a C-E-E-K tetrad in several members of the nitrilase superfamily of the nitrilase superfamily. **Appl. Environ. Microbiol**. **77**, 5761-5769. 2011.

17. Martínez-Gómez, A.I., Andújar-Sánchez, M., Clemente-Jiménez, J.M., Neira, J.L., Rodríguez-Vico, F., Martínez-Rodríguez, S. and las Heras-Vázquez, F.J. N-Carbamoyl-β-alanine amidohydrolase from Agrobacterium tumefaciens C58: a promiscuous enzyme for the production of amino acids. **J. Chromatogr. B Analyt. Technol. Biomed. Life Sci**. **879**, 3277-3282. 2011.

18. Doménech, R., Bocanegra, R., Velázquez-Campoy, A. and Neira, J.L. The isolated major homology region of the HIV capsid protein is mainly unfolded in solution and binds to the intact protein. **Biochim. Biophys. Acta 1814**, 1269-1278. 2011.

19. Doménech, R., Bocanegra, R., González-Muñiz, R., Gómez, J., Mateu, M.G. and Neira, J.L. Larger helical populations in peptides derived from the dimerization helix of the

capsid protein of HIV-1 results in peptide binding toward regions other than the "hotspot" interface. **Biomacromolecules 12**, 3252-3264. 2011.

20. Spínola-Amilibia, M., Rivera, J., Ortiz-Lombardía, M., Romero, A., Neira, J.L. and Bravo, J. The structure of BRMS1 nuclear export signal and SNX6 interacting region reveals a hexamer formed by antiparallel coiled coils. **J. Mol. Biol. 411**, 1114 -1127. 2011.
21. Bocanegra, R., Nevot, M., Doménech, R., López, I., Abián, O., Rodríguez-Huete, A., Cavasotto, C.N., Velázquez-Campoy, A., Gómez, J., Martínez, M.A., Neira, J.L. and Mateu, M.G. Rationally designed interfacial peptides are efficient in vitro inhibitors of HIV-1 capsid assembly with antiviral activity. **PLOS One,** e23877. 2011.
22. Saelices, L., Galmozzi, C. V., Florencio, F. J., Muro-Pastor, M. I. and Neira, J. L. The inactivating factor of glutamine synthetase IF17 is an intrinsically disordered protein, which folds upon binding to its target. **Biochemistry 50**, 9767-9778. 2011.
23. Espinosa, J, López-Redondo, ML, Miguel-Romero, L, Neira, JL, Marina, A, Contreras, A. Insights into the mechanism of activation of the phosphorylation-independent response regulator NblR. Role of residues Cys69 and Cys96. **Biochim Biophys Acta 1819**, 382-390. 2012.
24. Navarro, A, Encinar, JA, López-Méndez, B, Aguado-Llera, D, Prieto, J, Gómez, J, Martínez-Cruz, LA, Millet, O, González-Ros, JM, Fernández-Ballester, G, Neira, JL, Ferrer-Montiel, A. Mutation of Ser-50 and Cys-66 in Snapin Modulates Protein Structure and Stability. **Biochemistry 51**, 3470-3484. 2012
25. Aguado-Llera, D, Bacarizo, J, Gregorio-Teruel, L, Taberner, FJ, Cámara-Artigas, A, Neira, JL Biophysical characterization of the isolated C-terminal region of the transient receptor potential vanilloid 1. **FEBS Lett. 586**, 1154-1159. 2012.
26. Aguado-Llera, D, Doménech, R, Marenchino, M, Vidal, M, Neira, JL. Non-canonical residues of the marginally stable monomeric ubiquitin conjugase from goldfish are involved in binding to the C terminus of Ring 1B. **Biochim Biophys Acta 1824**, 991-1001. 2012.
27. Neira, JL, Sevilla, P, García-Blanco, F. The C-terminal sterile alpha motif (SAM) domain of human p73 is a highly dynamic protein, which acquires high thermal stability through a decrease in backbone flexibility. **Phys Chem Chem Phys 14**, 10308-10323. 2012.
28. Doménech, R, Martínez-Gómez, AI, Aguado-Llera, D, Martínez-Rodríguez, S, Clemente-Jiménez, JM, Velázquez-Campoy, A, Neira, JL. Stability and binding of the phosphorylated species of the N-terminal domain of enzyme I and the histidine phosphocarrier protein from the *Streptomyces coelicolor* phosphoenolpyruvate:sugar phosphotransferase system. **Arch Biochem Biophys 526**, 44-53. 2012.
29. Doménech, R, Martínez-Rodríguez, S, Velázquez-Campoy, A, Neira, JL. Peptides as inhibitors of the first phosphorylation step of the *Streptomyces coelicolor* phosphoenolpyruvate: sugar phosphotransferase system. **Biochemistry 51**, 7393-7402. 2012.
30. Barrera, FN, Neira, JL. Turbulent times in Southern European science. **Lancet 380**, 1229-1230. 2012.
31. Neira JL. NMR as a tool to identify and characterize protein holding intermediates. **Arch Biochem Biophys;** pii: S0003-9861(12)00331-1. 2012.
32. Nash, ME, Carroll, W.M., Velasco, D., Gomez, J., Gorelov, A.V., Elezov, D., Gallardo, A., Rochev, Y.A., Elvira, C. Synthesis and Characterization of a Novel Thermoresponsive Copolymer Series and their Application in Cell and Cell Sheet Regeneration. **J Biomat Sci: Polym E** (vol ahead-of-p) 1 – 16, 2012.

33. Renart, M.L., Montoya, E., Fernández, A.M., Molina, M.L., Poveda, J.A., Encinar, J.A., Ayala, J.L., Ferrer-Montiel, A.V., Gómez, J., Morales, A., González Ros J.M. Contribution of Ion Binding Affinity to Ion Selectivity and Permeation in KcsA, a Model Potassium Channel. **Biochemistry 51**, 3891 – 3900. 2012.

34. Souza, H., Souza, A.M.M., Gómez, J., Gonçalves, M. Complexation of WPI and microwave-assisted extracted agars with different physicochemical properties. **Carbohydr Polymer 89,** 1073 – 1080. 2012.

RESEARCH HIGHLIGHTS

Macromolecular interactions measured by calorimetric and spectroscopic techniques. Structure of biomolecules by NMR. Design of drugs. Biophysical and spectroscopic characterization of biomolecules and their complexes. Protein stability.

As an example of the research lines above described, we have carried out the dynamic studies of the SAM domain of p73 by using high resolution NMR studies. The α-splice variant of p73 (p73α), a homologue of the tumour suppressor p53, has close to its C terminus a sterile alpha motif (SAM), SAMp73, that is involved in protein-biomolecule interactions. The conformational stability of SAMp73 is low (~5 kcal mol^{-1}), although its thermal stability is high. To explain this high thermostability, we studied the dynamics of SAMp73 in a wide range of GdmCl (guanidine hydrochloride) concentrations and temperatures by NMR relaxation, NMR hydrogen-exchange (HX) and fluorescence lifetime approaches. The slowest exchanging residues of SAMp73 belong to the helical regions, and they did exchange by a global unfolding process. Moreover, SAMp73 was very flexible, with most of its amide protons affected by slow μs-ms conformational exchange. Within this time scale, the residues of SAMp73 with the largest exchange rates (R_{ex}) were involved in binding to other molecules; therefore, the flexibility in the μs-ms range was associated with biological functions. As the [GdmCl] increased, the pico-to-nanosecond flexibility of the backbone amide protons raised, but it did so differently depending on the residue. We were able to obtain, for the first time, the linear [GdmCl]-variation of the local conformational entropies, m_{s^2}, which ranged from 5.3 to 0.3 cal mol^{-1} K^{-1} M^{-1}, similar to those measured by using macroscopic techniques in other proteins. Conversely, the temperature dependence of the pico-to-nanoseconds dynamics of the backbone amide protons of SAMp73 indicates that the flexibility of some residues decreased with the temperature; these results explain the high thermostability of the protein.

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

Carmen Reyes Mateo Martínez

Ricardo Mallavia Marín

Mª José Martínez Tomé

POSTDOCTORAL FELLOWS

Rocío Esquembre Tomé

Ph.D STUDENTS

Rebeca Vázquez Guilló

Zehra Kahveci

TECHNICIANS

Elisa Pérez García

PUBLICATIONS

1. Tapia, M.J., Monteserín, M., Valente, A.J.M.; Burrows, H.D. and Mallavia, R. Binding of polynucleotides to conjugated polyelectrolytes and its applications in sensing. **Adv. Colloid Interfac. 158**, 94-107. 2010.
2. Salinas-Castillo, A.; Camprubí-Robles, M. and Mallavia, R. Synthesis of a new fluorescent conjugated polymer microsphere for chemical sensing in water media. **Chem. Comm. 46** ,1263-1265. 2010.
3. Ferrer, J.C., Salinas-Castillo, A. Alonso, J.L., Fernández de Ávila, S. and Mallavia, R. Direct synthesis of PbS nanocrystals capped with 4-fluorothiophenol in semiconducting polymer. **Mater. Chem. Phys. 112**, 459-462. 2010.

4. Monteserín, M., Tapia, M.J., Ribeiro, A.C.F., Santos, C.I.A.V., Valente, A.J.M., Burrows, H.D., Mallavia, R., Nilsson, M. and Söderman, O. Multicomponent Interdiffusion and Self-Diffusion of the Cationic Poly{[9,9-bis(6′-N,N,N-trimethylammonium) hexyl]fluorene-phenylene} Dibromide in a Dimethyl Sulfoxide + Water Solution. **J. Chem. Eng. Data. 55**, 1860-1866. 2010.

5. Álvarez, A.L., Romero, B., Arredondo, B., Quintana, X., Mallavia, R. and Otón, J.M. Electrical model of organic diodes with field-dependent carrier mobility in the presence of an electric filed at the injection interface. **Int. J. Numer. Model. El. 23**, 332- 339. 2010.

6. Tapia, M.J., Monteserín, M., Costoyas, A., Burrows, H.D., Marquez, A.T., Pais, A.A.C.C., Valente, A.J.M., Mallavia, R., Scherff, U., Pinazo, A., Pérez, L. and Morán, M.C. Effects of non-ionic commercial and ionic biocompatible arginine based surfactants on the photophysic of several poly(fluorene-1,4-phenylene)s. **J. Mol. Liq. 156**, 18-27. 2010.

7. Alonso, J.L., Ferrer, J.C., Salinas-Castillo, A., Mallavia, R. and Fernández de Ávila, S. Solvent dependent behaviour of poly(9-vinylcarbazole)-based polymer light emitting diodes. **Solid State Electron. 54**, 1269-1272. 2010.

8. Monteserín, M., Burrows, H.D., Mallavia, R, Di Paolo, R., Macanita, A. and Tapia, M.J. How to Change the Aggregation in the DNA/Surfactant/Cationic Conjugated Polyelectrolyte System through the Order of Component Addition: Anionic versus Neutral Surfactants. **Langmuir 26**, 11705-11714. 2010.

9. Martínez-Tomé, M.J., Esquembre, R., Mallavia, R. and Mateo, C. R. Development of a dual-analyte fluorescent sensor for the determination of bioactive nitrite and selenite in water samples. **J. Pharm. Biomed. Anal. 51**, 484-489. 2010.

10. Pastor, I., Salinas-Castillo, A., Esquembre, R., Mallavia, R. and Mateo, C.R. Multienzymatic system immobilization in sol-gel slides: Fluorescent superoxide biosensors development. **Biosensors and Bioelectronics 25,** 1526-1529. 2010.

11. Matallana González, M.C., Martínez-Tomé, M.J. and Torija Isasa M.E. Nitrate and nitrite content in organically cultivated vegetables. **Food Addit. Contam. B 3,** 1939-3210. 2010.

12. Martínez-Tomé, M.J., Esquembre, R., Mallavia, R. and Mateo C. R. Formation of Complexes between the Conjugated Polyelectrolyte Poly{[9,9-bis(6' –N,N,N-trimethylammonium)hexyl]fluorene-phenylene} Bromide (HTMA-PFP) and Human Serum Albumin. **Biomacromolecules 11**, 1494-1501. 2010.

13. Martínez-Tomé, M., Mariscal, M., Martínez-Tomé, J. and Martínez-Tomé, M.J. Proximate composition and anti-oxidant activities of organically- and conventionally-grown broccoli (Brassica oleracea L. var. italica). **J. Hortic. Sci. Biotech. 86**, 511-516. 2011.

14. Martínez-Tomé, M. J., Rodríguez, A., Jiménez, A. M.ª, Mariscal, M., Murcia, M.ª A. and García-Diz, L. Food habits and nutritional status of elderly people living in a Spanish Mediterranean city. **Nutr Hosp. 26**, 1175-1182. 2011.

15. Alvarez-Diaz, A., Salinas-Castillo, A., Camprubí-Robles, M., Costa-Fernandez, J.M., Pereiro, R., Mallavia, R. and Sanz-Medel, A. Conjugated polymer microspheres for "turn-off/turn-on"fluorescence optosensing of inorganic ions in aqueous media. **Anal. Chem. 83**, 2712-2718. 2011

16. Carrera, N., Salinas-Castillo, A., Albéniz, A.C., Espinet, P. and Mallavia, R. Fluorene-based stannylated polymers and their use as recyclable reagents in the Stille reaction. **J. Organomet. Chem. 696**, 3316-3321. 2011.

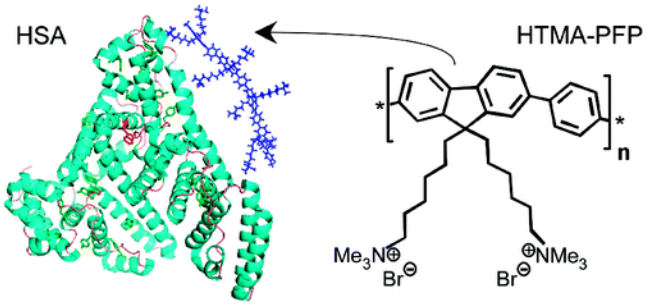
17. Valente, A.J.M., Burrows, H.D., Gomes, J.N.P.L., Pereira, R.F.P., Cerqueira, D., Jiménez, A., Burgos, N., Morán, C., .Mallavia, R., Filho, G.R. Cellulose acetate-poly {[9,9-bis (60-N,N,N-trimethylammonium) hexyl]fluorene-phenylene} bromide blends: Preparation, characterization and transport properties. **React Func Polym 72**, 420-426. 2012.

18. Neves, Â.C.B., Pinto, S.M.A., Henriques, C.A., Rosado, M.T.S., Mallavia, R., Burrows, H.D., Pereira, M.M., Calvete, M.J.F. Routes to synthesis of porphyrins covalently boundto poly(carbazole)s and poly(fluorene)s: Structural and computational studies on oligomers. **J Mol Struct 1029**, 199-208. 2012.

19. Esquembre, R., Pinto, S.N., Poveda, J.A., Prieto, M., Mateo, C.R. Immobilization and characterization of giant unilamellar vesicles (GUVs) within porous silica glasses. **Soft Matter 8**, 408-417. 2012.

RESEARCH HIGHLIGHTS

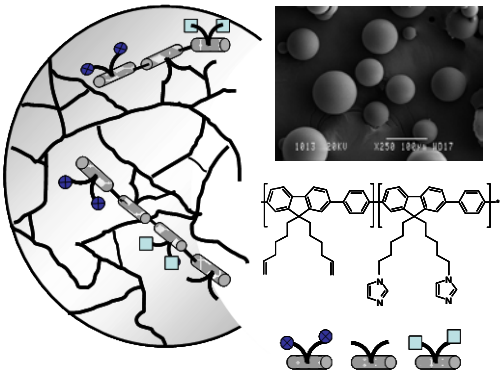
Formation of Complexes between the Conjugated Polyelectrolyte Poly{[9,9-bis(6' – N,N,N-trimethylammonium)hexyl]fluorene-phenylene} Bromide (HTMA-PFP) and Human Serum Albumin. Martínez-Tomé, M.J., Esquembre, R., Mallavia, R. and Mateo C. R. Biomacromolecules 11, 1494-1501. 2010.



In this work we present a spectroscopic study of the interaction in aqueous solution of HTMA-PFP, a fluorene based cationic conjugated polyelectrolyte, and Human Serum Albumin (HSA). The interaction was characterized from changes observed in both, the spectroscopic properties of HTMA-PFP and the intrinsic fluorescence of HSA. Interaction between both macromolecules is accompanied by an increasing of the fluorescence signal of HTMA-PFP, which suggests that hydrophobic interactions between the conjugated polymer backbone and the hydrophobic patches of HSA also contribute to the polymer-protein complex stabilization. In addition, this interaction produces a decreasing in the intrinsic fluorescence of HSA which is partially due to dynamic quenching and energy transfer mechanism between both macromolecules. Effects of HTMA-PFP on the thermal stability and conformation of folded protein were also explored from far-UV CD experiments. Results indicate that as polymer is added it binds to HSA and initiates unfolding. This unfolding process induces HTMA-PFP chains to become more extended, disrupting backbone interactions and increasing polymer fluorescence intensity.

Synthesis of a new fluorescent conjugated polymer microsphere for chemical sensing in water media. Salinas-Castillo, A.; Camprubí-Robles, M. and Mallavia, R. Chem. Comm. 46 (8), 1263-1265. 2010.

Noteworthy Chemistry, April 2010. A novel conjugated polymer microsphere of high value for fluorescent sensing in aqueous media has been synthesized. New conjugated polymers were functionalized in the side chain with imidazole moieties (recognition element) and a terminal double bond (covalently linked to an organic matrix) through a post-functionalization strategy.



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.

The idea that 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.

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PUBLICATIONS

1. Lucas, M., Encinar, J. A., Oyenarte, I., Gómez García, I., Astigarraga Arribas, E., Kortazar, D., Fernández, J. A., Mato, J. M., Martínez-Chantar, M. L. and Martínez-Cruz, L. A. Binding of 5´-methylthioadenosine and S-adenosyl-L-methionine to protein MJ0100 triggers an open-to-close conformational change in its CBS motif pair. **J. Mol. Biol. 396**, 800-820. 2010.
2. Renart, M.L., Triano, I., Poveda, J.A., Encinar, J.A., Fernandez, A.M., Ferrer-Montiel, A.V., Gomez, J. and Gonzalez-Ros, J.M. Ion binding to KcsA: implications in ion selectivity and channel gating. **Biochemistry 49**, 9480-9487. 2010.
3. Triano, F.N. Barrera, M.L. Renart, M.L. Molina, Fernandez-Ballester, G., Poveda, J.A., Fernandez, A.M., Encinar, J.A., Ferrer-Montiel, A.V., Otzen, D. and Gonzalez-Ros, J.M. Occupancy of non-annular lipid binding sites on KcsA greatly increases the stability of the tetrameric protein. **Biochemistry 49**, 5397-5404. 2010.
4. Alberola-Die, J., Martinez-Pinna, J.M., González-Ros, Ivorra I. and Morales, A. Multiple inhibitory actions of lidocaine on Torpedo nicotinic acetylcholine receptors transplanted to Xenopus oocytes". **J. Neurochem. 117**, 1009-1019. 2011.
5. Clemente-Casares, P., López-Jiménez, A.J., Bellón-Echeverría, I., Encinar, J.A., Martínez-Alfaro, E., Pérez-Flores, R., and Mas, A. De novo polymerase activity and oligomerization of Hepatitis C Virus RNA-dependent RNApolymerases from genotypes 1 to 5. **PLoS ONE 6**(4): e18515. 2011.
6. Fernandez-Ballester, G., Fernández-Carvajal, A.M., González-Ros, J.M., Ferrer-Montiel, A.V. Ionic channels as targets for drug design: a computational review. **Pharmaceutics 3**, 932-953. 2011.
7. Fernandez-Ballester, G., Fernández-Carvajal, A.M., González-Ros, J.M., Ferrer-Montiel, A.V. In silico-based direct evolution of peptidomimetics in drug discovery. **Curr. Topics Pharmacol. 15**, 35-55. 2011.
8. Gerona-Navarro, G., González-Muñiz, R., Fernández-Carvajal, A., González Ros, J.M., Ferrer-Montiel, A. Solid-phase synthesis of a library of amphipatic hydantoins. Discovery of new hits for TRPV1 blockade. **ACS Comb. Sci.** (formerly J. Comb. Chem.) **13**, 458-465. 2011.
9. Devesa, R. Planells-Cases, Fernández-Ballester, G., González-Ros, J.M., Ferrer-Montiel, A.V. and Fernández-Carvajal, A. The role of the Transient Receptor Potential Vanilloid 1 (TRPV1) in inflammation and sepsis. **J. Inflamm. Res. 4**, 67-81. 2011.
10. Vidal, M., Fernández-Carvajal, A., Moure, A., Gomis, A., Valente, P., Viana, F., Planells-Cases, R., González-Ros, J.M., Belmonte, C., Bujons, J., Ferrer-Montiel, A. and Messeguer A. Triazine-based TRPV1 Open Channel Blockers: Design, Synthesis, Evaluation and QSAR data. **J. Med. Chem. 54**, 7441-7452. 2011.

11. Martínez-Cruz, L.A., Encinar, J.A., Sevilla-Sierra, P., Oyenarte, I., Gómez-García, I., Aguado-Llera, D., García-Blanco, F., Gómez, J. and Neira, J.L. Nucleotide-induced conformational transitions in the CBS domain protein MJ0729 of Methanocaldococcus jannaschii. **Protein Eng Des Sel. 24**(1-2): 161-169. 2011.
12. Valente, P., Fernández-Carvajal, A.M., Quirce, S., Gomis, A., Camprubí, M., Viana, F., Fernández-Ballester, G., González-Ros, J.M., Belmonte, C., Planells-Cases, R. and Ferrer-Montiel, A.V. Membrane-tethered peptides patterned after the TRP domain potently and selectively inhibit TRPV1 channel activity. **The FASEB J. 25**, 1628-1640. 2011.
13. Esquembre R., Pinto S.N., Poveda J.A. , Prieto M. and C. Reyes Mateo Immobilization and characterization of giant unilamellar vesicles (GUVs) within porous silica glasses. **Soft Matter 8**, 408-417. 2012.
14. A. Fernández-Carvajal, G. Fernández-Ballester, I. Devesa, J.M González-Ros and A. Ferrer-Montiel: New Strategies to Develop Novel Pain Therapies: Addressing Thermoreceptors from Different Points of View. **Pharmaceuticals 5**, 16-48. 2012.
15. A. Navarro, J.A. Encinar, B. López, D.Aguado-Llera, J. Prieto, J. Gómez, L.A. Martínez-Cruz, O. Millet, J.M. González-Ros, G. Fernández-Ballester, J.L. Neira and A.V. Ferrer-Montiel : "Mutation of Ser-50 and Cys-66 in Snapin modulate protein structure and stability". **Biochemistry 51**, 3470-3484. 2012.
16. A. Calcutta, C.M. Jessen, M.A. Behrens, C.L.P. Oliveira, M.L. Renart, J.M. Gonzalez-Ros, D.E. Otzen, J.S. Pedersen, A. Malmendal and N.Chr. Nielsen: "Mapping of Unfolding States of Integral Helical Membrane Proteins by GPS-NMR and Scattering Techniques". **BBA Biomembranes 1818**, 2290-2301. 2012.
17. M.L. Renart, E. Montoya, A.M. Fernández, M.L. Molina, J.A. Poveda, J.A. Encinar, J.L. Ayala, A.V. Ferrer-Montiel, J. Gómez, A. Morales and J.M. González Ros: "On the contribution of ion binding affinity to ion selectivity and permeation in KcsA, a model potassium channel". **Biochemistry 51**, 3891-3900. 2012.
18. A.V. Ferrer-Montiel, A. Fernandez-Carvajal, R. Planells-Cases, G. Fernandez-Ballester, J.M. Gonzalez-Ros, A. Meseguer and R. Gonzalez-Muñiz: "Advances in regulating thermosensory TRP channels". **Expert Opinion Ther. Patents 22**, 999-1017. 2012.

PATENTS

Antonio Ferrer Montiel, Asia Fernández Carvajal, Gregorio Fernández Ballester, Jose Manuel González Ros, Carlos Belmonte Martínez, Felix Viana de la Iglesia, Ana Gomis Garcia, Pierluigi Valente, Maria Camprubi Robles. Modulating peptides of TRPV1 and it uses. Titular: UMH (80%), CSIC (20%). Registro: P201130052 (20/04/2011).

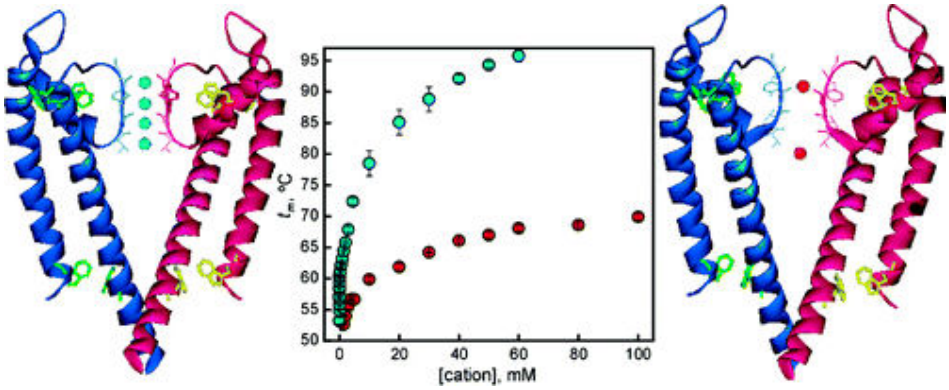
Antonio Ferrer Montiel, Asia Fernández Carvajal, Jose Manuel González Ros, Carlos Belmonte Martínez, Felix Viana de la Iglesia, Ana Gomis Garcia, Angel Messeguer Peypoch, Jordi Boullons Vilas, Miquel Vidal Mosquera. TRPV1 agonists, and uses thereof. UMH (80%), CSIC (20%). Registros: P201130537 (05/04/2011).

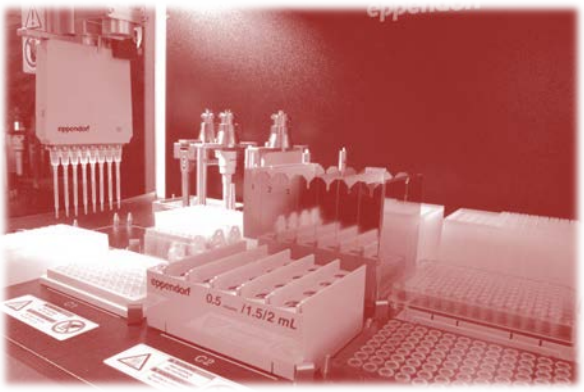
Carlos Belmonte Martínez, Juana Gallar Martinez, Antonio Ferrer Montiel, Asia Fernández Carvajal, Felix Viana de la Iglesia. Composición farmacéutica para el tratamiento de la epifora. PCT/ES02011/070627, WO2012/032209 A3.

RESEARCH HIGHLIGHTS

Ion binding to KcsA: implications in ion selectivity and channel gating. Renart, M.L., Triano, I., Poveda, J.A., Encinar, J.A., Fernandez, A.M., Ferrer-Montiel, A.V., Gomez, J. and Gonzalez-Ros, J.M. Biochemistry 49, 9480-9487. 2010.

Binding of K^+ and Na^+ to the potassium channel KcsA has been characterized from the stabilization observed in the heat-induced denaturation of the protein as the ion concentration is increased. KcsA thermal denaturation is known to include (i) dissociation of the homotetrameric channel into its constituent subunits and (ii) protein unfolding. The ion concentration-dependent changes in the thermal stability of the protein, evaluated as the Tm value for thermal-induced denaturation of the protein, may suggest the existence of both high- and low-affinity K^+ binding sites of KcsA, which lend support to the tenet that channel gating may be governed by K^+ concentration-dependent transitions between different affinity states of the channel selectivity filter. We also found that Na^+ binds to KcsA with a KD similar to that estimated electrophysiologically from channel blockade. Therefore, our findings on ion binding to KcsA partly account for K^+ over Na^+ selectivity and Na^+ blockade and argue against the strict "snug fit" hypothesis used initially to explain ion selectivity from the X-ray channel structure. Furthermore, the remarkable effects of increasing the ion concentration, K^+ in particular, on the Tm of the denaturation process evidence that synergistic effects of the metal-mediated intersubunit interactions at the channel selectivity filter are a major contributor to the stability of the tetrameric protein. This observation substantiates the notion of a role for ions as structural "effectors" of ion channels.





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.

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PUBLICATIONS

1. Pérez-Fons, L., Garzón, M.T., and Micol, V. Relationship between the antioxidant capacity and effect of rosemary (*Rosmarinus officinalis L.*) polyphenols on membrane phospholipid order. **J. Agric. Food Chem. 58**, 161-171. 2010.
2. Barrajón-Catalán, E., Menéndez-Gutiérrez, M.P., Falcó, A., Carrato, A., Saceda, M., Micol, V. Selective death of human breast cancer cells by lytic immunoliposomes: Correlation with their HER2 expression level. **Cancer Lett**. **290**, 192-203. 2010.
3. Caturla, N., Estepa, A. and Micol, V. The relationship between oleuropein antimicrobial activity and its effects on biological membranes. Eds. Victor R. Preedy and Ronald Ross Watson. Elsevier, Life Sciences, San Diego. ***Olives and Olive Oil in Health and Disease Prevention*** **150,** 1354-1354. 2010.
4. Beltrán-Debón, R., Alonso-Villaverde, C., Aragonès, G., Rodríguez-Medina, I., Rull, A., Micol, V., Segura-Carretero, A., Fernández-Gutiérrez, A., Camps J. and Joven J. The aqueous extract of *Hibiscus sabdariffa* calices modulates the production of monocyte chemoattractant protein-1 in humans. **Phytomedicine 17**, 186-91. 2010.
5. Funes , L, Micol, V., Quirantes-Piné, R., Segura-Carretero, A., Fernández-Gutiérrez, A. Incremento de la actividad de enzimas antioxidantes en células sanguíneas y determinación de metabolitos plasmáticos en ratas sobrealimentadas con *Lippia citriodora.* **Nutr. Hosp. 25(S1),** 133-134. 2010.
6. Funes, L., Laporta, O., Cerdán-Calero, M. and Micol, V. Effects of verbascoside, a phenyl-propanoid glycoside from lemon verbena, on phospholipid model membranes**. Chem. Phys. Lipids 163,** 190-9. 2010.
7. Fernández-Arroyo, S., Barrajón, E., Micol, V., Segura-Carretero, A. and Fernández-Gutiérrez, A. High-performance liquid chromatography with diode array detection coupled to electrospray time-of-flight and ion-trap tandem mass spectrometry to identify phenolic compounds from a *Cistus ladanifer* aqueous extract. **Phytochem. Anal. 21**, 307-313. 2010.
8. Fu, S., Arráez-Román, D., Segura-Carretero, A., Micol, V., Menéndez, J.A, and Fernández-Gutiérrez, A. Qualitative screening of phenolic compounds in olive leaf extracts by hyphenated liquid chromatography and preliminary evaluation of cytotoxic activity against human breast cancer cells. **Anal. Bioanal. Chem. 397**, 643-654. 2010.
9. Barrajón-Catalán, E., Fernández-Arroyo, S., Saura, D., Guillén, E., Fernández-Gutiérrez, A., Segura-Carretero, A. and Micol, V. *Cistaceae* aqueous extracts containing ellagitannins show antioxidant and antimicrobial capacity, and cytotoxic activity against human cancer cells. **Food Chem. Toxicol. 48**, 2273-82. 2010.
10. Maestre, R., Micol, V., Funes, L. and Medina, I. Incorporation and interaction of grape seed extract antioxidants in membranes and relation with their efficacy in muscle foods. **J. Agric. Food Chem. 58,** 8365-74. 2010.
11. Herranz, M., Barrajón-Catalán, E., Beltrán-Debón, R., Joven, J., and Micol, V. Stevia is a source for alternative sweeteners: potential medicinal effects. **AGROFood Ind. Hi-tech 21,** 4-8. 2010.
12. Valero, M., Micol, V., Saura, D., Muñoz, N, Lorente, J., and Martí, N. Comparison of antimicrobial treatments for citrus juices. **CAB Reviews:** Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources **5**. 2010.

13. Barrajón-Catalán, E., Fernández-Arroyo, S., Guillén, E., Saura, D. and Micol, V. A systematic study of the composition of aqueous extracts deriving from several *Cistus* genus species: evolutionary implications. **Phytochem. Anal. 22,** 303-12. 2011.

14. Funes, L., Carrera-Quintanar, L., Cerdán-Calero, M., Ferrer, M. D., Drobnic, F., Pons, A., Roche, E. and Micol, V. Effect of Lemon verbena supplementation on muscular damage markers, proinflammatory cytokines release and neutrophils' oxidative stress in chronic exercise. **Eur. J. Appl. Physiol. 111,** 695-705. 2011.

15. Caturla, N., Funes, L., Pérez-Fons, L. and Micol, V. A randomized, double-blind, placebo-controlled study of the effect of a combination of lemon verbena extract and fish oil omega-3 on joint management. **J. Altern. Complement. Med**. **17**, 1051-63. 2011.

16. Beltrán-Debón, R., Rull, A., Rodríguez-Sanabria, F., Iswaldi, I., Herranz-López, M., Aragonès, G., Camps, J., Alonso-Villaverde, C., Menéndez J.A., Micol, V., Segura-Carretero, A. and Joven, J. Continuous administration of polyphenols from aqueous rooibos (*Aspalathus linearis*) extract ameliorates dietary induced metabolic disturbances in hyperlipidemic mice. **Phytomedicine 18**, 414. 2011.

17. Fernández-Arroyo, S., Rodriguez-Medina, I.C., Beltrán-Debón, R., Pasini, F., Joven, J., Micol, V., Segura-Carretero, A. and Fernández-Gutiérrez, A. Quantification of the polyphenolic fraction and invitro antioxidant and in vivo antihyperlipemic activities of *Hibiscus sabdariffa* aqueous extract. **Food Res. Int. 44,** 1490. 2011.

18. Mestre-Alfaro A., Ferrer M.D., Sureda A., Tauler P., Martínez E., Bibiloni M.M., Micol, V., Tur, J.A., and Pons, A. Phytoestrogens enhance antioxidant enzymes after swimming exercise and modulate sex hormone plasma levels in female swimmers. **Eur. J. Appl. Physiol. 111**, 2281-94. 2011.

19. Oliveras-Ferraros, C., Fernández-Arroyo, S., Vazquez-Martin, A., Lozano-Sánchez, J., Cufí, S., Joven, J., Micol, V., Fernández-Gutiérrez, A., Segura-Carretero, A., and Menendez, J.A. Crude phenolic extracts from extra virgin olive oil circumvent de novo breast cancer resistance to HER1/HER2-targeting drugs by inducing GADD45-sensed cellular stress, G2/M arrest and hyperacetylation of Histone H3. **Int. J Oncol. 38**, 1533. 2011.

20. Vegara, S., Funes, L., Martí, N., Saura, D., Micol, V., and Valero, M. Bactericidal activities against pathogenic bacteria by selected constituents of plant extracts in carrot broth. **Food Chem. 128**, 872-877. 2011.

21. Martí, N. , Saura, D., Fuentes, E., Lizama, V., García, E., Mico-Ballester, M.J., and Lorente, J. Fiber from tangerine juice industry. **Ind. Crops Prod. 33**, 94-98. 2011.

22. Mena, P., García-Viguera, C., Navarro-Rico, J., Moreno, D.A., Bartual, J., Saura, D. and Martí, N. Phytochemical characterisation for industrial use of pomegranate (*Punica granatum* L.) cultivars grown in Spain. **J. Sci. Food Agric. 10**, 1893-1906. 2011.

23. Garrido, M.D., Auqui, M., Martí, N., and Linares, M.B. Effect of two different red grape pomace extracts obtained under different extraction systems on meat quality of pork burgers. **LWT – Food Sci. Tech**. **10**, 2238-2243. 2011.

24. Herranz, M., Fernández-Arroyo, S., Pérez-Sánchez, A., Barrajón-Catalán, E., Beltrán-Debón, R., Menéndez, J.A., Alonso-Villaverde, C., Segura-Carretero, A., Joven, J., Micol, V. Synergism of plant-derived polyphenols in adipogenesis: perspectives and implications. **Phytomedicine 19,** 253-261. 2012.

25. Giner, MJ, Vegara, S., Funes, L., Martí, N., Saura, D., Micol, V., Valero, M. Antimicrobial activity of food-compatible plant extracts and chitosan against naturally occurring micro-organisms in tomato juice. **J. Sci. Food Agri 92**, 1917-23**.** 2012.

26. Carrera-Quintanar, L., López-Fuentes, M., Climent, V., Herranz-López, M., Micol, V., Pons, A., Sogorb, F., Roche, E. Oxidative damage is present in plasma and circulating neutrophils 4 weeks after a high mountain expedition. **Eur. J. Appl. Physiol., 112,** 2923-32**.** 2012.

27. Carrera-Quintanar L, Funes L, Viudes E, Tur J, Micol V, Roche E, Pons A. Antioxidant effect of lemon verbena extracts in lymphocytes of university students performing aerobic training program. **Scand. J. Med. Sci. Sports. 22,** 454-61. 2012.

28. Cufí S, Vazquez-Martin A, Oliveras-Ferraros C, Quirantes R, Segura-Carretero A, Micol V, Joven J, Bosch-Barrera J, Del Barco S, Martin-Castillo B, Vellon L, Menendez JA. Metformin lowers the threshold for stress-induced senescence: A role for the microRNA-200 family and miR-205. **Cell Cycle** 11(6). 2012.

29. Taamalli, A., Arráez-Román, D., Barrajón-Catalán, E., Ruiz-Torres, V., Pérez-Sánchez, A., Herrero, M., Ibáñez, E., Micol, V., Zarrouk, M., Segura-Carretero, A., Fernández-Gutiérrez, A. Use of advanced techniques for the extraction of phenolic compounds from Tunisian olive leaves: Phenolic composition and cytotoxicity against human breast cancer cells. **Food Chem. Toxicol. 50**, 1817-25**.** 2012.

30. Joven, J., Espinel, E., Rull, A., Aragonès, G., Rodríguez-Gallego, E., Camps, J., Micol, V., Herranz-López, M., Menéndez, J.A., Borrás, I., Segura-Carretero, A., Alonso-Villaverde, C., Beltrán-Debón, R. Plant-derived polyphenols regulate expression of miRNA paralogs miR-103/107 and miR-122 and prevent diet-induced fatty liver disease in hyperlipidemic mice. **Biochim Biophys Acta - General Subjects 1820**, 849-9**.** 2012.

31. Fernández-Arroyo, S. Herranz-López, M., Beltrán-Debón, R., Borrás-Linares, I., Barrajón-Catalán, E., Joven, J., Fernández-Gutiérrez, A., Segura-Carretero, A., Micol, V. Bioavailability study of a polyphenol-enriched extract from *Hibiscus sabdariffa* in rats and associated antioxidant status. **Mol. Nutr. Food Res. 56**, 1590-5. 2012.

32. Corominas-Faja, B., Quirantes-Piné, R., Oliveras-Ferraro, C., Vázquez-Martín, A., Cufí, S., Martín-Castillo, B., Micol, V., Joven, J., Segura-Carretero, A., Menéndez, J.A. Metabolomic fingerprint reveals that metformin impairs one-carbon metabolism in a manner similar to the antifolate class of chemotherapy drugs. **Aging 4**, 7. 2012.

33. 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**, 121-6. 2012.

34. Quirantes-Piné R, Verardo V, Arráez-Román D, Fernández-Arroyo S, Micol V, Caboni MF, 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. 2012.

35. Joven J, Rull A, Rodriguez-Gallego E, Camps J, Riera-Borrull M, Hernández-Aguilera A, Martin-Paredero V, Segura-Carretero A, Micol V, Alonso-Villaverde C, Menéndez JA; 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. 2012.

36. 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.

37. Hussam Ahmad-Qasem, M., Cánovas, J., Barrajón-Catalán, E., Micol V, Cárcel, 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.** 2012 (doi: 10.1016/j.ifset.2012.11.008).

38. Mena, P., Gil-Izquierdo, A., Moreno, D.A., Martí, N., García-Viguera, C. Assessment of the melatonin production in pomegranate wines. **LWT-Food Sci. Tech. 47**, 13-18. 2012.
39. Mena, P., Martí, N., Saura, D., Valero, M., García-Viguera, C. Combinatory effect of thermal treatment and blending on the quality of pomegranate juices. **Food Bioprocess Tech. 5,** 1-14. 2012.
40. Saura, D., Martí, N., Valero, M., González, A., Carbonell, A., Laencina, J. Separation of aromatics compounds during the clarification of lemon juice by cross-flow filtration. **Ind. Crops Prod. 36**, 543-548. 2012.
41. Mena, P., Gironés-Villaplana, A., Martí, N., García-Viguera, C. Pomegranate varietal wines: Phytochemical composition and quality parameters. **Food Chem. 133**, 108-115. 2012.
42. Martí, N., Lizama, V., Verdú, J.A., Muñoz, N., Aleixandre, J.L., Saura, D. Prediction of Phenolic Composition of *Monastrell* and *Tempranillo* Wines: Correlation Between Phenolic Content and Traditional Variables of Fruit Maturity. **Int. J. Food Prop**. 2012 (doi**:**10.1080/10942912.2011.570467).

PATENTS

Inventores:	N. Martí, V. Micol, M. Valero, N. Muñoz, L. Funes, D. Saura.
Título:	Producción de extractos de células de uva enriquecidas en estilbenos.
Titular:	Mitra Sol., S.L.
Registros:	P2010000146

Inventores:	E. Barrajón, N. Martí, V. Micol, M. Valero, N. Muñoz, D. Saura.
Título:	Extractos de plantas del género *Cistus* enriquecidos con polifenoles con actividades biológicas.
Titular:	Químicas del Vinalopó, S.L.
Registros:	ES2373184

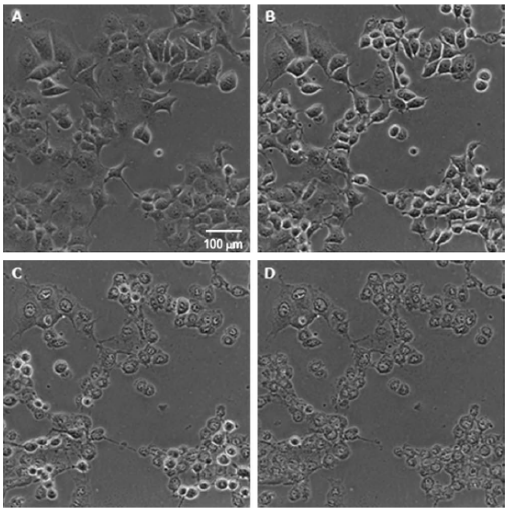
Inventores:	D. Saura, N. Martí, P. Mena, C. García-Viguera, C. García-Ruiz, V. Micol, M. Valero.
Título:	Combinación sinérgica de flavonoides y vitamin C.
Titular:	Mitra Sol., S.L.
Registros:	P201001031.

Inventores:	D. Saura.; N. Martí; V. Micol, M. Valero; E. Bernal.
Título:	Equipo de expansión instantánea a vacío y ultrasonidos.
Titular:	JBT FoodTech Ltd.
Registros:	P201200830

RESEARCH HIGHLIGHTS

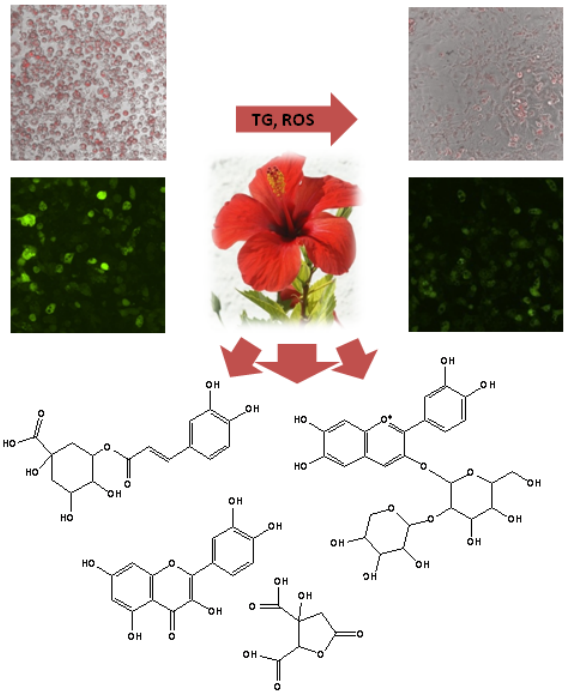
Selective death of human breast cancer cells by lytic immunoliposomes: Correlation with their HER2 expression level. Barrajón-Catalán E, Menéndez-Gutiérrez MP, Falco A, Carrato A, Saceda M, Micol V. Cancer Lett. 290, 192-203. 2010.

In this study we target HER2-overexpressing (the human epidermal growth factor receptor 2) human breast cancer cells with pegylated immunoliposomes bearing trastuzumab (Herceptin) and containing melittin from bee venom. These immunoliposomes decreased cancer cells viability in a dose-response manner and in correlation to their level of HER2 expression. The morphological changes observed in the treated cells suggested a cytolytic process. This preclinical approach may suppose an effective strategy for the treatment of HER2-overexpressing tumors. Trastuzumab resistant breast cancer cells (JIMT-1), can also be targeted using this approach.



Synergism of plant-derived polyphenols in adipogenesis: perspectives and implications. Herranz-López M, Fernández-Arroyo S, Pérez-Sanchez A, Barrajón-Catalán E, Beltrán-Debón R, Menéndez JA, Alonso-Villaverde C, Segura-Carretero A, Joven J, Micol V. Phytomedicine 19, 253-261. 2012.

We present here the full characterization of bioactive components of *Hibiscus sabdariffa* (HS) aqueous extracts, a widely recognised medicinal plant, and document their effects in a model of adipogenesis from 3T3-L1 cells and in hypertrophic and insulin-resistant adipocytes. Aqueous extracts were up to 100 times more efficient in inhibiting triglyceride accumulation when devoid of fibre and polysaccharides. Significant differences were also observed in reactive oxygen species generation and adipokine secretion. We also found that, when polyphenols were fractionated and isolated, the benefits of the whole extract were greater than the sum of its parts, which indicated a previously unnoticed synergism. In conclusion, polyphenols have interactive and complementary effects, which suggest a possible application in the management of complex diseases and efforts to isolate individual components might be irrelevant for clinical medicine and/or human nutrition.



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.

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Gema Osuna Tenorio
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PUBLICATIONS

1. Ferrandiz, C., Fernández-Carvajal, A. and Ferrer-Montiel, A. Rab4 Interacts With The Human P-Glycoprotein And Modulates Its Surface Expression In Multidrug Resistant K562 Cells. **Int J. Cancer 128,** 192-205. 2010.
2. Camprubí-Robles, M., Ferrer-Montiel, A. and Planells-Cases, R. Contribution of ion channel trafficking to nociceptor sensitization. **Open Pain Journal 3**, 108-116. 2010.
3. Laínez, S., Valente, P., Ontoria-Oviedo, I., Estevez-Herrera, J, Camprubí-Robles, M., Ferrer-Montiel, A. and Planells-Cases R. GABAA receptor-associated protein (GABARAP) modulates TRPV1 expression and channel activity. **FASEB J. 24,** 1958-1970**.** 2010.
4. Triano I., Barrera F. N., Renart M. L., Molina M. L., Fernández-Ballester G., Poveda J. A., Fernández A. M., Encinar J. A., Ferrer-Montiel A., Otzen D. and González-Ros J. M. Occupancy of non-annular lipid binding sites on kcsa greatly increases the stability of the tetrameric protein. **Biochemistry 49,** 5397-5404. 2010.
5. Pérez de Vega MJ, García-López MT, Zaccaro L, Royo M, Albericio F, Fernández-Carvajal A, Ferrer-Montiel A and González-Muñiz R. Solid-Phase Synthesis of New Trp(Nps)- Containing Dipeptide Derivatives as TRPV1 Channel Blockers. **Molecules** 15, 4924-4933. 2010.
6. Renart, M.L., Triano, I, Poveda, J.A., Encinar, J.A., Fernández, A.M., Ferrer-Montiel, A.V.**,** Gómez J. and González Ros J.M. Ion binding to KcsA: implications in ion selectivity and channel gating. **Biochemistry 49**, 9480-9487. 2010.
7. Planells-Cases, R, Camprubí-Robles, M., and Ferrer-Montiel, A. TRP Channel Trafficking. In "TRP channels in health and disease implications for diagnosis and therapy". Ed., A. Szallasi**: Nova Publishers**. 2011.
8. Planells-Cases R., Valente P., Ferrer-Montiel, A, Qin F. and Szallasi A. Complex regulation of TRPV1 and related thermoTRPs: implications for therapeutic intervention. In TRP Channels. **Adv. Exp. Med. Biol. 704**, 1958-1970. 2011.
9. Valente, P, Fernández-Carvajal A, Camprubí-Robles M, Gomis A, Fernandez-Ballester G, Viana F, Gonzalez Ros JM, Belmonte C, Planells-Cases, R, Ferrer-Montiel A. Membrane-tethered peptides patterned after the TRP domain (TRPducins) selectively inhibit TRPV1 channel activity. **FASEB J.** 25, 1628-1640. 2011.
10. Goswami, C., Kuhn, J., Dina, O., Fernández-Ballester, G., Ferrer-Montiel A., Levine, J.D., Hucho, T. PKCε induces destabilization of microtubules channel-independently via TRPV1**. J. Neurochem 117**, 995-1008. 2011.

11. Zaccaro L, García-López T, González-Muñiz R, García-Martínez C, Ferrer-Montiel A, Albercio F, Royo M. New modulators of TRPV1 receptors: structure-activity relationships using a rational combiantorial approach. **Biorg. Med. Chem. Lett. 21**, 3541-3545. 2011.

12. Gerona-Navarro G, González-Muñiz R, Fernández-Carvajal A, González-Ros JM, Ferrer-Montiel A, Carreño C, Albericio F, Royo M. Solid Phase synthesis of a library of amphipatic hydantoins. Discovery of new hits for TRPV1 blockade. **ACS Comb. Scien**. **13,** 458-465. 2011.

13. Devesa I, Planells-Cases R , González-Ros, JM, Ferrer-Montiel A, Fernandez-Carvajal A The role of the transient receptor potential vanilloid 1 (TRPV1) in inflammation and sepsis. **J. Inflammation. Res. 4,** 67-81. 2011.

14. Vidal M, Fernández-Carvajal A, Moure A, Valente P, Fernandez-Ballester G, Gonzalez Ros JM, Planells-Cases R, Bujons J, Ferrer-Montiel A and Messeguer A. Triazine-based TRPV1 antagonists: design, synthesis, evaluation and QSAR data**. J. Med. Chem 54,** 7441-7452. 2011.

15. Fernández-Ballester G, Fernández-Carvajal A, González-Ros JM and Ferrer-Montiel A. Ionic channels as targets for drug design: a review on computational methods. **Phamaceutics 3,** 932-953. 2011.

16. Fernández-Ballester G, Fernández-Carvajal A, Devesa I, Valenzuela B, Duart MJ, González-Ros JM and Ferrer-Montiel A. *In silico*-based direct evolution of peptides and peptidomimetics in drug discovery. **Curr. Topics. Pharmacol 15,** 35-55. 2011.

17. Fernández-Carvajal A, Fernández-Ballester G, Devesa I, González Ros JM, Ferrer-Montiel A. New strategies to develop novel pain therapies: addressing thermoreceptors from different points of view. **Pharmaceuticals 5,** 16-48. 2012.

18. Giudici AM, Molina ML, Ayala JL, Montoya E, Renart ML, Fernández AM, Encinar JA, Ferrer-Montiel AV, Poveda JA, González-Ros JM. Detergent-labile, supramolecular assemblies of KcsA: Relative abundance and interactions involved. **Biochim Biophys Acta 1828**, 193-200. 2012.

19. Ferrer-Montiel A, Fernández-Carvajal A, Planells-Cases R, Fernández-Ballester G, Messeguer A, González-Ros JM, González-Muñiz R. Advances in modulating thermosensory TRP channels. **Exp. Opin. Ther. Pat.** 22, 999-1017. 2012.

20. Renart ML, Montoya E, Fernández AM, Molina ML, Poveda JA, Encinar JA, Ayala JL, Ferrer-Montiel A, Gómez J, Morales A and González Ros JM. On the contribution of ion binding affinity to ion selectivity and permeation in KcsA, a model potassium channel. **Biochemistry** 51, 3891-3900. 2012.

21. Sanz-Salvador, L, Andrés-Borderia, A, Ferrer-Montiel A and Planells-Cases R. Agonist-dependent desensitization of trpv1 targets the receptor to lysosomes for degradation. **J. Biol. Chem.** 287, 19462-19471. 2012.

22. Navarro A, Encinar JA, López B, Aguado-Llera D, Prieto J, Gómez J, Martínez-Cruz LA, Millet O, González-Ros, JM, Fernández-Ballester G, Neira JL, and Ferrer-Montiel A**.** Mutation of Ser-50 and Cys-66 in Snapin modulate protein structure and stability. **Biochemistry 51**, 3470-3484. 2012.

23. Ponsati B, Carreño C, Curto-Reyes V, Valenzuela B, Duart MJ, Van Den Nest W, Fernandez J, Borsini F, Caprioli, Di Serio, Veretchy, Bonsi, Baamonde A, Menendez L, Barros F, De la Peña P, Borges R, Felipo V, Planells-Cases R, Ferrer-Montiel A. Compound DD04107, an inhibitor of neuronal exocytosis, displays safe in vivo,

long-lasting analgesic activity against chronic inflammatory and neuropathic pain. **J. Pharmacol. Exp. Ther.** 341, 634-645. 2012.

PATENTS

Inventores:	Antonio Ferrer-Montiel, Asia Fernández-Carvajal, Carlos Belmonte Martínez, Félix Viana, Juana Gallar
Titulo:	Pharmaceutical composition for the treatment of the dry ice.
Titular:	UMH (80%), CSIC (20%)
Registros:	P2010-31341 (08/09/2010)

Inventores:	Antonio Ferrer-Montiel, Asia Fernández-Carvajal, Gregorio Fernandez Ballester, José Manuel González Ros, Carlos Belmonte Martínez, Félix Viana, Ana Gomis, Pierluigi Valente y María Camprubí-Robles.
Titulo:	Peptides modulators of TRP receptors and their uses
Titular:	UMH (50%), DiverDrugs (40%), CSIC (10%)
Registros:	P2011-30052 (19/01/2011)

Inventores:	Antonio Ferrer-Montiel, Asia Fernández-Carvajal, Gregorio Fernandez Ballester, José Manuel González Ros, Carlos Belmonte Martínez, Félix Viana, Ana Gomis, Rosa María Planells-Cases, Miquel Vidal, Jordi Bujons, Angel Messeguer
Titulo:	Compounds modulators of TRP receptors and their uses.
Titular:	UMH (33%), CSIC (33%), CIPF (33%)
Registros:	P2011-30537 (05/04/2011)

Inventores:	Antonio Ferrer-Montiel, José Maria García Antón
Titulo:	Peptides modulators of PGC-1alfa
Titular:	Lipotec
Registros:	P2011-30439 (25/03/2011)

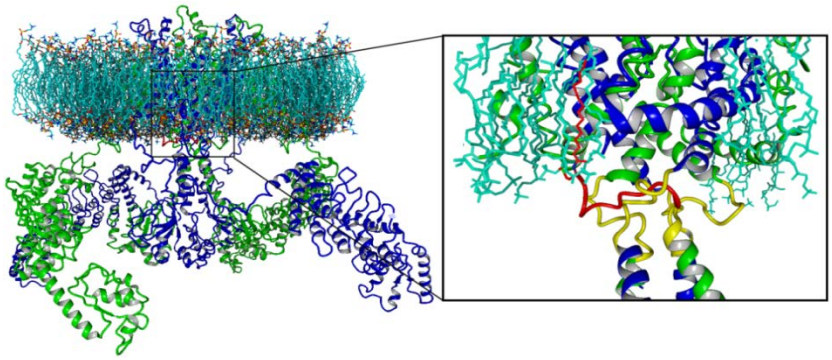
Inventores:	Antonio Ferrer-Montiel, José Maria García Antón
Titulo:	Peptides useful in the treatment and/or care of the skin and/or mucoses and their use in cosmetic or pharmacological compositions.
Titular:	Lipotec
Registros:	P2011-3044 (25/03/2011)

RESEARCH HIGHLIGHTS

Membrane-tethered peptides patterned after the TRP domain (TRPducins) selectively inhibit TRPV1 channel activity. Valente, P, Fernández-Carvajal A, Camprubí-Robles M, Gomis A, Fernandez-Ballester G, Viana F, Gonzalez Ros JM, Belmonte C, Planells-Cases, R, Ferrer-Montiel A. FASEB J. 25, 1628-1640. 2011.

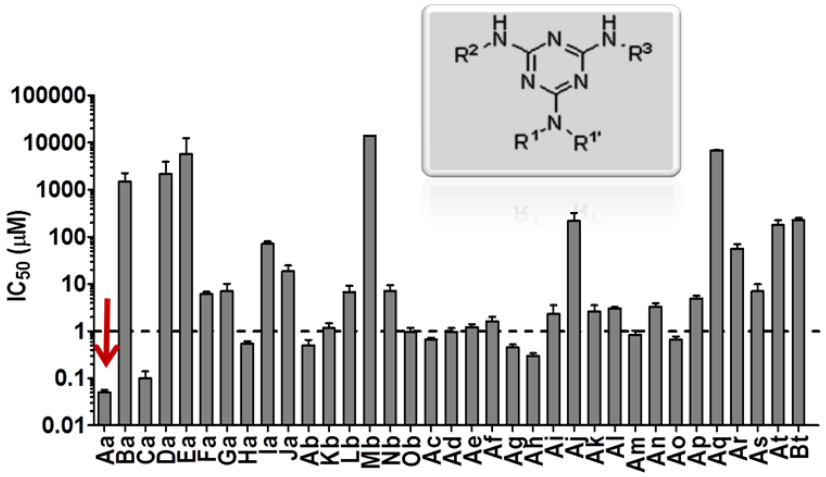
The design and validation of a family of allosteric modulators of TRPV1 channels with in vivo anti-nociceptive activity was reported. These compounds were coined with the name of TRPducins and they represent palmitoylated short peptides patterned after the TRP domain located in the C-terminal region of the receptor, adjacent to the pore gate. These peptides selectively inhibit the channel activity with potency in recombinant and native systems. Furthermore, they attenuated *in vivo* the thermal hyperalgesia and pruritus that develops in a chronic liver disease. TRPducins expand the pepducin concept from the

GPCR family to the field of ion channels, and pave the way for the specific targeting membrane proteins critically involved in cell signaling.



Triazine-based TRPV1 antagonists: design, synthesis, evaluation and QSAR data.
Vidal M, Fernández-Carvajal A, Moure A, Valente P, Fernández-Ballester G, González Ros JM, Planells-Cases R, Bujons J, Ferrer-Montiel A and Messeguer A. J. Med. Chem 54, 7441-7452. 2011

This article describes the design and development of TRPV1 uncompetitive antagonists that act as open channel blockers. In particular, triazine Aa is reported that blocks the channel activity with nanomolar activity, and exhibits an acceptable receptor selectivity. This compound also blocked native receptors and displayed in vivo anti-nociceptive activity against thermal nociception and pruritus in a model of chronic liver disease. These compounds are the first reported open channel blockers with a significant therapeutic potential.



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.

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PUBLICATIONS

1. Chico, V., Martinez-Lopez, A., Ortega-Villaizan, M., Falco, A., Perez, L., Coll, J. M. and Estepa, A.. Pepscan mapping of viral hemorrhagic septicemia virus glycoprotein G major lineal determinants implicated in triggering host cell antiviral responses mediated by type I interferon. **J Virol 84**, 7140-7150. 2010.

2. Encinas, P., Rodriguez-Milla, M. A., Novoa, B., Estepa, A., Figueras, A. and Coll, J. M.. Zebrafish fin immune responses during high mortality infections with viral haemorrhagic septicemia rhabdovirus. A proteomic and transcriptomic approach. **BMC Genomics 11**, 518-534. 2010.

3. Caturla, N., Estepa, A., and Micol, V. The Relationship between Oleuropein Antimicrobial Activity and its Effects on Biological Membranes. In Olives and olive oil in health and disease prevention. Chapter 150, pp. 1345-1354. Ed. Elsevier (Editors, V. Preedy, and C. Whatson). 2010. ISBN-13: 978-0-12-374420-3.

4. Ortega-Villaizan, M., Chico, V., Martinez-Lopez, A., Falco, A., Perez, L., Coll, J. M. and Estepa, A. In vitro analysis of the factors contributing to the antiviral state induced by a plasmid encoding the viral haemorrhagic septicaemia virus glycoprotein G in transfected trout cells. **Vaccine 29,** 737-743. 2011.

5. Balseiro, P., Falco, A., Romero, A., Dios, S., Martinez-Lopez, A., Figueras, A., Estepa, A. and Novoa, B. (2011). Mytilus galloprovincialis Myticin C: A Chemotactic Molecule with Antiviral Activity and Immunoregulatory Properties. **PLoS ONE 6,** e23140. 2011.

6. García, I., Galiana, A., Falcó, A., Estepa, A. and Perez, L. Characterization of an infectious 1 pancreatic necrosis (IPN) virus carrier cell culture with resistance to superinfection with heterologous viruses. **Veterinary Microbiol. 149**. 2011.

7. Encinas, P., Gomez-Casado, E., Estepa, A. and Coll, J. M.. An ELISA for detection of trout antibodies to viral haemorrhagic septicemia virus using recombinant fragments of their viral G protein**. J Virol Methods 176,** 14-23. 2011.

8. Encinas, P., Gomez-Sebastian, S., Nunez, M. C., Gomez-Casado, E., Escribano, J. M., Estepa, A. and Coll, J.. Antibody recognition of the glycoprotein g of viral haemorrhagic septicemia virus (VHSV) purified in large amounts from insect larvae. **BMC research notes 4**, 210. 2011.

9. Encinas, P., Gomez-Casado, E., Fregeneda, G., Olesen, N. J., Lorenzen, N., Estepa, A. and Coll, J. M.. Rainbow trout surviving infections of viral haemorrhagic septicemia virus (VHSV) show lasting antibodies to recombinant G protein fragments. **Fish Shellfish Immunol 30**, 929-935. 2011.

10. Gomez-Casado, E., Estepa, A. and Coll, J. M.. A comparative review on European-farmed finfish RNA viruses and their vaccines. **Vaccine 29,** 2657-2671. 2011.

11. Martinez-Alonso, S., Martinez-Lopez, A., Estepa, A., Cuesta, A. and Tafalla, C.. The introduction of multi-copy CpG motifs into an antiviral DNA vaccine strongly up-regulates its immunogenicity in fish. **Vaccine 29,** 1289-1296. 2011.

12. Falco A., Ortega-Villaizan M., Coll J.M., and Estepa A. Antigenicity and Immunogenicity of the Envelope Glycoprotein (gpG) of Viral Haemorrhagic Septicaemia Rhabdovirus (VHSV). Ed. Nova Science Publishers, Inc.NY (USA); 2011 (ISBN: 978-1-61761-591-7).

13. Estepa, A, Tafalla, C and Coll, JM. Defence mechanism against viral infections in fish: the trout/ viral haemorrhagic septicaemia (VHSV) rhabdovirus model. In Fish Defenses Volume 2: Pathogens, Parasites and Predators Chapter 3 pp 63-109. Ed. Science publishers (USA); 2011 (ISBN: 978-1-57808-407-4).

14. Martínez López, A., Chinchilla, B., Encinas, P., Gómez-Casado, E., Estepa, A., Coll JM. Replacement of the human cytomegalovirus promoter with fish enhancer core elements to control the expression of the G gene of viral haemorrhagic septicemia virus (VHSV). **J. Biotechnol**. **164**, 171-178. 2012.

15. Ortega-Villaizan, M., Martínez-López, A., García-Valtanen, P., Chico, V., Pérez, L., Coll JM, Estepa, A. Ex vivo transfection of trout pronephros leukocytes, a model for cell culture screening of fish DNA vaccine candidates. **Vaccine 30**, 5983-5990. 2012.

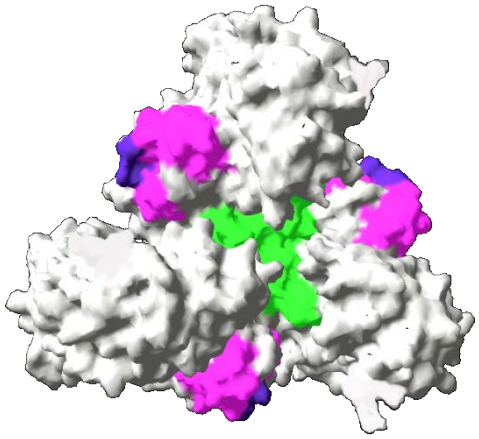
16. Pereiro, P., Martínez-López, A., Falcó, A., Dios, S., Figueras, A., Coll, J.M., Novoa, B., Estepa, A. Protection and antibody response induced by intramuscular DNA vaccine encoding for viral haemorrhagic septicaemia virus (VHSV) G glycoprotein in turbot (*Scophthalmus maximus*). **Fish Shellfish Immunology. 32**, 1088-1094. 2012.

17. Martínez-López, A., Encinas P., García-Valtanen P., Gómez-Casado, E., Estepa, A. Improving the safety of viral DNA vaccines: development of vectors containing both 5' and 3' homologous regulatory sequences from non-viral origin. **Appl Mycrobiol Biotechnol.** 2012 (doi: 10.1007/s00253-012-4403-7).

18. Falcó A., Martínez-López, A., Coll, J.M., Estepa, A. The potential for antimicrobial peptides to improve fish health in aquaculture. Infectious disease in aquaculture. pp. 457-479. Cambridge Woodhead Publishing. 2012. ISBN 978-0-8579-016-4.

RESEARCH HIGHLIGHTS

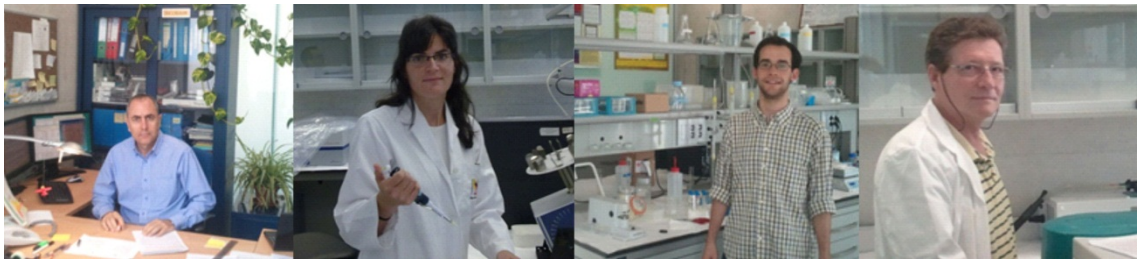
Pepscan mapping of viral hemorrhagic septicemia virus glycoprotein G major lineal determinants implicated in triggering host cell antiviral responses mediated by type I interferon. Chico, V., Martinez-Lopez, A., Ortega-Villaizan, M., Falco, A., Perez, L., Coll, J. M. and Estepa, A. Journal of virology 84, 7140-7150. 2012.



Surface glycoproteins of enveloped virus are potent elicitors of type I interferon (IFN)-mediated antiviral responses in a way that may be independent of the well-studied genome-mediated route. However, the viral glycoprotein determinants responsible for initiating the IFN response remain unidentified. In this study, we have used a collection of 60 synthetic 20-mer overlapping peptides (pepscan) spanning the full-length of the glycoprotein G (gpG) of viral haemorrhagic septicaemia (VHS) virus to investigate what regions of this protein are implicated in triggering the type I interferon (IFN)-associated immune responses. Briefly, two regions with ability to increase several-fold the basal expression level of the IFN-stimulated mx gene and to restrict the spread of virus among responder cells were mapped to amino acid residues 280 to 310 and 340 to 370 of the gpG of VHSV. In addition, the results obtained suggest that an interaction between VHSV gpG and integrins might trigger the host IFN-mediated antiviral response after VHSV infection. Since it is known that type I IFN plays an important role in determining/modulating the protective antigen-specific immune responses, the identification of viral glycoprotein determinants directly implicated in the type I IFN induction might be of special interest for designing new adjuvants and/or more efficient and cost-effective viral vaccines as well as to improve our knowledge on how to stimulate the innate immune system.

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.

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Miguel Ramos Baddouh

PUBLICATIONS

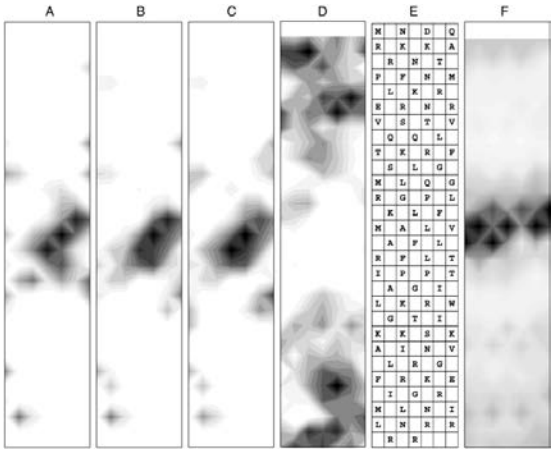
1. Guillén, J, González-Alvarez, A, Villalaín, J. A membranotropic region in the C-terminal domain of hepatitis C virus protein NS4B interaction with membranes. **Biochim Biophys. Acta. Biomembranes 1798**, 327-37. 2010.
2. Palma-Guerrero, J, Lopez-Jimenez, JA, Pérez-Berná, AJ, Huang, IC, Jansson, HB, Salinas, J, Villalaín, J, Read, ND, Lopez-Llorca, LV. Membrane fluidity determines sensitivity of filamentous fungi to chitosan. **Mol. Microbiol. 75**, 1021-32. 2010.
3. Palomares-Jerez, MF, Guillén, J, Villalaín, J. Interaction of the N-terminal segment of HCV protein NS5A with model membranes. **Biochim Biophys. Acta. Biomembranes**. **1798,** 1212-24. 2010.
4. Villalaín, J. Membranotropic effects of arbidol, a broad anti-viral molecule, on phospholipid model membranes. **J. Phys. Chem. B**. **114,** 8544-54. 2010.
5. Nemésio, H, Palomares-Jerez, F, Villalaín, J. The membrane-active regions of the dengue virus proteins C and E. **Biochim. Biophys. Acta. Biomembranes 1808,** 2390-402. 2011.
6. Palomares-Jerez, MF, Villalaín, J. Membrane interaction of segment H1 (NS4B(H1)) from hepatitis C virus non-structural protein 4B. **Biochim Biophys. Acta. Biomembranes 1808**, 1219-29. 2011.
7. Muñoz, F, Palomares-Jerez, MF, Daleo, G, Villalaín, J, Guevara, MG. Cholesterol and membrane phospholipid compositions modulate the leakage capacity of the swaposin domain from a potato aspartic protease (StAsp-PSI). **Biochim. Biophys. Acta. 1811**, 1038-44. 2011.
8. Ordóñez, MV, Guillén, J, Nercessian, D, Villalaín, J, Conde, RD. Secondary structure determination by FTIR of an archaeal ubiquitin-like polypeptide from Natrialba magadii. **Eur Biophys J. 40**, 1101-7. 2011.
9. Palomares-Jerez F., Villalaín, J. The membrane spanning domains of protein NS4B from Hepatitis C virus. **Biochim Biophys Acta. Biomembranes 1818**, 2958-2966. 2012.
10. Nemésio, H., Palomares-Jerez, F., Villalaín, J. NS4A AND NS4B proteins from dengue virus: Membranotropic regions. **Biochim Biophys. Acta. Biomembranes 1818**, 2818-2830. 2012.
11. Palomares-Jerez, F., Nemésio, H., Villalaín, J. Interaction with membranes of the full c-terminal domain of protein NS4B from Hepatitis C virus. **Biochim Biophys Acta. Biomembranes 1818**, 2536-2549. 2012.

RESEARCH HIGHLIGHTS

The membrane-active regions of the dengue virus proteins C and E. Nemésio, H, Palomares-Jerez, F, Villalaín, J. Biochim Biophys Acta. Biomembranes 1808, 2390-2402 (2011).

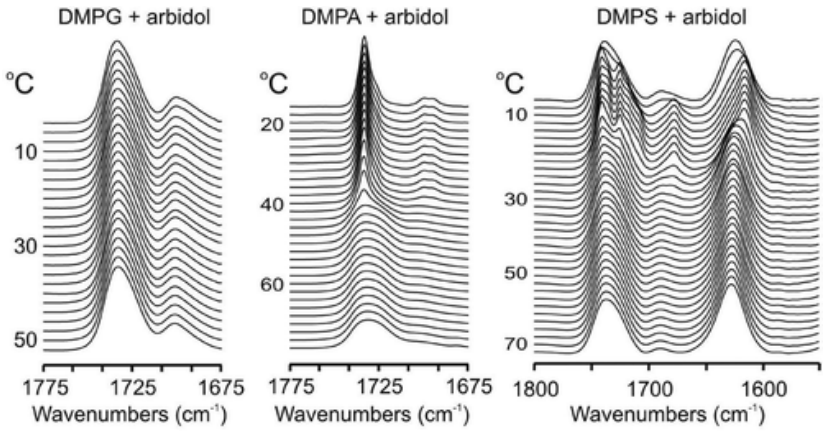
In this work we identified the membranotropic regions of proteins C and E of DENV virus by performing an exhaustive study of membrane rupture induced by two C and E-derived peptide libraries on model membranes having different phospholipid compositions as well as its ability to modulate the DEPE L(β)-L(α) and L(α)-H(II) phospholipid phase transitions. Protein C presents one hydrophobic leakage-prone region coincidental with a

proposed membrane interacting domain, whereas protein E presents five membrane-rupture zones coincidental with different significant zones of the protein, i.e., the fusion peptide, a proline-rich sequence, a sequence containing a hydrophobic pocket as well as the stem and transmembrane domains of the protein. These membrane-active segments should have a vital role in viral membrane fusion, formation of the replication complex and morphogenesis and therefore be attractive targets for development of new anti-viral compounds.



Membranotropic effects of arbidol, a broad anti-viral molecule, on phospholipid model membranes. Villalaín, J. J. Phys. Chem B. 114, 8544-8554. 2010.

This article describes the biophysical characterization of the interaction of a broad and potent antiviral molecule, arbidol, with biomembranes. We show that it incorporates rapidly into membranes and interacts and modifies the physicochemical properties of the phospholipids in the membrane, having a significant effect on negatively charged phospholipids but a minor one on zwitterionic phospholipids, and participates in hydrogen bonding either with water or the phospholipid or both, decreasing the hydrogen bonding network of the phospholipids giving place to a phospholipid phase similar to the dehydrated solid one. These data suggest that the potent antiviral effects of arbidol are mediated at least in part through its membranotropic effects, giving place to the formation of perturbed membrane structures and these modifications should be responsible for its broad antiviral activity.



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

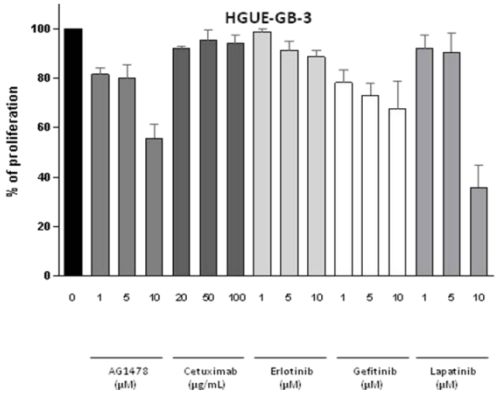
1. Menéndez-Gutiérrez MP, Ferragut JA, García-Morales P, Martínez-Lacaci I, Ferragut JA, Saceda M. Serin proteases in histone deacetylase inhibitor-induced apoptosis still an unresolved question. **Mol Cancer Ther. 9,** 241-24. 2010.
2. Carrasco-García E, Saceda M, Grasso S, Rocamora-Reverte L, Conde M, Gómez-Martínez A, García-Morales P, Ferragut JA, Martínez-Lacaci I. Small tyrosine kinase inhibitors interrupt EGFR signaling by interacting with erbB3 and erbB4 in glioblastoma cell lines. **Exp Cell Res. 317**, 1476-89. 2011.
3. Simó C, Ibáñez C, Gómez-Martínez A, Ferragut JA, Cifuentes A. Is metabolomics reachable? Different purification strategies of human colon cancer cells provide different CE-MS metabolite profiles. **Electrophoresis. 32**, 1765-77. 2011.
4. Manzano JI, Carvalho L, García-Hernández R, Poveda JA, Ferragut JA, Castanys S, Gamarro F. Uptake of the antileishmania drug tafenoquine follows a sterol-dependent diffusion process in Leishmania. **J. Antimicrob Chemother. 66**, 2562-5. 2011.
5. Rocamora-Reverte, L., Carrasco-García, E., Ceballos-Torres, J., Prashar, S., Goran, Kaluđerović, G.N., Ferragut, J.A., Gómez-Ruiz, S. Study of the anticancer properties of tin (IV) carboxylate complexes on a panel of human tumor cell lines. **ChemMedChem 7,** 301-310. 2012.
6. Cerezo D, Lencina M, Ruiz-Alcaraz AJ, Ferragut JA, Saceda M, Sanchez M, Cánovas M, García-Peñarrubia P, Martín-Orozco E. Acquisition of MDR phenotype by leukemic cells associates with an increase of caspase-3 activity and a collateral sensitivity to cold stress. **J. Cell. Biochem. 113**, 1416-1425. 2012.
7. Herrero, M., Castro-Puyana, M., Rocamora-Reverte, L., Ferragut, J.A., Cifuentes, A., Ibáñez, E. Formation and relevance of 5-hydroxymethylfurfural in bioactive subcritical water extracts from olive leaves. **Food Res Int 47**, 31–37. 2012.
8. Fernández-Arroyo, S., Gómez-Martínez, A., Rocamora-Reverte, L., Quirantes-Piné, R., Segura-Carretero, A., Fernández-Gutiérrez, A., Ferragut, J.A. Application of nanoLC-ESI-TOF-MS for the metabolomic analysis of phenolic compounds from extra-virgin olive oil in treated colon-cancer cells. **J. Pharm Biomed Anal 63,** 128-134. 2012.
9. Ibáñez C, Simó C, García-Cañas V, Gómez-Martínez A, Ferragut JA, Cifuentes A. CE/LC-MS Multiplatform for Broad Metabolomic Analysis of Dietary Polyphenols Effect on Colon Cancer Cells Proliferation. **Electrophoresis 33,** 2328-2336. 2012.
10. Valdés A, Simó C, Ibáñez C, Rocamora-Reverte L, Ferragut JA, García-Cañas V, Cifuentes A. Effect of dietary polyphenols on K562 leukemia cells: A Foodomics approach. **Electrophoresis 33**, 2314-2327. 2012.

11. Ibáñez C, Valdés A, García-Cañas V, Simó C, Celebier M, Rocamora-Reverte L, Gómez-Martínez A, Herrero M, Castro-Puyana M, Segura-Carretero A, Ibáñez E, Ferragut JA, Cifuentes A. Global Foodomics strategy to investigate the health benefits of dietary constituents**. J Chrom A 1248,** 139-153. 2012.
12. Valdés A, García-Cañas V, Rocamora-Reverte L, Gómez-Martínez A, Ferragut JA, Cifuentes A. Effect of rosemary polyphenols on human colon cancer cells: transcriptomic profiling and functional enrichment analysis. **Genes Nutr** 2012 (doi: 10.1007/s12263-012-0311-9).
13. Balaguer TM, Gómez-Martínez A, García-Morales P, Lacueva J, Calpena R, Reverte LR, Riquelme NL, Martinez-Lacaci I, Ferragut JA, Saceda M. Dual regulation of P-glycoprotein expression by Trichostatin A in cancer cell lines. **BMC Molecular Biology 13**, 25. 2012.
14. Grasso, S., Menéndez-Gutiérrez, M.P., Carrasco-García, E., Mayor-López, L., Tristante, E., Rocamora-Reverte, L., García-Morales, P., Ferragut, J.A., Saceda, M., Martínez-Lacaci, I. Cell Death and Cancer. Novel Therapeutic Strategies (2012). Apoptosis and medicine, pp: 67-110. (T.M. Ntuli ed.) InTech-Open Access Publisher, Rijeka, Croatia, ISBN 980-953-307-491-2.

RESEARCH HIGHLIGHTS

Small tyrosine kinase inhibitors interrupt EGFR signalling by interacting with erbB3 and erbB4 in glioblastoma cell lines. Estefanía Carrasco-García, Miguel Saceda, Silvina Grasso, Lourdes Rocamora-Reverte, Mariano Conde, Ángeles Gómez-Martínez, Pilar García-Morales, José A. Ferragut, Isabel Martínez-Lacaci. **Exp Cell Res. 317**, 1476-89. 2011.

Signalling through the epidermal growth factor receptor (EGFR) is relevant in glioblastoma. We have determined the effects of small-molecule EGFR tyrosine kinase inhibitors (AG1478, gefitinib, erlotinib and lapatinib) in glioblastoma cell lines and in primary cultures obtained from patients and found that these cells were very sensitive to these drugs. However, the EGFR monoclonal antibody, cetuximab had no effect on cell proliferation. Activity of downstream signalling molecules of EGFR such as Akt and especially ERK1/2 was interrupted with EGFR tyrosine kinase inhibitors, whereas cetuximab treatment could not sustain this blockade over time. Small-molecule EGFR inhibitors were able to prevent phosphorylation of erbB3 and erbB4, whereas cetuximab only hindered EGFR phosphorylation, suggesting that EGFR tyrosine kinase inhibitors may mediate their anti-proliferative effects through other erbB family members. We can conclude that small-molecule EGFR inhibitors may be a therapeutic approach for the treatment of glioblastoma patients.



Other activities

PhD THESES

"Implicación del dominio TRP en la región carboxilo terminal de TRPV1 en la oligomerización y acoplamiento funcional del termorreceptor". **Nuria García Sanz.** Supervisors: Antonio Ferrer-Montiel and Rosa Planells-Cases, 15 December 2010.

"Iones y fosfolípidos como efectores en la estructura y estabilidad del canal de potasio KcsA". **María Lourdes Renart Pérez**. Supervisor: José Manuel González-Ros, 16 December 2010.

"Caracterización estructural y funcional de la proteína vesicular Snapin" **Aaron Navarro i García.** Supervisors: Antonio Ferrer-Montiel and Gregorio Fernández-Ballester, 16 September 2011.

"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.

"Caracterización analítica de extractos vegetales y evaluación de su actividad en modelos celulares y animales". **Salvador Fernández Arroyo**. Supervisors: Antonio Segura, Alberto Fernández and Vicente Micol, 26 March 2012.

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

"Estrategias para el diseño de nuevos antivirales y antimicrobianos". **Rosa Doménech Mata**. Supervisor: José Luis Neira, 16 November 2012.

"Biophysical characterization of the membranotropic regions of the non-structural proteins NS5A and NS4B from hepatitis C virus". **María Francisca Palomares Jerez**. Supervisor: José Villalaín, 14 December 2012.

SCIENCE COMMUNICATION

Organization of meetings

Córdoba, Spain, September 14, 2010
II FORO DEL EMPRENDEDOR. XXXIII CONGRESO DE LA SOCIEDAD ESPAÑOLA DE BIOQUÍMICA Y BIOLOGÍA MOLECULAR.

- **A. Ferrer.** Co-organizer

Elche, Spain, December 2-3, 2010

TRP CHANNELS AND SENSORY BIOLOGY

- **A. Ferrer.** Co-organizer

Imola, Italy, July 2011
3nd ITALIAN-SPANISH-PORTUGUESE WORSHOP IN BIOPHYSICS AND MOLECULAR BIOLOGY OF ION CHANNELS AND TRANSPORTERS

- **A. Ferrer.** Co-organizer

Barcelona, Spain, September 4, 2011
III FORO DEL EMPRENDEDOR
XXXIII CONGRESO DE LA SOCIEDAD ESPAÑOLA DE BIOQUÍMICA Y BIOLOGÍA MOLECULAR.

- **A. Ferrer. Co-organizer**

Alicante, Spain, February 1-3, 2012
XIII IBERIAN PEPTIDE MEETING

- **J. Villalain** and **A. Ferrer.** Co-organizers

Sevilla, Spain, September 4-9, 2012
22nd IUBMB and 37th FEBS Congress

- **A. Ferrer.** Co-organizer

Sevilla, Spain, September 4-9, 2012
IV FORO DEL EMPRENDEDOR. 22nd IUBMB and 37th FEBS Congress

- **A. Ferrer.** Co-organizer

Valencia, Spain, September 12-14, 2012
INTERNATIONAL WORKSHOP ON TRANSIENT RECEPTOR POTENTIAL CHANNELS

- **A. Ferrer.** Co-organizer

Bilbao, Spain, September 19-21, 2012
Biospain 2012 International Meeting/ Congreso de la Sociedad Española de Biotecnología (BIOTEC 2012).

- **J.M. Sanz**. Organizing Committee.

La Habana, Cuba, September 24-28, 2012
II Congreso Internacional LABIOFAM 2012. Simposio de productos naturales en la terapia contra el cáncer

- **V. Micol**. Organizing Committee.

La Habana, Cuba, September 24-28, 2012
II Congreso Internacional LABIOFAM 2012. Simposio de productos naturales en la terapia contra el cáncer

- **A. Estepa**. Organizing Committee.

Universidad Miguel Hernández. Elche, Spain, October 19, 2012
…Y tú qué investigas? I JORNADAS IBMC para el fomento de las vocaciones científicas

- **A. Ferrer**, Organizer. **A. Estepa**, Co-organizer.

Marjal Costa Blanca EcoCamping Resort. Elche, Alicante, October 25, 2012
III JORNADAS DE GASTRONOMIA SALUDABLE DE LA EPSO (UMH).

- **N. Martí.** Organizer.

Lisbon, Portugal, November 21-23
II International Conference on Antimicrobial Research (ICAR2012).
(http://www.formatex.org/icar2012)

- **A. Estepa**, Co-organizer.

Elche, Spain, January-December 2012
Research seminars Program (IBMC-UMH)

- **R. Mallavia**, Organizer.

Invited talks and courses

Madrid, Spain, February 2010.
Facultad Medicina. Universidad Complutense de Madrid.

- **A. Ferrer**. "Ying y Yang in thermal sensation".

Madrid, Spain, April 23, 2010
Instituto de Química Médica, CSIC.

- **A. Ferrer. "**TermoTRPs: Ying and Yang in thermal sensation".

Valencia, Spain, October 26, 2010
Sociedad Española de químicos cosméticos. Workshop "Evolución de la Neurocosmética".

- **A. Ferrer. "**Inflamación neurogénica y piel sensible: un paradigma para nuevos cosmecéuticos"**.**

Baeza, Spain, November 2-4, 2010.
Universidad International de Andalucía. Workshop on "Ion channels and diseases of the central nervous system".

- **A. Ferrer.** "Complex regulation of TRPV1: Implications for nociception and pain".

Elche, Spain, December 2, 2010
Jornada: Alternativas Tecnológicas a la Situación Actual.

- **A. Ferrer**. "Los laboratorios universitarios como nichos de negocio".

Elche, Spain, December 2-3, 2010.
Workshop: TRP Channels and Sensory Biology.

- **A. Ferrer**. "TRP domain: implications for TRPV1 channel function".
- **A. Fernández-Carvajal.** "Modulators of TRPV1".
- **G. Fernández Ballester. "**Molecular modeling of TRPV1".

Elche, Spain, December 10, 2010
Instituto de Bioingeniería, Universidad Miguel Hernández.

- **A. Ferrer**. "Bases moleculares del dolor".

Tenerife, Spain, February 2-4, 2011
Workshop: Trends and Challenges in Ion Channel Research. III Reunión de la Red Nacional de Canales Iónicos.

- **A. Ferrer**. "TRPducins a novel paradigm to modulate ion channel activity".

Murcia, Spain, June 2-4, 2011
XXV Congreso de la Sociedad de Biofísica de España. Simposio en Canales iónicos.

- **A. Ferrer**. "Papel del dominio TRP de TRPV1 en la función".

Valencia, Spain, September 18-21, 2011.
XVI Congress of the SEQT.

- **A. Ferrer**. "TRPducins: a novel paradigm to modulate ion channel activity".

Alicante, Spain, October 21, 2011.
Instituto de Neurociencias de Alicante, UMH-CSIC.

- **A. Ferrer**. "Pharmacological modulation of Ion Channels".

New Delhi, India, November 22-24, 2011.
17th Technological Summit & Technology Platform. India-Spain Join Scientific workshop on Health and Medical Research.

- **A. Ferrer**. "Pharmacology of Pain Management".

Bilbao, Spain, December 13-14, 2011.
Bioforo Pain: from individual perception to treatment through molecular biology.

- **A. Ferrer**. "Good vs. bad pain: molecular insights and pharmacology".

Alicante 1-3 February, 2012.
XIII Iberian Peptide Meeting,

- **A. Fernández-Carvajal.** "Peptidomimetics design and function: peptides patterned after the TRP domain of TRPV1 channel".

Universidad de Murcia, Spain, February 2012.
Conferencia invitada. Departamento de Bioquímica y Biología Molecular A.

- **J.M. Sanz.** "Nanobiotecnología de proteínas: un pequeño gran universo"

Universidad de Murcia, Spain, February 2012.
Conferencia invitada. Departamento de Bioquímica y Biología Molecular A.

- **V. Micol** "Sinergia de compuestos polifenólicos en modelos celulares de adipogénesis".

Universidad Miguel Hernández, Elche, Spain, February 2012.
Conferencia invitada. Instituto de Bioingeniería.

- **J.M. Sanz.** "Nanobiotecnología de proteínas: un pequeño gran universo"

Universidad de Granada, CIDAF, Granada, Spain, 3 March, 2012
Jornada: "Nuevas tendencias en alimentación funcional: legislación, producción y marketing".

- **V. Micol. "**Desarrollo de un ingrediente funcional aplicado a patologías relacionadas con el síndrome metabólico".

Barcelona, Spain, March 9, 2012.
Universidad de Barcelona. Hot topics "NEUROPATHIC PAIN".

- **A. Ferrer**. A TR(i)P to pain transduction.

Napoles, Italy, June 7-10, 2012
13th Naples Workshop on Bioactive Peptides.

- **A. Ferrer**. "TRPducins: a new peptide-based paradigm to modulate ion channel activity".

Segovia, Spain, June 9-11, 2012
Frontiers in Ion Channel Research. New findings and new challenges.

- **A. Ferrer**. "Allosteric modulation of TRPV1channels as a novel pharmacological strategy".

Barcelona, Spain, July 2-7, 2012
XII Congress Sociedad de Biofísica de España.

- **A. Ferrer**. "Structure-function relationships in a thermoTRP channel" Barcelona.

Sevilla, Spain, September 4-9. 2012.
22nd IUBMB and 37th FEBS Meeting.

- **A. Ferrer**. "TRPducins: a novel paradigm to modulate ion channel signaling".

Sevilla, Spain, September 4-9 2012.
22nd IUBMB and 37th FEBS Meeting.

- **A. Ferrer**. "A bioentrepreneurial experience: learning from failure".

Valencia, Spain, September 12-14-9 2012.
International Workshop on Transient Receptor Potential Channels

- **G. Fernández-Ballester.** "Structural insights into the dynamics of the TRPA1 activation mechanism".

Bilbao, October 4, 2012,
CIC BioGune.

- **A. Ferrer**. "Molecular Basis of Thermosensation".

La Habana, Cuba, September 24, 2012
Congreso internacional LABIOFAM 2012. Simposio Productos naturales en la terapia del cáncer.

- **V. Micol**. "Productos naturales y su vehiculización en liposomas para la terapia antitumoral. Curso precongreso".

La Habana, Cuba, September 26, 2012
Congreso internacional LABIOFAM 2012. Simposio Productos naturales en la terapia del cáncer.

- **A. Estepa**. "Nuevas estrategias de vacunación DNA frente a virus en peces".

La Habana, Cuba, September 27, 2012
Congreso internacional LABIOFAM 2012. Simposio Productos naturales en la terapia del cáncer.

- **V. Micol**. "Efecto de polifenoles de origen vegetal en la adipogénesis y la hiperlipemia. Aplicaciones en patologías asociadas al síndrome metabólico".

Novelda, Alicante, Octubre 16, 2012
VI Semana de la Ciencia Casino de Novelda.

- **R. Mallavia**. "¿Nanotecnología, y esto qué es?"

Tarragona, Spain, October 25, 2012

- **R. Mallavia.** *"Diseño, síntesis, caracterización y aplicaciones de polifluorenos". Universitat Rovira i Virgili.*

Tbilisi State University, Tbilisi, Georgia, November 1-3, 2012
European Project MAPB Meeting. Program TEMPUS IV

- **D. Saura**. "Nutraceuticals Ingredients"

Yereban State University, Yereban, Armenia, November 3-5, 2012
European Project MAPB Meeting. Program TEMPUS IV

- **D. Saura**. "Nutraceuticals Ingredients"

Tbilisi State University, Tbilisi, Georgia, November 1-3, 2012
European Project MAPB Meeting. Program TEMPUS IV

- **N. Martí**. "Functional Beverages"

Yereban State University, Yereban, Armenia, November 3-5, 2012
European Project MAPB Meeting. Program TEMPUS IV

- **D. Saura**. "Functional Beverages"

Universidad de Granada, Spain, February, 2012
Advanced Course. EXPERTO EN ALIMENTOS FUNCIONALES Y NUTRACÉUTICOS.

- **D. Saura**. Módulo VII. Bebidas Funcionales.

Universidad de Granada, Spain, February, 2012
Advanced Course. EXPERTO EN ALIMENTOS FUNCIONALES Y NUTRACÉUTICOS.

- **N. Martí**. Módulo VII. Bebidas Funcionales.

Molina de Segura, Murcia, December 23, 2012
Centro Integrado de Formación y Experiencias Agrarias, CIFEA. Centro de Referencia del Ministerio de Agricultura. Consejería de Agricultura de la Comunidad de Murcia.

- **D. Saura**. "Introducción al análisis sensorial desde el punto de vista fisiológico. Curso de Analisis Sensorial."

Molina de Segura, Murcia, December 17-21, 2012
Centro Integrado de Formación y Experiencias Agrarias, CIFEA. Centro de Referencia del Ministerio de Agricultura. Consejería de Agricultura de la Comunidad de Murcia.

- **D. Saura**. "Curso de aprovechamiento de subproductos de la industria transformadora de tomate, cebolla, brócoli y alcachofa."

Molina de Segura, Murcia, December 17-21, 2012
Centro Integrado de Formación y Experiencias Agrarias, CIFEA. Centro de Referencia del Ministerio de Agricultura. Consejerí Agricultura de la Comunidad de Murcia.

- **N. Martí**. "Curso de aprovechamiento de subproductos de la industria transformadora de tomate, cebolla, brócoli y alcachofa."

Universidad Pablo de Olavide, Sevilla, Spain, November-December, 2012
Master Universitario en "Ciencia y Tecnología de Aceites y Bebidas Fermentadas".

- **D. Saura**. Módulo II. Conocimiento avanzado de los agentes y procesos de transformación de bebidas fermentadas y zumos. Módulo III. Tecnología de bebidas fermentadas y zumos.

Universidad Pablo de Olavide, Sevilla, Spain, November-December, 2012
Master Universitario en "Ciencia y Tecnología de Aceites y Bebidas Fermentadas".

- **N. Martí**. Módulo III. Tecnología de bebidas fermentadas y zumos.

Science dissemination: outreach activities

Centro Cultural Virgen de Carmen, Torrevieja, Alicante, Spain, 23 November, 2010
II Ciclo de Divulgación Científica. Semana de la Ciencia (MICINN). A. C. Ars Creatio.

- **V. Micol.** "¿Nuevas estrategias nanotecnológicas para el tratamiento del cáncer".

Centro Cultural Virgen del Carmen, Torrevieja, Alicante, Spain, 22 November, 2011
III Ciclo de Divulgación Científica. Semana de la Ciencia (MICINN). A. C. Ars Creatio.

- **V. Micol.** "¿Podemos evitar las complicaciones asociadas a la obesidad a través de la dieta?".

Elche, Spain, October 19, 2012
…Y tú qué investigas? I JORNADAS IBMC SOBRE VOCACIONES CIENTÍFICAS

- **A. Ferrer**. The Spanish Ion Channel Initiatitive

Elche, Spain, November 29, 2012
Jornada de Divulgación "*Ciencia con tapas*"

- **A. Ferrer**.

Artículos de divulgación científica. A.C. Ars Creatio.

- **R. Mallavia.** "Polímeros que fluorecen en el azul: polifluorenos". Revista Digital de la Asociación *Ars Creati,* nº 28, Otoño 2012 (ISSN: 1885-4524).
- **L. Pérez García-Estañ. "**Cómo diseñar vacunas para peces. Modelos celulares de infecciones virales*"*. Revista Digital de la Asociación *Ars Creatio*, nº 28, Otoño 2012 (ISSN: 1885-4524).

Free Communications

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

- National: 31
- International: 82

Awards

Premio Bruker España SA 2012. Sociedad de Biofísica de España (SBE). **A. Ferrer**

GOVERNMENTAL PROJECTS AND FUNDING

Proyectos del Plan Nacional de I+D+i. Ministerio de Ciencia e Innovación. "Estudio de interacciones funcionalmente relevantes en proteínas de membrana: Allanando el camino a nuevas aproximaciones al descubrimiento de fármacos". (BFU2008-00602/BMC; 2009-2011). IP: **J.M. González-Ros.**

Proyectos del Plan Nacional de I+D+i. Dirección General de Investigación. MEC "Analisis de la capacidad antimicrobiana e inmunomoduladora de polifenoles glicosilados de especies vegetales mediterráneas: actividad in vitro e in vivo. Aplicaciones en alimentación funcional" (Ref: AGL2007—60778; 2007-2010). IP: **V. Micol.**

Generalitat Valenciana. Ayudas Complementarias a Proyectos Nacionales. "Ayuda Complementaria al Proyecto AGL2007—60778 (2010). IP: **V. Micol.**

The Spanish Ion Channel Initiative (SICI). Ministerio de Ciencia e Innovación. Proyectos CONSOLIDER-INGENIO 2010 (CSD2008-00005; 2008-2013). Coordinator and IP: **A. Ferrer**.

Proyectos del Plan Nacional de I+D+i. Ministerio de Ciencia e Innovación. "Polifenoles de origen alimentario: Una aproximación nutrigenómica sobre su actividad frente a cáncer de colon y leucemia". (MCINN AGL2008-05108-CO3-02/ALI; 2008-2011). IP: **J. A Ferragut.**

Comisión Europea (FP7). "Combating Antibiotics Resistant Pneumococci by Novel Strategies Based on in vivo and in vitro Host – Pathogen Interactions (CAREPNEUMO)" (Project HEALTH-F3-2009-223111) (March 2009-February 2012). IP subproyecto UMH: **J.M. Sanz.**

Proyecto del Subprograma Acción integrada 2009. Ministerio de Ciencia e Innovación. "Blend films of fluorene copolymers for optoelectronic and sensing applications" (Ref: PT2009-0002; 2010-2012). IP: **R. Mallavia.**

Proyectos de Investigación Fundamental no Orientada 2010. 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; 2011-2013). IP: **J.M. Sanz.**

Proyectos de Investigación Fundamental no Orientada 2011. Ministerio de Ciencia e Innovación. **"**Polielectrolitos conjugados multifuncionales y nanoestructurados como plataformas terapéuticas "(Ref: MAT2011-23007; 2012-2014). **IP: R. Mallavia.**

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" (Ref: AGL2011-28921-C03-ACU; 2012-2014). IP: **A. Estepa.**

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" (Ref: CTQ2011-24393); 2012 - 2014). IP: **F. J. Gómez.**

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 2011. Ministerio de Economía y competitividad: "The potassium channel KcsA: A versatile workbench to progress in ion channel structure, function and drug discovery studies "(Proyecto BFU2011-25920, 2012-2014). IP: **J.M. González Ros.**

Proyectos de Investigación Fundamental no Orientada 2012. Ministerio de Economía y competitividad. "Mechanisms and pharmacological modulation of inflammatory nociceptor sensitization" (BFU2012-39092-C02-01; 2013-2015). IP: **A. Ferrer**.

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

Proyectos de Infraestructuras del Ministerio de Economía y Competitividad. "Adquisición infraestructura. Patch Clamp automático" (UMHE10-3E-409; 2011-2012). IP: **A. Ferrer**.

Generalitat Valenciana. Ayudas para la contratación de personal de apoyo en organismos de investigación de la Entidad de realización: Universidad Miguel Hernández de Elche (2010) IP: **J.M. Sanz.**

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. "Adquisición infraestructura para Parque Científico Elche" (PPC/2010/023, 2010). IP: **A. Ferrer.**

Generalitat Valenciana. "Adquisición infraestructura para Parque Científico Elche" (PPC/2011/044, 2011). IP: **A. Ferrer**.

Generalitat Valenciana. "Adquisición infraestructura para Parque Científico Elche" (PPC/2012/008, 2012). IP: **A. Ferrer**.

Proyectos ISIC. Generalitat Valenciana. "Plataforma de investigación en piel - SKIN RESEARCH PLATFORM (SRP)." (ISIC/2012/009; 2012). IP. **A Ferrer**.

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**

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.**

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.**

Generalitat Valenciana. Ayudas FEDER Julio 2012 para la adquisición o renovación de equipamiento científico-técnico para grupos de investigación e investigadores principales de proyectos de investigación (UMH). IP: **A. Ferrer.**

Generalitat Valenciana. Ayudas FEDER Noviembre 2012 para la adquisición o renovación de equipamiento científico-técnico para grupos de investigación e investigadores principales de proyectos de investigación (UMH). IP: **V. Micol.**

Generalitat Valenciana. Ayudas FEDER Noviembre 2012 para la adquisición o renovación de equipamiento científico-técnico para grupos de investigación e investigadores principales de proyectos de investigación (UMH). IP: **J.M. González-Ros.**

PRIVATE FUNDING

Contracts

Acuerdo específico de transferencia de know-how y de asesoramiento. NUTRACITRUS, SL. (23/05/2005- 22/05/2010). IP: **D. Saura.**

Contrato para la realización de ensayos de extracción de zumos cítricos. Evolución de calidad del zumo y de la pulpa. Funded by JOHN BEAN TECHNOLOGIES FOODTECH, SL. (10/12/2010-31/12/2011). IP: **D. Saura.**

Addenda al contrato para la realización de ensayos de extracción de zumos cítricos. Evolución de calidad del zumo y de la pulpa. Funded by: JOHN BEAN TECHNOLOGIES FOODTECH SL. (01/01/2012-31/12/2012). IP: **D. Saura.**

Convenio de colaboración para el proyecto "Producción de zumo de caqui (*Diospyros kaki* l.) y de industrialización de la granada (*Punica granatum* L.)". Funded by FUNDACION DE LA COMUNIDAD VALENCIANA PARA LA INVESTIGACION AGROALIMENTARIA (AGROALIMED) (01/12/2009-31/12/2011). IP: **D. Saura.**

Contrato para la realización del "Proyecto de investigación y desarrollo para la obtención de extractos vegetales con principios activos interesantes para la creación de una gama ecológica de higiene y cosmética. Protección UV". Funded by QUIMICAS DEL VINALOPO, SL (18/03/2010-31/12/2010). IP: **V. Micol.**

Contrato para la realización del "Proyecto de investigación y desarrollo para la obtención de extractos vegetales con principios activos interesantes para la creación de una gama ecológica de higiene y cosmética. Protección UV". Funded by QUIMICAS DEL VINALOPO, SL (04/02/2011-31/12/2011). IP: **V. Micol.**

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.**

Recombinant expression of the peptides identified in the *Rhopalurus junceus* scorpion venom. Funded by: LABIOFAM S.A. (La Habana, Cuba S.A. (La Habana, Cuba). (01/07/2011-31/08/2012). IP: **A. Estepa.**

"Identificación y Desarrollo De Productos Cosméticos". Diverdrugs. (2006-2013). IP: **A. Ferrer.**

"Desarrollo de compuestos capaces de inducir la lectura de codones de terminación temprana (PTCs)". BCN Peptides (2008-2012). 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.**

Characterisation of the biological activity of human cytokines overexpressed in plants. Funded by: AGRENVEC S.L. (Madrid, Spain). **A. Estepa.**

Contrato de Apoyo Tecnológico para la realización del trabajo "Ensayo para determinar la descomposición de la materia orgánica producida por un producto enzimático". Funded by: Asociación de Investigación de la Industria Textil (AITEX, Alicante). (08/03/12-07/09/12). IP: **V. Micol.**

Contrato de "Asesoramiento en el diseño, formulación, preparación y aplicaciones de ingredientes funcionales para los sectores nutracéutico y cosmético". Funded by MONTELOEDER SL. (19/07/11-18/01/12). IP: **V. Micol.**

Contrato de Asesoramiento y Apoyo Tecnológico en la preparación del Proyecto" Obtención de un ingrediente funcional para el tratamiento y la prevención de la esteatosis hepática (higado graso) con aplicaciones en los sectores alimentarios, nutracéutico y farmacéutico". Funded by MONTELOEDER SL. (02/04/12-31/03/14). IP: **V. Micol.**

Contrato de asesoramiento y asistencia técnica en el área de caracterización de fibras dietéticas. Funded by Cítricos de Murcia, SA. (27/03/2009-26/04/2011). IP: **N. Martí.**

Contrato para actividades de asesoramiento y asistencia técnica en el Área de Tecnología de Alimentos. (16/10/2009-15/02/2010). Funded by Federación Española de Industrias de la Alimentación y Bebidas. IP: **N. Martí.**

Cuantificación de hidroxitirosol en muestras líquidas por Cromatografía Líquida de alta resolución y columna de fase reserva (C18). (20/09/12). EXTRACTIA HEALTH SL. **V. Micol**

Determinación de la capacidad antioxidante mediante la utilización del ensayo Oxygen Radical Absorbance Capacity de muestras biológicas o alimentarias (26/01/2011). AMGAT CITRUS PRODUCTS, SA. IP: **V. Micol.**

SCIENTIFIC AND EDUCATIONAL COMMITTEES

R&D and Educational Committees

National Committee of Biochemistry. Ministerio de Ciencia e Innovación. (2008-2010). **A. Ferrer.**

National Committee of Biophysics. Ministerio de Ciencia e Innovación. (2007-2010). **A. Ferrer.**

Comisión Nacional de Evaluación la Actividad Investigadora (Sexenios Tecnológicos). Ministerio Economía y Competitividad. (2011-2014). **A. Ferrer.**

Agencia Nacional de Evaluación y Prospectiva (ANEP) (2010-2012). Ministerio de Economía y Competitividad. **V. Micol., A. Estepa.**

Instituto de la Pequeña y Mediana Industria de la Generalitat Valenciana (IMPIVA) (2011). **V. Micol, C.R. Mateo, A. Estepa, J. Sanz.**

Comité Evaluador de la ANECA para becas de Formación del Profesorado Universitario en Biomedicina. Coordinador (2012-). **J.M. González Ros**

Comité de Evaluación de la ANECA. Programa Nacional de Formación de Recursos Humanos de Investigación. Ministerio de Economía y Competitividad. **J. A. Ferragut** (2012), **J. L. Neira.**

Comité de Acreditación de Profesor Titular de la ANECA. Área de Ciencias de la Salud. Ministerio de Educación. **J. Sanz** (2012).

R&D Management

National Plan on Biomedicine of Ministerio de Educación y Ciencia (2003-2007) and Ministerio de Ciencia e Innovación (2008-2011). Co-manager R&D National Projects (SAF, PETRI, TRACE, AACC) (2007- 2013). **A. Ferrer**

Red Española de Canales Iónicos. Coordinator (2011-2013). **A. Ferrer**

Scientific Advisor of the company MONTELOEDER, SL. (2002-2012). **V. Micol**

Scientific Society Councils

Sociedad Española de Bioquímica y Biología Molecular. (2007-2010). **A. Ferrer**
Sociedad de Biofísica de España. (2007-2010, 2012-2018). **A. Ferrer**
Presidente-electo Sociedad de Biofísica de España. (2014-2018). **A. Ferrer**

Sociedad Española de Biotecnología (SEBIOT), Junta Directiva (2010-2012). **J. Sanz**.

Editorial Boards

Open Enzyme Inhibition Journal (2007-). **J.L. Neira**

ISRN Biochemistry (2012-). **J.L. Neira**

Archives of Biochemistry and Biophysics (2010-2012). **J.L. Neira**

Archives of Biochemistry and Biophysics, EDITOR (2012-2015). **J.L. Neira**

Journal of Pharmacological Sciences. **A. Ferrer**

The Open Journal of Pain. **A. Ferrer**

AgroFood Industry Hi-Tech. TeknoScienze. **V. Micol**

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