

# Scientific Report Biophysics Unit

(CSIC, UPV/EHU)



[www.ehu.es/biofisica](http://www.ehu.es/biofisica)

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# Message from the Director



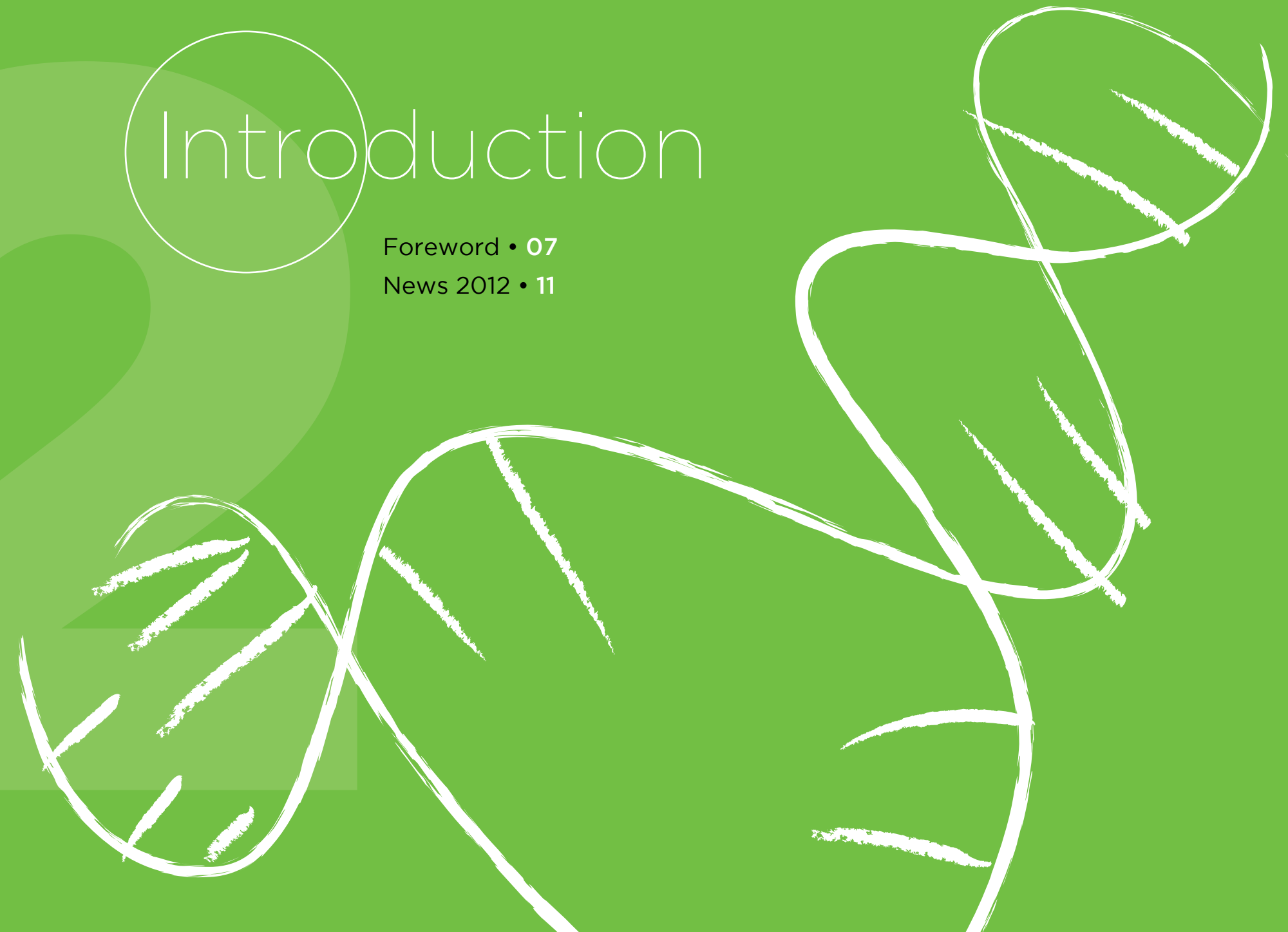
It is with great pleasure that I write these words of greetings for our readers. The Biophysics Unit has just completed ten years in its present building, and will be moving very soon to its new location, also within the Leioa Campus of the University of the Basque Country.

The Biophysics Unit is thriving with devoted scientists, young and old, and with enthusiastic students, technicians and administrators. The generous patronage of our many sponsors, and the firm support of our joint parent institutions, Consejo Superior de Investigaciones Científicas and Universidad del País Vasco/Euskal Herriko Unibertsitatea make possible our sustained activity, even in these difficult times.

Our main asset is our human capital. Thus our chief reason for optimism is the increasing number of highly-qualified scientists that, mainly with the help of Ikerbasque, are steadily joining our Institute. I very much hope the Biophysics Unit will continue its vigorous growth for the benefit of Basque Science and of human welfare.

# Introduction

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## Foreword

The Unidad de Biofísica is a joint centre of the Spanish National Research Centre (CSIC) and the University of the Basque Country (UPV/EHU).

The following pages contain a summary of the current research lines, together with the list of staff, students and visitors, and our recent publications and other activities. This Annual Report intends to serve a two-fold purpose, providing the reader with information about our activities, and supplying our sponsors with the necessary data about the end-product of their funding. We shall be glad to answer any questions or provide further information, and would be delighted to welcome you personally in our laboratory.

# Presentación

La Unidad de Biofísica es un centro mixto del Consejo Superior de Investigaciones Científicas (CSIC) y de la Universidad del País Vasco (UPV/EHU).

Las páginas que siguen contienen un resumen de las líneas de investigación, junto con la relación de

trabajadores, estudiantes y visitantes, y nuestras publicaciones y actividades recientes. Esta Memoria anual tiene un doble propósito, proporcionar información sobre nuestras actividades a los lectores en general, y transmitir en particular a nuestros patrocinadores los datos necesarios sobre los resultados producto de su generosidad. Con mucho gusto responderemos a cualquier pregunta y proporcionaremos información complementaria, y por supuesto estaremos encantados de recibirles personalmente.

# Aurkezpena

Biofisika Unitatea Consejo Superior de Investigaciones Científicas (CSIC) eta Euskal Herriko Unibertsitateko (UPV/EHU) zentro bateratua da.

Hurrengo orrietan Biofisika Unitatean gaur egun dauden ikerketa lerroen laburpena,

ikertzaile, ikasle eta bisitarien zerrenda, eta gure argitarapen eta ekintzen berri eskaintzen da. Urteroko txosten honek helburu bikoitza du: irakurle orori gure ekintzen berri ematea, eta bereziki, gure laguntzaileei beraien eskuzabaltasunari esker lortutako datuak jakinaraztea. Atsegin handiz, edozein galdera erantzuteko, informazio osagarria eskaintzeko, edota pertsonalki errezibitzeko prest gaude.

# Biophysics Unit (CSIC-UPV/EHU)

## 10<sup>th</sup> Anniversary Event

The Biophysics Unit organized a scientific event last 23th October 2012 to celebrate the tenth anniversary of the current facilities in the Campus. This research centre was created in 1999 through a partnership agreement between the University of the Basque Country (UPV/EHU) and the National Research

Council of Spain (CSIC). Then 10 years ago the Biophysics Unit opened the present building in Leioa Campus.

The event, attended by more than 150 guests from areas of science, business and administration (Basque Government, University and Regional Government of Biscay), was aimed to spread and promote information about biophysics and to recognize the professional career of the affiliated scientists and their respective research teams.

# News 2012

The scientific sessions held in the Graduation Hall of the Faculty of Science and Technology UPV/EHU, had as a special guest Professor Alberto Diaspro, head of the Nanophysics Department of the Italian Institute of Technology, Genoa, and former president of the European Biophysical Societies Association (EBSA). Lectures were also given by scientists from the Biophysics Unit, Dr. Álvaro Villarroel,

Dr. Vadim Frolov and Dr. José Luis Nieva. The event had an important impact in the media. The coverage resulted in international references such as press agency 'Europa Press', and in national and local media: El Correo, Deia, El Pais, El Economista, 20 Minutos, Terra Noticias web portal, Onda Cero, Onda Vasca or Radio Euskadi, among others. The Biophysics Unit is now addressing a powerful development and expansion plan that will be resulting in the move to a new building next year, in the nearby Scientific Park, that will be opened in December 2013.



## New building

The new building has made good progress through 2012, and will be completed in the summer 2013. After moving the current laboratories and facilities, the new building should be operational from January 2014.

## Awards and Honours

**F.M. Goñi** was declared an Illustrious Biscayan (Bizkaitar Argia) by the Biscayan Government.

**J.M.G. Vilar** was awarded the Werfen-Izasa-Beckman-Coulter prize.

**E. Rodríguez-Hortelano** received the Best Poster Award at the XII International Congress of the Spanish Biophysical Society, (Barcelona, Spain, July 2012).

## Research Highlights 2012

### “Sphingomyelin organization is required for vesicle biogenesis at the Golgi complex”

J.M. Durán, F. Campelo, J. van Galen, T. Sachsenheimer, J. Sot, M.V. Egorov, C. Rentero, C. Enrich, R.S Polishchuk, F.M. Goñi, B. Brügger, F. Wieland and V. Malhotra.

*EMBO J.* **31**, 4535-4546 (2012).

Scientists in the Unidad de Biofísica, together with other Spanish and German groups, have shown that the organization of sphingomyelin and cholesterol in defined domains in the Golgi complex are essential for the formation of transport vesicles in this subcellular organelle.

### “Classical swine fever virus p7 protein is a viroporin involved in virulence in swine”

D.P. Gladue, L.G. Holinka, E. Largo, I. Fernandez Sainz, C. Carrillo, V. O'Donnell, R. Baker-Branstetter, Z. Lu, X. Ambroggio, G.R. Risatti, J.L. Nieva and M.V. Borca.

*J. Virol.* **86**, 6778-6791 (2012).

The classical swine fever virus is very important from the point of view of economy. This work, in collaboration with laboratories from the U.S. shows that p7, a small viral hydrophobic protein, is involved in the virulence process in swine.

### “A new view of the lethal apoptotic pore”

G. Basañez, L. Soane and J.M. Hardwick.

*PLoS Biology.* **10**, Issue 9, e1001399 (2012).

The authors propose a novel concept of the apoptotic pore, according to which the pore would consist of proteins and lipids, against the currently prevailing view of a purely proteic apoptotic pore.

# Organization

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Eskerrik asko Marije

# Lines of Research

2011-2012



## Sphingolipids and membrane domains

A. Alonso,  
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In recent years the interest for membrane domains has increased, in particular transient domains known as rafts. The hypothesis of "rafts" suggests that these microdomains are enriched in sphingolipids and in cholesterol. Sphingomyelinases are enzymes that break down sphingomyelin into ceramides and water soluble products. Ceramides are membrane lipids, but their activity is mainly seen through cytosolic proteins. Our group studies, on the one hand, the characteristics of sphingomyelinases, and on the other hand, the changes induced by ceramides in the physical properties of membranes, in order to identify the molecular bases of the physiological activity of ceramides. We are also analysing the tendency of various different sphingolipids (ceramides, sphingosine) to form domains in the lipid bilayer plane.

### REFERENCES

**"Imaging the early stages of phospholipase C/sphingomyelinase activity on vesicles containing coexisting ordered-disordered and gel-fluid domains"** M. Ibarguren, D.J. López, L.R. Montes, J. Sot, A.I. Vasil, M.L. Vasil, F.M. Goñi and A. Alonso. *J. Lipid Res.* **52**, 635-645 (2011).

**"Binding of  $\beta$ -Amyloid (1-42) peptide to negatively charged phospholipid membranes in the liquid-ordered state: modeling and experimental studies"**. H. Ahyayauch, M. Raab, J.V. Busto, N. Andracka, J.L. R. Arrondo, M. Masserini, I. Tvaroska and F.M. Goñi. *Biophys. J.* **103**, 453-463 (2012).

**"Accumulated bending energy elicits neutral sphingomyelinase activity in human red blood cells"** D.J. López, M. Egido-Gabas, I. López-Montero, J.V. Busto, J. Casas, M. Garnier, F. Monroy, B. Larijani, F.M. Goñi and A. Alonso. *Biophys. J.* **102**, 2077-2085 (2012).



# Membrane protein folding and stability. Structural motif engineering and design

### REFERENCES

“Par j 1 and Par j 2, the two major allergens in *Parietaria judaica*, bind preferentially to monoacylated negative lipids” R.González-Rioja, J.A.Asturias, A.Martínez, F.M.Goñi & A.R.Viguera. *FEBS J.* **276**, 1762-1775 (2009).

“NMR assignment and backbone dynamics of the pore-forming domain of colicin A” A.Ibañez de Opakua, T.Diercks, A.R.Viguera & F.J.Blanco. *Biomol NMR assign* **4**, 33-36 (2010).

Protein folding has been the subject of intensive research. Well designed combinations of experimental and computational studies are enabling folding to be followed at atomic resolution, with the result that general rules are emerging. This insight, however, pertains to water-soluble proteins and it is unclear how the unifying mechanisms extend to the many proteins that reside in membranes. Understanding membrane protein folding in vitro will not only begin to overcome the problems of overexpression, purification and solubilization of membrane proteins, but also bring new techniques to membrane protein research. We have chosen the pore-forming fragment of colicin A as a model to study protein-lipid complex formation and stability. We investigate the kinetics and thermodynamics of folding aiming to obtain mechanistic detail, with an emphasis on  $\alpha$ -helical proteins.

# Structural studies of Biomolecules using IR spectroscopy

### REFERENCES

“Sphingosine-1-phosphate as an amphipathic metabolite: its properties in aqueous and membrane environments”. M. García-Pacios, M.I. Collado, J.V. Busto, J. Sot, A. Alonso, J.L.R. Arrondo and F.M. Goñi. *Biophys. J.* **97**, 1398-1407 (2009).

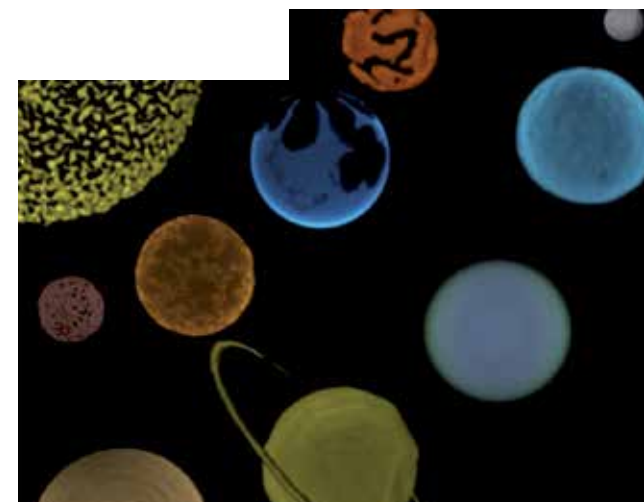
“Membrane insertion stabilizes the structure of TrwB, the R388 conjugative plasmid coupling protein” A.J. Vecino, I. de la Arada, R.L. Segura, F.M. Goñi, F. de Cruz, J.L. R. Arrondo and I. Alkorta. *Biochim. Biophys. Acta* **1808**, 1032-1039 (2011).

“A conventional and 2DCOS infrared approach to the kinetics of protein misfolding” I. de la Arada, N. Andraka, M. Garcia Pacios and J.L.R. Arrondo. *Current Protein & Peptide Science* **12**, 181-187 (2011).

In the nineteen eighties, our laboratory pioneered the application of infrared spectroscopy to the study of the structure of lipids and proteins. Currently we are developing the new technology of two-dimensional IR spectroscopy (2DCOS), applying it to the analysis of the structure and conformational changes of proteins, lipids and their complexes.

The main areas on which we are currently focusing our attention are:

- Study of sphingomyelin-cholesterol mixtures
- Membrane proteins and lipoproteins
- Amyloidogenesis
- Protein-DNA interactions



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## Protein folding and the role of molecular chaperones

### REFERENCES

**“Nucleoplasmin binds histone H2A-H2B dimers through its distal face”**. I. Ramos, J. Martín-Benito, R. Finn, L. Bretaña, K. Aloria, J.M. Arizmendi, J. Ausió, A. Muga, J.M. Valpuesta, A. Prado. *J Biol. Chem.* **285**, 33771-33778 (2010).

**“A quantitative analysis of the effect of nucleotides and the M domain on the association equilibrium of ClpB”** U. del Castillo, C. Alfonso, S.P. Acebron, A. Martos, F. Moro, G. Rivas and A. Muga. *Biochemistry* **50**, 1991-2003 (2011).

**“The effect of amyloidogenic peptides on bacterial aging correlates with their intrinsic aggregation propensity”** A. Villar-Pique, N.S. de Groot, R. Sabaté, S.P. Acebrón, G. Celaya, X. Fernández-Busquets, A. Muga and S. Ventura. *J. Mol. Biol.* **421**, 270-281 (2012).

Living systems host a crowd of molecular chaperones that act with different mechanisms and serve to maintain protein homeostasis. Our group studies nuclear and cytosolic chaperones. Among the cytosolic chaperones we are interested in members of the Hsp60, Hsp70 and Hsp100 families. In particular, we are analysing the functional cycle of these proteins and how they interact with substrates and modulate their conformation. We are also trying to understand how Hsp70 and Hsp100 proteins collaborate, forming a productive network, to disaggregate and refold cellular protein aggregates. Among nuclear chaperones we focus on nucleoplasmin, a histone-chaperone involved in the exchange of basic proteins bound to DNA and therefore in the regulation of the condensation state of chromatin. In particular, we are interested in the nucleoplasmin-mediated histone exchange mechanism. These studies are carried out using a combination of biochemical (expression and purification of proteins, mutagenesis, hybrid oligomeric proteins) and biophysical (fluorescence, IR spectroscopy, calorimetry...) techniques.

## Insights into the structure, function and nucleocytoplasmic traffic of nuclear proteins

○ M.A. Urbaneja,  
S. Bañuelos

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**“Recognition of nucleoplasmin by its nuclear transport receptor importin  $\alpha/\beta$ : insights into a complete import complex”**. J. Falces, I. Arregi, P.V. Konarev, M.A. Urbaneja, D.I. Svergun, S.G. Taneva and S. Bañuelos. *Biochemistry* **49**, 9756-9769 (2010).

**“The nuclear transport machinery recognizes nucleoplasmin-histone complexes”**. I. Arregi, J. Falces, S. Bañuelos, M.A. Urbaneja and S.G. Taneva. *Biochemistry* **50**, 7104-7110 (2011).

**“A global survey of CRM1-dependent nuclear export sequences in the human deubiquitinase family”** I. García-Santisteban, S. Bañuelos and J.A. Rodríguez. *Biochem. J.* **441**, 209-217 (2012).

Nuclear chaperones are involved among other functions in the chromatin remodeling that takes place during various physiological processes such as fertilization (e.g. mediated by nucleoplasmin) and ribosome assembly and cell proliferation control (e.g. mediated by nucleophosmin). Like other nuclear proteins, they are synthesized in the cytoplasm and rely on carriers (in the case of nucleoplasmin / nucleophosmin family, importin  $\alpha/\beta$  heterodimer carrier) to be imported into the cell nucleus. Nucleophosmin is a “shuttling” protein: it needs to be imported and exported continuously. Protein function is frequently regulated by cell localization, and failure in this traffic may trigger diseases. Nucleophosmin mislocalization and dysfunction have been related to several types of human cancer. Based on biochemical, molecular biology and biophysical approaches we are studying nucleophosmin structure, function and interaction with nuclear transport receptors, trying to understand the basis of its pathogenic alterations.

○ H. Ostolaza,  
C. Martín

## The role of cell membranes in bacterial pathogenesis

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**“*Bordetella* adenylate cyclase toxin promotes calcium entry into both CD11b+ and CD11b- cells through cAMP-dependent L-type-like calcium channels”**. C. Martín, G. Gómez-Bilbao and H. Ostolaza. *J. Biol. Chem.* **285**, 357-364 (2010).

**“Adenylate cyclase toxin promotes internalisation of integrins and raft components and decreases macrophage adhesion capacity”** C. Martín, K.B. Uribe, G. Gómez-Bilbao and H. Ostolaza. *PLoS one* **6**, e17383 (2011).

In recent years, our group has been studying the phenomenon of the interaction of a pathogenic toxin, *Escherichia coli*  $\alpha$ -haemolysin, with erythrocytes and model membranes. This is an example of protein that it is initially synthesised as a water-soluble protein, but on coming into contact with a membrane binds to it, behaving from then on as an intrinsic protein. Our efforts are focussed on studying the structural requirements of the toxin for this transformation from the soluble to the membrane-bound state to take place, as well as the parameters that may modulate the interaction with the target membrane. Recently, we have broadened the scope of our work to include another member of the RTX family, the adenylate cyclase toxin from *Bordetella pertussis*.

## Mechanism of action of peptide toxins acting at the membrane level

Our research is focussed on the interaction of equinatoxin-II with cell and model membranes. Equinatoxin-II, a toxin produced by the anemone *Actinia equine*, forms pores in the membrane. Using site-directed mutagenesis, we are designing mutants that we hope will help us identify those residues directly involved in the insertion process. On the other hand, we are also investigating the biophysical parameters of the membrane that favour this type of interaction, and, in particular, the coexistence of lipid phases within the bilayer.

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**“Crystallization and preliminary crystallographic analysis of fragaceatoxin C, a pore-forming toxin from the sea anemone *Actinia fragacea*”**. A.E. Mechaly, A. Bellomio, K. Morante, J.M. González-Mañas and D.M.A. Guérin. *Acta Cryst.* **65**, 357-360 (2009).

**“Structural insights into the oligomerization and architecture of eukaryotic membrane pore-forming toxins”** A.E. Mechaly, A. Bellomio, D. Gil-Cartón, K. Morante, M. Valle, J.M. González Mañas and D.M.A. Guérin. *Structure* **19**, 181-191 (2011).

J.M. González-Mañas ○

I. Alkorta,  
F.M. Goñi

## Inter-domain relationships in integral membrane proteins

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**“Reconstitution in liposome bilayers enhances nucleotide binding affinity and ATP-specificity of TrwB conjugative coupling protein”** A.J. Vecino, R.L. Segura, B. Ugarte-Urbe, S. Águila, I. Hormaeche, F. de la Cruz, F.M. Goñi, and I. Alkorta *BBA Biomembranes* **1798**, 2160-2169 (2010).

**“Membrane insertion stabilizes the structure of TrwB, the R388 conjugative plasmid coupling protein”** A.J. Vecino, I. de la Arada, R.L. Segura, F.M. Goñi, F. de Cruz, J.L. R. Arrondo and I. Alkorta. *Biochim. Biophys. Acta* **1808**, 1032-1039 (2011).

**“Membrane insertion stabilizes the structure of TrwB, the R388 conjugative plasmid coupling protein”**

A.J. Vecino, I. de la Arada, R.L. Segura, F.M. Goñi, F. de Cruz, J.L. R. Arrondo and I. Alkorta. *Biochim. Biophys. Acta* **1808**, 1032-1039 (2011).

**“Deletion of a single helix from the transmembrane domain causes large changes in membrane insertion properties and secondary structure of the bacterial conjugation protein TrwB”**

A.J. Vecino, R.L. Segura, I. de la Arada, F. de la Cruz, F.M. Goñi, J.L.R. Arrondo, I. Alkorta, *Biochim. Biophys. Acta* **1818**, 3158-3166 (2012).

The purpose of this project is to determine the role of the various protein components that are part of the bacterial conjugation system of the R388 plasmid. In particular, we are interested in the membrane protein TrwB. This protein, the first member of the coupling family of proteins to be purified, is involved in the transfer of DNA from the donor to the recipient cell. Clarifying its role in the process of conjugation will contribute to solving the problem of antibiotic resistance shown by an increasing number of bacterial strains (in collaboration with F. De la Cruz, University of Cantabria).

## Mechanisms for virus-induced membrane fusion

J.L. Nieva

Our objective is to determine the molecular mechanism by which membrane glycoproteins of some viruses (HIV, Ebola) induce the fusion of the cell and viral membranes. Prediction tools have been developed to detect the domains that are inserted into the target membrane. Specifically, we seek to understand their behaviour as antigenic determinants, and to develop inhibitory agents that would block their destabilizing interaction. A branch of this field consists of the characterisation of similar domains that may be involved in the infective power of the prion protein. In parallel, we are studying the mechanism of cell membrane permeabilisation, induced by certain viral products (viroporins) during infection (this work on viroporins is in collaboration with L. Carrasco, CBM, Madrid).

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**“Recognition of membrane-bound fusion-peptide/MPER complexes by the HIV-1 neutralizing 2F5 antibody: implications for anti-2F5 immunogenicity”** N. Huarte, A. Araujo, R. Arranz, M. Lorizate, H. Quendler, R. Kunert, J.M. Valpuesta and J.L. Nieva. *PLoS One.* **7** (12):e52740. doi:10.1371/journal.pone.0052740 (2012).

## Mitochondrial membranes, apoptosis and cancer

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**“A new view of the lethal apoptotic pore”** G. Basañez, L. Soane and J.M. Hardwick. *PLOS Biology*, **10**, Issue 9, e1001399 (2012).

During apoptosis, mitochondrial membranes undergo dramatic changes in permeability and morphology. The principal components involved in these processes are the BCL-2 family of proteins, with assistance from an increasing number of mitochondrial protein/lipid effectors. Despite the remarkable progress made in uncovering the molecular underpinnings of apoptotic cell death in the last decade, identification of the precise mechanisms by which BCL2 family proteins regulate the structure and functioning of mitochondrial membranes remains a key and controversial issue in the field of cell death. Given the inherent complexity of the cellular apoptotic network, we use in vitro reconstituted systems with physiologically relevant characteristics to try to elucidate the mode of action of specific members of the BCL2 family and/or their effectors at the membrane level, using a multidisciplinary approach based on biophysical techniques. Considering the important role played by BCL2 family proteins in tumorigenesis and in cellular responses to chemotherapy, the information gained in these studies may facilitate progress in the fight against cancer.

## X-ray crystallography and crystallisation of proteins and virus

Learning about the structure of macromolecules of biological interest (enzymes, receptors, large molecular aggregates such as viruses) enables the mechanisms of the biochemical functions they perform to be interpreted. Protein crystallography, currently the most advanced and powerful technique for determining atomic structures, is used by our group to study a wide range of macromolecules. We are currently working on the resolution of the structure of several proteins of interest in the Biophysics Unit (membrane protein Scramblase and the eukaryotic toxin FraC) and we are collaborating with national and international centres on other structural projects (Triatoma virus, Potassium Channel KcsA and Acyl-CoA binding protein, among others). In parallel with this crystallography work, we are developing new experimental devices and procedures to enhance protein crystallization.

Along with the basic research described before, our group initiated new research lines associated to the development of biomolecular tools based on Dicrostoviruses. These lines comprise the production of natural biopesticides against insect pests, the creation of new molecular tools to enhance the production of recombinant proteins, and the development of a VLP-based platform for rational design of vaccines.

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**“Structural insights into the oligomerization and architecture of eukaryotic membrane pore-forming toxins”** A.E. Mechaly, A. Bellomio, D. Gil-Cardón, K. Morante, M. Valle, J.M. González Mañas and D.M.A. Guérin. *Structure* **19**, 181-191 (2011).

**“Capsid protein identification and analysis of Triatoma Virus (TrV) mature virions and naturally occurring empty particles”** J. Agirre, K. Aloria, J.M. Arizmendi, I. Iloro, F. Elortza, G.A. Marti, E. Neumann, F.A. Rey and D.M.A. Guérin. *Virology* **409**, 91-101 (2011).

**“Pores of the toxin FraC assemble into 2D hexagonal clusters in both crystal structures and model membranes”** A.E. Mechaly, A. Bellomio, K. Morante, J. Agirre, J.M. González-Mañas and D.M.A. Guérin. *J. Structural Biology* **180**, 312-317 (2012).

## Identification and characterization of proteins and lipids associated to regulators of cell excitability

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**“A pore residue of the KCNQ3 potassium M-channel subunit controls surface expression”.**

J.C. Gómez-Posada, A. Etxeberria, M. Roura-Ferrer, P. Areso, M. Masin, D. Ruth; R.D. Murrell-Lagnado and Á. Villarroel. *J Neurosci*. **30**, 9316-9323 (2010).

**“The Kv7.2/Kv7.3 heterotetramer assembles with a random subunit arrangement”**

A.P. Stewart, J.C. Gómez-Posada, J. McGeorge, M.J. Rouhani, A. Villarroel, R.D. Murrell-Lagnado and J. M. Edwardson. *J Biol Chem*. **287**, 11870-11877 (2012).

**“Surface expression and subunit specific control of steady protein levels by the Kv7.2 helix A-B linker”**

P. Aivar, J. Fernández-Orth, C. Gomis-Perez, A. Alberdi, A. Alaimo, M.S. Rodríguez, T. Giraldez, P. Miranda, P. Areso and A. Villarroel. *PLoS One* **7**, Issue 10, e47263 (2012).

Among ionic channels, those that are potassium selective are, by far, the most diverse group. They play a key role in processes such as immune response, cell differentiation, excitability and cell death, among others. More than 60 genes for potassium channels are known in the human genome, which together with the fact that up to four different subunits can combine to form a channel, means that there are a large numbers of variants. Despite this impressive redundancy in “potassium permeation”, mutations in some subunits cause hereditary diseases, indicating that the rest of the channels cannot substitute for them. These diseases are known as channelopathies. To date, around 10 potassium channelopathies have been identified and four of these are due to mutations in genes of the KCNQ family, the gene products of which are Kv7.1-Kv7.5.

Our research is focused on the molecular study of these proteins that regulate cell excitability. In humans, mutations of these proteins cause arrhythmia, epilepsy and deafness, depending on the isoform affected and their distribution within the tissue. Our objective is to identify the network of proteins associated with these channels, by analysing the physiological consequences of these interactions through mutagenesis-function studies, and the use of electrophysiological, imaging, biochemical and high-resolution biophysical techniques. In addition, we aim to determine the role played by lipids in the regulation of these channels. Currently, we are establishing the channel regions involved in biogenesis, assembly, membrane insertion and subcellular localization, as well as in the regulation by lipid second messengers. We hope to identify the proteins and lipids that interact specifically with each of these domains, and these may become targets for the therapeutic drug development. In the longer term, our objective is to determine the three-dimensional structure of these macro-complexes. As an intermediate stage, en route to future crystallization, we are investigating new strategies for high-yield production of large quantities of water-soluble, properly folded macro-complexes.

## Advanced techniques of fluorescence spectroscopic micro and nanoscopy

My main research interest is the development and application of novel micro and nanoscopic optical methodologies to the quantitative investigation of the spatial organisation and dynamics of inter- and intra-molecular interactions in living cells. The quantitative description of proteins behaviour and interactions in the living cell adds to the in-vitro information obtained through traditional biochemistry techniques and results in a better understanding of the molecular, cellular and physiological mechanisms of disease.

The Biophotonics lab is endowed with a multiphoton Leica TCS-SP5 microscope with advanced imaging capabilities such as Fluorescence Correlation Spectroscopy (FCS) and Fluorescence Lifetime Imaging (FLIM). We are also currently setting up a PALM microscope for nanoscopic imaging.

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**“Quantification of Molecular interactions in the living cell: to fit or not to fit”** G. de las Heras, S. Padilla-Parra, J. Requejo-Isidro. *Reviews in Fluorescence* **2012** (Eds. C.D. Geddes, J.R. Lakowicz) (Springer Science, New York, 2013).

**“Fluorescence lifetime imaging reveals that the environment of the ATP binding site of myosin in muscle senses force”** D. Ibañez-García, J. Requejo-Isidro, M.R. Webb, T.G. West, P. French and M.A. Ferenczi. *Biophys J*. **99**, 2163-2169 (2010).

## Systems Biophysics and Computational Biology

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**“Accurate prediction of gene expression by integration of DNA sequence statistics with detailed modeling of transcription regulation”.**

J.M.G. Vilar. *Biophys J.* **99**, 2408-2413 (2010).

**“Control of gene expression by modulated self-assembly”** J.M.G. Vilar and L. Saiz. *Nucl. Acids. Res.* **39**, 6854-6863 (2011).

**“Far-from-equilibrium processes without net thermal exchange via energy sorting”** J.M.G. Vilar and J.M. Rubi. *J. Chem. Phys.* **136**, 064115 (2012)

Our research activity is focused on computational and mathematical analysis of biological systems at their various levels of organization, from molecular properties to cell behaviour and the role these play in the cell population dynamics. The main objective is to deepen our understanding of the underlying mechanisms and to use this information for the controlling and designing cellular processes. For this, we use the latest computational technologies with a wide range of methods including molecular dynamics, structural bioinformatics, stochastic simulation algorithms and mathematical analysis of dynamic systems. Using these computational biophysical techniques, together with corresponding experimental results, we are studying proteins, nucleic acids and lipids, as well as their interactions, their collective properties and the dynamics of their macromolecular complexes in networks of gene expression and signal transduction.

## Structural Glycobiology

Glycans are not only one of the major components of the cell but also are essential molecules that modulate a variety of important biological processes in all living organisms. These oligo- and polysaccharides are used primarily as energy storage and metabolic intermediates as well as being key structural components in bacteria and plants. Moreover, as a consequence of protein and lipid glycosylation, glycans generate a significant amount of structural diversity in biological systems. These structural features are particularly apparent in molecular recognition events including cell-cell, cell-matrix and cell-molecule interactions during critical stages of development, the immune response and host-pathogen interactions. Most of the enzymes encoded in eukaryotic/prokaryotic/archaeal genomes responsible for the biosynthesis of glycan structures are glycosyltransferases. The long-term goal of our research program is to understand how glycosyltransferases function to control health and disease at the molecular level. We are particularly interested in investigating the structural and mechanistic properties of glycosyltransferases with special emphasis on the study of integral and peripheral membrane-associated enzymes. To this end, we are using a multidisciplinary approach including molecular biology, protein biochemistry, protein biophysics and structural biology.

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**“Glycolytic and non-glycolytic functions of the fructose-1,6-bisphosphate aldolase of *Mycobacterium tuberculosis*, and essential enzyme produced by replicating and non-replicating bacilli”** M.P. Santangelo, P.M. Gest, M.E. Guerin, M. Coinçon, H. Pham, G. Ryan, S.E. Puckett, J.S. Spencer, M. Gonzalez-Juarrero, R. Daher, A.J. Lenaerts, D. Schnappinger, M. Therisod, S. Ehrt, J. Sygusch and M. Jackson. *J. Biol. Chem.* **286**, 40219-40231 (2011).

**“Mechanistic insights into the retaining glucosyl-3-phosphoglycerate synthase from mycobacteria”** S. Urresti, D. Albesa-Jové, F. Schaeffer, H.T. Pham, D. Kaur, P. Gest, M.J. van der Woerd, A. Carreras-Gonzalez, S. Lopez-Fernandez, P.M. Alzari, P.J. Brennan, M. Jackson and M. E. Guerin. *J Biol. Chem.* **287**, 24649-24661 (2012).

## Nanomechanics of cell membrane systems

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**“Domain-driven morphogenesis of cellular membranes”** A.V. Shnyrova, V.A. Frolov and J. Zimmerberg. *Curr Biol.* **19** (17):R772-80 (2009).

**“Lipid Polymorphisms and Membrane Shape”** V.A. Frolov, A.V. Shnyrova and J. Zimmerberg. *Cold Spring Harb Perspect Biol.* **3**:a004747 (2011).

**“Dynamin: functional design of a membrane fission catalyst”** S.L. Schmid and V.A. Frolov. *Annu. Rev. Cell Dev. Biol.* **27**, 79-105 (2011).

Morphological flexibility of cell membranes provides the foundation for the spatial organization of living cells. The signature morphologies of cellular endomembrane systems are created at the nanoscale where specialized proteolipid complexes assemble to control membrane curvature, shape and topology. Our main focus is on fundamental molecular mechanisms of membrane remodeling by such complexes operating at submicron scales, where pathways of membrane deformations are defined by forces applied by individual protein complexes, carefully organized in time and space, and elastic resistance of the lipid bilayer. We apply novel experimental approaches combining nanomanipulations, electrophysiology and time-resolved fluorescence, confocal and TIRF microscopy to characterize mechanical properties and dynamics of biomimetic and cell membranes at the nanoscale, with particular attention to topological membrane remodeling, fusion and fission, dynamics of the force- and geometry-induced demixing of membrane components and diffusion in complex media. We reconstitute the morphological activity of the prototype proteins controlling membrane remodeling, such as dynamin and matrix protein of enveloped viruses, using nanofabricated lipid templates to resolve subtle features of the proteolipid interactions, creation and sensing of membrane curvature by proteins, and dynamics of protein complexes on membrane surfaces.

Finally, we carry out theoretical analysis of the proteolipid interactions utilizing phenomenological membrane models and simulations.

## Role of lipids in membrane protein activity and function

Our main objective is to decipher the molecular mechanism by which specific membrane lipids govern membrane protein structure and function. Despite remarkable advances made in membrane biology, intramembrane protein-lipid interaction still one of the major gaps of knowledge in membrane biology on account of the complex scenario where lipids and proteins interact. Unlocking this mystery is the key of the vast majority of human diseases. For such a challenging goal, a combination of multidisciplinary approaches is required. Among others, biochemistry, biophysics, molecular biology, chemical biology, cell biology and structural biology techniques are currently used. In addition, we develop functionalized small molecules as tools for lipid and membrane research. Unravelling the biological functions of such lipid/protein complexes in health and disease will help to lay the basis for the development of novel, selective and improved therapies for a set of human diseases.

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**“Specificity of intramembrane protein-lipid interactions”** F.X. Contreras, A.M. Ernst, F. Wieland, B. Brügger. *Cold Spring Harb Perspect Biol.* **3** doi:pii: a004705 (2011).

**“Molecular recognition of a single sphingolipid species by a protein’s transmembrane domain”** F.X. Contreras, A.M. Ernst, P. Haberkant, P. Björkholm, E. Lindahl, B. Gönen, C. Tischer, A. Elofsson, G. von Heijne, C. Thiele, R. Pepperkok, F. Wieland B. Brügger *Nature* **481**, 525-529 (2012).



## Role of lipids in HIV-1 life cycle and in the development of new antiviral strategies

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**“Recognition of membrane-bound fusion-peptide/MPER complexes by the HIV-1 neutralizing 2F5 antibody: implications for anti-2F5 immunogenicity”** N. Huarte, A. Araujo, R. Arranz, M. Lorzate, H. Quendler, R. Kunert, J.M. Valpuesta and J.L. Nieva. *PLoS One*. **7**(12):e52740. doi: 10.1371/journal.pone.0052740 (2012).

**“Siglec-1 is a novel dendritic cell receptor that mediates HIV-1 trans-infection through recognition of viral membrane gangliosides”** N. Izquierdo-Useros, M. Lorzate, M.C. Puertas, M.T. Rodríguez-Plata, N. Zangger, E. Erikson, M. Pino, I. Erkizia, B. Glass, B. Clotet, O.T. Keppler, A. Telenti, H.G. Kräusslich and J. Martínez-Picado. *PLoS Biol*. **10**(12):e1001448. doi: 10.1371/journal.pbio.1001448 (2012).

**“Sialyllactose in viral membrane gangliosides is a novel molecular recognition pattern for mature dendritic cell capture of HIV-1”** N. Izquierdo-Useros, M. Lorzate, F.X. Contreras, M.T. Rodríguez-Plata, B. Glass, I. Erkizia, J.G. Prado, J. Casas, G. Fabriàs, H.G. Kräusslich and J. Martínez-Picado. *PLoS Biol*. **10**(4):e1001315. doi: 10.1371/journal.pbio.1001315 (2012).

HIV-1 virus is delimited by a lipid envelope in which fusion proteins (env) are embedded. We have recently identified that sialyllactose, a molecule exposed in specific gangliosides highly enriched in the HIV-1 membrane, is essential for viral uptake into mature mDCs are potent antigen presenting cells that constantly interact with T cells to initiate immune responses. However, HIV-1 has evolved strategies to subvert mDC antiviral activity and promote infection of CD4+ T cells. Our principal research lines are the following (1) In vivo and in vitro studies of the lipid environment of the HIV-1 fusion protein and the role of lipids in the function and activity of this protein. The information gained from these studies will be used to develop new immunogenic formulations able to generate neutralizing responses. (2) Development of nanoliposomal systems able to deliver antiretroviral drugs within the cell in mDCs context. (3) Design and development of lipidomimetic and raftophilic compounds as viral infection inhibitors.

## Structure and mechanism of membrane-associated processes

Membranes are the biological barriers of all cells and organelles and allow for compartmentalization and separation of biological processes. Sophisticated biological mechanisms have been developed in the course of evolution to translocate these barriers. In the outer membrane of Gram-negative bacteria and mitochondria, insertase complexes are the basis for protein biogenesis. These complexes recognize preproteins and assemble them in the membrane in an energy-independent way. We study these complexes regarding their mechanism by a spectrum of biophysical and biochemical techniques.

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**“Recent insights into iron metabolism and biomineralization processes in Dps enzymes”** K. Zeth. *Biochem. J*. **445**, 297-311 (2012).

**“Structure and translocation mechanism of pesticin from *Y. pestis*, a bacterial lysozyme homolog”** S.I. Patzer, R. Albrecht, V. Braun and K. Zeth. *J. Biol. Chem*. **287**, 23381-96 (2012).

# Scientific Highlights

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## Publications 2011/2012

**“Capsid protein identification and analysis of mature Triatoma virus (TrV) virions and naturally occurring empty particles”**

J. Agirre, K. Aloria, J.M. Arizmendi, I. Iloro, F. Elortza, R. Sanchez-Eugenia, G.A. Marti, E. Neumann, F.A. Rey and D.M.A. Guérin.  
*Virology* 409, 91-101 (2011).

**“Effects of bilayer composition and physical properties on the phospholipase C and sphingomyelinase activities of *Clostridium perfringens*  $\alpha$ -toxin”**

P. Urbina, M. Flores-Díaz, A. Alape-Girón, A. Alonso and F.M. Goñi.  
*Biochim. Biophys. Acta* 1808, 279-286 (2011).

**“Multiple stages of detergent-erythrocyte membrane interaction-A spin label study”**

P.S.C. Preté, C.C. Domingues, N.C. Meirelles, S.V.P. Malheiros, F.M. Goñi, E. de Paula and S. Schreier.  
*Biochim. Biophys. Acta* 1808, 164-170 (2011).

**“Structural insights into the oligomerization and architecture of eukaryotic membrane pore-forming toxins”**

A.E. Mechaly, A. Bellomio, D. Gil-Cartón, K. Morante, M. Valle, J.M. González Mañas and D.M.A. Guérin.

*Structure* **19**, 181-191 (2011).

**“Analysis of confiscated fireworks using Raman spectroscopy assisted with SEM-EDS and FTIR”**

K. Castro, S. Fernández-Ortiz de Vallejuelo, I. Astondoa, F.M. Goñi and J.M. Madariaga.

*J. Raman Spectrosc.* **42**, 2000-2005 (2011).

**“Multiple phospholipid substrates of phospholipase C/sphingomyelinase HR<sub>2</sub> from *Pseudomonas aeruginosa*”**

D.J. López, M.I. Collado, M. Ibarguren, A.I. Vasil, M. L. Vasil, F.M. Goñi and A. Alonso.

*Chem. Phys. Lipids* **164**, 78-82 (2011).

**“Membrane insertion stabilizes the structure of TrwB, the R388 conjugative plasmid coupling protein”**

A.J. Vecino, I. de la Arada, R.L. Segura, F.M. Goñi, F. de Cruz, J.L. R. Arrondo and I. Alkorta.

*Biochim. Biophys. Acta* **1808**, 1032-1039 (2011).

**“Adenylate cyclase toxin promotes internalisation of integrins and raft components and decreases macrophage adhesion capacity”**

C. Martín, K.B. Uribe, G. Gómez-Bilbao and H. Ostolaza.

*PLoS one* **6**, e17383 (2011).

**“Reconstitution of proapoptotic BAK function in liposomes reveals a dual role for mitochondrial lipids in the BAK-driven membrane permeabilization process”**

O. Landeta, A. Landajuela, D. Gil, S. Taneva, C. DiPrimo, B. Sot, M. Valle, V.A. Frolov, and G. Basañez.

*J. Biol. Chem.* **286**, 8213-8230 (2011).

**“Optimal resting-growth strategies of microbial populations in fluctuating environments”**

N. Geisel, J.M.G. Vilar, J.M. Rubi.

*PLOS one* **6**, e18622 (2011).

**“Imaging the early stages of phospholipase C/sphingomyelinase activity on vesicles containing coexisting ordered-disordered and gel-fluid domains”**

M. Ibarguren, D.J. López, L.R. Montes, J. Sot, A.I. Vasil, M.L. Vasil, F.M. Goñi and A. Alonso.

*J. Lipid Res.* **52**, 635-645 (2011).

**“Control of gene expression by modulated self-assembly”**

J.M.G. Vilar and L. Saiz.

*Nucl. Acids. Res.* **39**, 6854-6863 (2011).

**“Glycolytic and non-glycolytic functions of the fructose-1,6-bisphosphate aldolase of *Mycobacterium tuberculosis*, and essential enzyme produced by replicating and non-replicating bacilli”**

M.P. Santangelo, P.M. Gest, M.E. Guerin, M. Coinçon, H. Pham, G. Ryan, S.E. Puckett, J.S. Spencer, M. Gonzalez-Juarrero, R. Daher, A.J. Lenaerts, D. Schnappinger, M. Therisod, S. Ehrt, J. Sygusch and M. Jackson.

*J. Biol. Chem.* **286**, 40219-40231 (2011).

**“Are these liquids explosive? Forensic analysis of confiscated indoor fireworks”**

K. Castro, S. Fdez-Ortiz de Vallejuelo, I. Astondoa, F.M. Goñi, J.M. Madariaga.

*Anal. Bioanal. Chem.* **400**, 3065-3071 (2011).

**“The nuclear transport machinery recognizes nucleoplasmin-histone complexes”**

I. Arregui, J. Falces, S. Bañuelos, M.A. Urbaneja and S.G. Taneva.

*Biochemistry* **50**, 7104-7110 (2011).

**“La ciencia en tiempo de crisis” F.M. Goñi. In: “La idea de la crisis revisitada: Variaciones e interferencias”**

(A. Davila Legeren Coord.)

*Servicio Editorial de la Universidad del País Vasco, Bilbao, Spain*, 17-27 (2011).

**“Trafficking coordinate description of intracellular transport control of signaling networks”**

J.M.G. Vilar and L. Sainz.

*Biophys. J.* **101**, 2315-2323 (2011).

**“Microcalorimetry of blood serum proteome: a modified interaction network in the multiple myeloma case”**

S. Todinova, S. Krumova, L. Gartcheva, C. Roberst and S.G. Taneva.

*Anal. Chem.* **83**, 7992-7998 (2011).

**“Kv7 channels can function without constitutive calmodulin tethering”**

J.C. Gómez-Posada, P. Aivar, A. Alberdi, A. Alaimo, A. Etxeberría, J. Fernández-Orth, T. Zamalloa, M. Roura-Ferrer, P. Villace, P. Areso, O. Casis and A. Villarreal.

*PLoS one*, **6**(9) e25508 (2011).

**“Stochastic simulations of mixed-lipid compartments: from self-assembling vesicles to self-producing protocells”**

K. Ruiz-Mirazo, G. Piedrafita, F. Ciriaco and F. Mavelli.

In Arabnia H. R. (Ed.) "Software Tools and Algorithms for Biological Systems" (Book series: Advances in Experimental Medicine & Biology, AEMB). Springer. (Chapter 70: pp. 689-696) (2011).

**"G $\alpha$  activity is reduced in erythrocyte membranes of patients with psedohypoparathyroidism due to epigenetic alterations at the *GNAS* locus"**

C. Zazo, S. Thiele, C. Martín, E. Fernández-Rebollo, L. Martínez-Indart, R. Werner, I. Garin, Spanish PHP Group, O. Hiort and G. Pérez de Nanclares.

*J. Bone Miner Res* **26**, 1864-1870 (2011).

**"Work-Hamiltonian connection for anisoparametric processes in manipulated microsystems"**

J.M.G. Vilar and J.M. Rubi.

*J. Non-Equilib. Thermodyn.* **36**, 123-130 (2011).

**"The impact of the paradigm of complexity on the foundational frameworks of biology and cognitive science"**

A. Moreno, K. Ruiz-Mirazo, and X. Barandiaran.

In: C. Hooker (ed) Complex Systems. Vol X of the D. Gavia, P. Thagard & J. Woods (eds) Handbook of the Philosophy of Science. Elsevier. (pp. 311-334) ISBN: 978-0-444-52076-0 (2011).

**"Low-density lipoprotein density determination by electric conductivity"**

J.A. Fernández-Higuero, A.M. Salvador, J.L.R. Arrondo and J.C. Milicua.

*Anal Biochem.* **417**, 283-285 (2011).

**"Lipids, a missing link in prion propagation"**

J. Castilla and F.M. Goñi.

*Chem. & Biol.* **18**, 1345-1346 (2011).

**"El polinomio imposible"**

F.M. Goñi.

*CIC Network* **10**, 4-5 (2011).

**"Crystal structure of the allosteric-defective chaperonin GroELE434K mutant"**

A. Cabo-Bilbao, A.E. Mechaly, J. Agirre, S. Spinelli, B. Sot, A. Muga and D.M.A. Guérin.

*J. Biophys. Struct. Biol.* **3**, 66-71 (2011).

**"Interaction of anti-HIV-1 antibody 2F5 with phospholipid bilayers and its relevance for the mechanism of virus neutralization"**

R. Maeso, N. Huarte, J.P. Julien, R. Kunert, E.F. Pai and J.L. Nieva.

*AIDS Res. Hum. Retroviruses* **27**, 863-876 (2011).

**"Destabilization exerted by peptides derived from the membrane-proximal external region of HIV-1 gp41 in lipid vesicles supporting fluid phase co-existence"**

B. Apellániz, A.J. García-Sáez, S. Nir, and J.L. Nieva.

*Biochim. Biophys. Acta.* **1808**, 1797-1805 (2011).

**"A new paradigm in molecular recognition? Specific antibody binding to membrane-inserted HIV-1 epitopes"**

J.L. Nieva, B. Apellaniz, N. Huarte and M. Lorizate.

*J. Mol. Recognit.* **24**, 642-646 (2011).

**"Mitchell y la energía en Biología"**

A. Alonso.

*CIC Network* **9**, 74-78 (2011).

**"Membrane integration of Poliovirus 2B viroporin"**

L. Martínez-Gil, M. Bañó-Polo, N. Redondo, S. Sánchez-Martínez, J.L. Nieva, L. Carrasco and I. Mingarro.

*J. Virol.* **85**, 11315-11324 (2011).

**"Life"**

K. Ruiz-Mirazo and A. Moreno. In: Encyclopedia of Astrobiology (Gargaud, M., Amils, R., Cernicharo Quintanilla, J.,

Cleaves, H.J., Irvine, W.M., Pintí, D., Viso, M., Eds.).

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**"Lipid polymorphisms and membrane shape"**

V.A. Frolov, A.V. Shnyrova and J. Zimmerberg.

*Cold Spring Harb Perspect Biol;* **3**:a004747 (2011).

**"Membrane-transferring regions of gp41 as targets for HIV-1 fusion inhibition and viral neutralization"**

N. Huarte, M. Lorizate, E. Pérez-Payá, and J.L. Nieva.

*Curr. Top. Med. Chem.* **11**, 2985-2996 (2011).

**"Assessment of soil quality using microbiol properties and attributes of ecological relevance"**

C. Garbisu, I. Alkorta and L. Epelde.

*Applied Soil Ecology* **49**, 1-4 (2011).

**"Membrane-proximal external HIV-1 gp41 motif adapted for destabilizing the highly rigid viral envelope"**

B. Apellániz, A. Ivankin, S. Nir, D. Gidalevitz and J.L. Nieva.

*Biophys J.* **101**, 2426-2435 (2011).

**“Unexpected wide substrate specificity of *C. perfringens*  $\alpha$ -toxin phospholipase C.”**

P. Urbina, M.I. Collado, A. Alonso, F.M. Goñi, M. Flores-Díaz, A. Alape-Girón, J.M. Ruysschaert and M.F. Lensink.  
*Biochim Biophys Acta*. **1808**, 2618-2627 (2011).

**“Dynammin: functional design of a membrane fission catalyst”**

S.L. Schmid and V.A. Frolov.  
*Annu. Rev. Cell Dev. Biol.* **27**, 79-105 (2011).

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K. Ruiz-Mirazo. In: Encyclopedia of Astrobiology (Gargaud, M., Amils, R., Cernicharo Quintanilla, J., Cleaves, H.J., Irvine, W.M., Pinti, D., Viso, M., Eds.).  
*Springer*. Heidelberg, Germany. Vol 3, pp. 1353-1354 (2011).

**“Allosteric communication between the nucleotide binding domains of caseinolytic peptidase B”**

J.A. Fernandez-Higuero, S.P. Acebron, S.G. Taneva, U. del Castillo, F. Moro and A. Muga.  
*J. Biol. Chem* **286**, 25547-25555 (2011).

**“A quantitative analysis of the effect of nucleotides and the M domain on the association equilibrium of ClpB”**

U. del Castillo, C. Alfonso, S.P. Acebron, A. Martos, F. Moro, G. Rivas and A. Muga.  
*Biochemistry* **50**, 1991-2003 (2011).

**“A conventional and 2DCOS infrared approach to the kinetics of protein misfolding”**

I. de la Arada, N. Andraka, M. Garcia Pacios and J.L.R. Arrondo.  
*Current Protein & Peptide Science* **12**, 181-187 (2011).

**“Variation of lipid membrane composition caused by strong bending”**

P.V. Bashkirov, K.V. Chekashkina, S.A. Akimov, P.I. Kuzmin and V.A. Frolov.  
*Biologicheskie Membrany* **28**, 145-152 (2011).

**“On the transition from prebiotic to proto-biological membranes: from “Self-assembly” to “Self-production”**

G. Piedrafita, F. Mavelli, F. Morán and K. Ruiz-Mirazo.  
ECAL'09 Proceedings of the 10th European conference on Advances in artificial life: Darwin meets von Neumann - Springer-Verlag Berlin, Volume Part I pp 256-264 (2011).

**“Functional characterization of splicing and ligand-binding domain variants in the LDL receptor”**

A. Etxebarria, L. Palacios, M. Stef, D. Tejedor, K.B. Uribe, A. Oleaga, L. Irigoyen, B. Torres, H. Ostolaza and C. Martin.  
*Hum Mutat.* **33**, 232-43 (2012).

**“Far-from-equilibrium processes without net thermal exchange via energy sorting”**

J.M.G. Vilar and J.M. Rubi.  
*J. Chem. Phys.* **136**, 064115 (2012).

**“A global survey of CRM1-dependent nuclear export sequences in the human deubiquitinase family”**

I. García-Santisteban, S. Bañuelos and J.A. Rodríguez.  
*Biochem. J.* **441**, 209-217 (2012).

**“Model systems of precursor cellular membranes: long-chain alcohols stabilize spontaneously formed oleic acid vesicles”**

A. Rendón, D. Gil Carton, J. Sot, M. García-Pacios, L.R. Montes, M. Valle, J.L.R. Arrondo, F.M. Goñi and K. Ruiz-Mirazo  
*Biophys. J.* **102**, 278-286 (2012).

**“The Kv7.2/Kv7.3 heterotetramer assembles with a random subunit arrangement”**

A.P. Stewart, J.C. Gómez-Posada, J. McGeorge, M.J. Rouhani, A. Villarroel, R.D. Murrell-Lagnado and J. M. Edwardson.  
*J Biol Chem.* **287**, 11870-11877 (2012).

**“Accumulated bending energy elicits neutral sphingomyelinase activity in human red blood cells”**

D.J. López, M. Egido-Gabas, I. López-Montero, J.V. Busto, J. Casas, M. Garnier, F. Monroy, B. Larjani, F.M. Goñi and A. Alonso.  
*Biophys. J.* **102**, 2077-2085 (2012).

**“*In situ* synthesis of fluorescent membrane lipids (ceramides) using click chemistry”**

M. Garrido, J.L. Abad, A. Alonso, F.M. Goñi, A. Delgado and L.R. Montes.  
*J Chem Biol* DOI 10.1007/s12154-012-0075-0 (2012).

**“Lipid bilayers in the gel phase become saturated by Triton X-100 at lower surfactant concentrations than those in the fluid phase”**

H. Ahyayauch, M.I. Collado, A. Alonso and F.M. Goñi.  
*Biophys. J.* **102** 1-7 (2012).

**“Lípidos que regulan su propio metabolismo (y el ajeno)”**

F.M. Goñi.  
*SEBBM* (2012).

**“Recognition of membrane-bound fusion-peptide/MPER complexes by the HIV-1 neutralizing 2F5 antibody: implications for Anti-2F5 immunogenicity”**

N. Huarte, A. Araujo, R. Arranz, M. Lorizate, H. Quendler, R. Kunert, J.M. Valpuesta and J.L. Nieva.

*PLoS One*, **7**, e52740. doi: 10.1371 (2012).

**“Theoretical conditions for the stationary reproduction of model protocells”**

F. Mavelli and K. Ruiz-Mirazo.

*Integrative Biology*, DOI: 10.1039/c2ib20222k (2012).

**“Mechanistic insights into the retaining glucosyl-3-phosphoglycerate synthase from mycobacteria”**

S. Urresti, D. Albesa-Jové, F. Schaeffer, H.T. Pham, D. Kaur, P. Gest, M.J. van der Woerd, A. Carreras-Gonzalez, S. Lopez-Fernandez, P.M. Alzari, P.J. Brennan, M. Jackson and M. E. Guerin.

*J Biol. Chem.* **287**, 24649-24661 (2012).

**“Viroporins: structure and biological functions”**

J.L. Nieva, V. Madan and L. Carrasco.

*Nat Rev Microbiol.* **10**, 563-74 (2012).

**“Viability conditions for a compartmentalized protometabolic system: a semi-empirical approach”**

G. Piedrafita, K. Ruiz-Mirazo, P.A. Monnard, A. thel Cornish-Bowden and F. Montero.

*PLoS ONE* **7**, Issue 6, e39480 (2012).

**“Phospholipases C and sphingomyelinases: Lipids as substrates and modulators of enzyme activity”**

F.M. Goñi, L.R. Montes and A. Alonso.

*Prog Lipid Res* **51**, 238-266 (2012).

**“Autonomy in evolution: from minimal to complex life”**

K. Ruiz-Mirazo and A. Moreno.

*Synthese* **185** (1): 21-52 (available online: DOI 10.1007/s11229-011-9874-z) (2012).

**“Charge pair interactions in transmembrane helices and turn propensity of the connecting sequence promote helical hairpin insertion”**

M. Bañó-Polo, L. Martínez-Gil, B. Wallner, J.L. Nieva, A. Elofsson and I. Mingarro.

*J. Mol. Biol.* doi:pii: S0022-2836(12)00915-1 (2012).

**“Mechanical properties of lipid bilayers and regulation of mechanosensitive function. From biological to biomimetic channels”**

D. Balleza.

*Channels* **6**, 1-14 (2012).

**“Regulation of Type IV secretion ATPase TrwD by magnesium: implications for the catalytic mechanism for the secretion ATPase superfamily”**

J. Ripoll-Rozada, A. Peña, S. Rivas, F. Moro, F. de la Cruz, E. Cabezón and I. Arechaga.

*J. Biol. Chem.* **287**, 17408-17414 (2012).

**“Mechanism of membrane perturbation by the HIV-1 gp41 membrane-proximal external region and its modulation by cholesterol”**

A. Ivankin, B. Apellániz, D. Gidalevitz and J.L. Nieva.

*Biochim Biophys Acta.* **1818**, 2521-2528 (2012).

**“A dynamic model of long-range conformational adaptations triggered by nucleotide binding in GroEL-GroES”**

L. Skjaerven, A. Muga, N. Reuter and A. Martinez.

*Proteins* **80**, 2333-2346 (2012).

**“Targeting of Kv7.5 (KCNQ5)/KCNE channels to surface microdomains of cell membranes”**

M. Roura-Ferrer, L. Solé, A. Oliveras, Á. Villarroel, N. Comes and A. Felipe.

*Muscle Nerve.* **45**, 48-54 (2012).

**“The effect of amyloidogenic peptides on bacterial aging correlates with their intrinsic aggregation propensity”**

A. Villar-Pique, N.S. de Groot, R. Sabaté, S.P. Acebrón, G. Celaya, X. Fernández-Busquets, A. Muga and S. Ventura.

*J. Mol. Biol.* **421**, 270-281 (2012).

**“Membrane-active peptides derived from picornavirus 2B viroporin”**

S. Sánchez-Martínez, V. Madan, L. Carrasco and J.L. Nieva.

*Curr Protein Pept Sci.* **13**, 1-12 (2012).

**“Binding of  $\beta$ -Amyloid (1-42) peptide to negatively charged phospholipid membranes in the liquid-ordered state: modeling and experimental studies”**

H. Ahyayauch, M. Raab, J.V. Busto, N. Andracka, J.L. R. Arrondo, M. Masserini, I. Tvaroska and F.M. Goñi.

*Biophys. J.* **103**, 453-463 (2012).

**“A new view of the lethal apoptotic pore”**

G. Basañez, L. Soane and J.M. Hardwick.  
*PLOS Biology*, **10**, Issue 9, e1001399 (2012).

**“Surface expression and subunit specific control of steady protein levels by the Kv7.2 helix A-B linker”**

P. Aivar, J. Fernández-Orth, C. Gomis-Perez, A. Alberdi, A. Alaimo, M.S. Rodríguez, T. Giraldez, P. Miranda, P. Areso and A. Villarroel.  
*PLOS One* **7**, Issue 10, e47263 (2012).

**“Classical swine fever virus p7 protein is a viroporin involved in virulence in swine”**

D.P. Gladue, L.G. Holinka, E. Largo, I. Fernandez Sainz, C. Carrillo, V. O'Donnell, R. Baker-Branstetter, Z. Lu, X. Ambroggio, G.R. Risatti, J.L. Nieva and M.V. Borca.  
*J. Virol*, **86**, 6778-6791 (2012).

**“Futuro, pasado, ... y memoria”**

F.M. Goñi. In.  
“*Qué es Jakiunde*”. Servicio Editorial de la UPV/EHU, Bilbao, 75-79 (2012).

**“Insights into sphingolipid miscibility: separate observation of sphingomyelin and ceramide N-acyl chain melting”**

S.S.W. Leung, J.V. Busto, A. Keyvanloo, F.M. Goñi and J. Thewalt.  
*Biophys J*, **103**, 2465-2474 (2012).

**“Pores of the toxin FraC assemble into 2D hexagonal clusters in both crystal structures and model membranes”**

A.E. Mechaly, A. Bellomio, K. Morante, J. Agirre, D. Gil-Cartón, M. Valle, J.M. González-Mañas and D.M. Guérin.  
*J. Struct. Biol* **180**, 312-317 (2012).

**“Calorimetry-based profiling of blood plasma from colorectal cancer patients”**

S. Todinova, S. Krumova, P. Kurtev, V. Dimitrov, L. Djongov, Z. Dudunkov, S.G. Taneva.  
*Biochim. Biophys. Acta* **1820**, 1879-1885 (2012).

**“Sphingomyelin organization is required for vesicle biogenesis at the Golgi complex”**

J.M. Duran, F. Campelo, J. van Galen, T. Sachsenheimer, J. Sot, M.V. Egorov, C. Rentero, C. Enrich, R.S Polishchuk, F.M. Goñi, B. Brügger, F. Wieland and V. Malhotra.  
*EMBO J*, **31**, 4535-4546 (2012).

**“Deletion of a single helix from the transmembrane domain causes large**

**changes in membrane insertion properties and secondary structure of the bacterial conjugation protein TrwB”**

A.J. Vecino, R. de L. Segura, I. de la Arada, F. de la Cruz, F.M. Goñi, J.L. Arrondo and I. Alkorta.  
*Biochim Biophys Acta*, **1818**, 3158-3166 (2012).

**“Biología sintética: enfrentándose a la vida para comprenderla, utilizarla o extenderla”**

K. Ruiz-Mirazo and A. Moreno.  
*Pasajes* **38**, 28-37 (2012).

**“Fluorescent labeling of Acanthamoeba assessed *in situ* from corneal sectioned microscopy”**

S. Marcos, J. Requejo-Isidro, J. Merayo-Llves, A.U. Acuña, V. Hornillos, E. Carrillo, P. Pérez-Merino, S. del Olmo-Aguado, C. del Aguila, F. Amat-Guerri and L. Rivas.  
*Biomed Opt Express*, **3**, 2489-2499 (2012).

**“An infrared microspectroscopy 2DCOS study of the effect of radiation on normal and cancer cells”**

N. Andraka, J. González-Velasco, J. Celeiro, J.L.R. Arrondo and P. Bilbao.  
*Vibrational Spectroscopy*, **60**, 189-192 (2012).



# PhD Theses 2011/2012

"Implicación del equilibrio conformacional del fragmento formador de poros de la colicina A en su mecanismo de acción"

**Alain Ibañez de Opakua López de Abetxuko**

Supervisor: Ana Rosa Viguera  
6 July 2011.

"Implicación de la membrana en el mecanismo de neutralización del VIH por el anticuerpo anti-MPER 2F5"

**Rubén Maeso Gallego**

Supervisor: José Luis Nieva  
18 July 2011.

"Interacción de DnaK y DnaJ con sustratos proteicos. Regulación de la estructura y función de RepE"

**Judit Perales Calvo**

Supervisors: Arturo Muga / Fernando Moro  
6 February 2012.

"Delivery of small nucleic acids by conjugation to carbohydrates and lipids as novel research and therapeutic tools"

**Begoña Ugarte Uribe**

Supervisor: Itziar Alkorta  
28 May 2012.

"Functional and structural characterization of peptides derived from HIV-1 gp41 membrane proximal and transmembrane domains. Implications for anti-HIV inhibitor and immunogen development"

**Beatriz Apellaniz Unzalu**

Supervisor: José Luis Nieva  
11 June 2012.

"Purification and characterization of the structure and function of a novel actinoporin isolated from the sea anemone *Actinia fragacea*"

**Koldobika Morante Sagasti**

Supervisor: Juan Manuel González-Mañas  
27 September 2012.

"Molecular determinants of KV7.2 surface expression"

**Juncal Fernández Orth**

Supervisor: Álvaro Villarroel  
12 November 2012.

"Ensamblaje de complejos de transporte nucleocitoplasmático con chaperones de histonas"

**Jorge Falces Ramos**

Supervisors: M. Ángeles Urbaneja / Sonia Bañuelos  
26 November 2012.

"Diseño y análisis de un modelo proteico para el estudio de la interacción lípido-proteína"

**Iván Bermejo Luhía**

Supervisor: Ana Rosa Viguera  
20 December 2012.



# Patents

2011/2012

**INVENTORS:**

Gemma Fabriás Domingo, Félix M. Goñi Urcelay, Nuria Izquierdo Useros, Amadeu Llebaria Soldevilla, Santos Mañes Brotón, Javier Martínez Picado.

**TITLE:**

“Methods and compositions for the treatment of AIDS”.

**APPLICANT:**

Laboratorios del Dr. Esteve, S.A.

**PCT APPLICATION Number:**  
PCT/EP2011/051237.

**PRIORITY DATE:** 28-01-2011  
**PRIORITY COUNTRY:** SPAIN

**INVENTORS:**

Luis Alberto Anel Bernal, María José Martínez Lorenzo, Luis Martínez Lostao, Gorka Basáñez Asúa, María Angeles Alava Martínez de Contrasta, Luis Larrad Mur, Javier Naval Iraberri y Andrés Piñeiro Antón.

**TITLE:**

“Liposomes covered with the extracellular domain of the Apo2L/TRAIL protein”.

**APPLICANT:**

University of Zaragoza, UPV/EHU, CSIC.

**PCT APPLICATION Number:**  
US-2012-0189690-A1.

**PRIORITY DATE:** 07-26-2012  
**PRIORITY COUNTRY:** USA



## Conferences and courses

### Organization of Meetings

**II International Workshop on Chagas Disease, Triatomines, T. Cruzi, and Triatoma virus.**

COCHABAMBA, BOLIVIA,  
17-20 SEPTEMBER 2012

- D.M.A. Guérin. Organizer

### 4<sup>th</sup> Annual Meeting “Nanoparticles for therapy and diagnosis of Alzheimer disease (NAD)”

BILBAO, BIZKAIA, SPAIN,  
25-27 SEPTEMBER, 2012  
• Bial Industrial Farmacéutica, F.M. Goñi and H. Ahyayauch. Organizers.



## Invited Talks

### MM4TB FP7 MEETING

• D. Albesa-Jové “Molecular gymnastics at the PimA surface”  
Bratislava, Slovakia,  
12-13 January, 2012

### NATIONAL INSTITUTES OF HEALTH

• V. Frolov “Nanomechanics of Membrane Fission: Lessons from Dynamin”  
Bethesda, USA  
20 January, 2012

### KEYSTONE SYMPOSIA: MEMBRANES IN MOTION

• V. Frolov “Catalytic pathway of membrane remodeling by a minimal dynamin complex”  
Tahoe City, USA  
23 January, 2012

### BIOENGINEERING DEPARTMENT. INSTITUT QUIMIC SARRIÀ. UNIVERSITY RAMON LLULL

• M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”  
Barcelona, Spain  
23 February, 2012

### LELOIR INSTITUTE FOUNDATION

• M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”  
Buenos Aires, Argentina  
19 April, 2012

### UNIVERSITY OF BUENOS AIRES - DEPARTMENT OF BIOLOGICAL CHEMISTRY

• M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”  
Buenos Aires, Argentina  
23 April, 2012

### • D.M.A. Guérin “Triatoma Virus (TrV): un nuevo modelo viral dentro de los picornavirales”

CNB, Madrid, Spain  
24 April, 2012

### TALLER DEL BECARIO “DESARROLLA TU CAPACIDAD DE COMUNICACIÓN EN CIENCIA”

• F.M. Goñi “Seminario sobre redacción de un artículo científico”  
Sevilla, Spain  
3-4 May, 2012

### “SEVENTH INTERNATIONAL VIRUS ASSEMBLY SYMPOSIUM”

• D.M.A. Guérin “Cryo-EM reconstructions of Triatoma Virus empty capsids indicate that this virus doesn’t match picornavirus RNA delivery models”  
Menorca, Islas Baleares, Spain  
13-17 May, 2012



NATIONAL CANCER INSTITUTE (NCI) AND NATIONAL SCIENCE FOUNDATION (NSF) INTERNATIONAL ASSESSMENT OF PHYSICAL SCIENCES AND ENGINEERING ADVANCES IN LIFE SCIENCES AND ONCOLOGY

- J.M.G. Vilar “Computational systems biophysics at the molecular, cellular, and cell-population levels”

Barcelona, Spain  
28-30 May 2012

XXIII SITGES CONFERENCE ON STATISTICAL MECHANICS: UNDERSTANDING AND MANAGING RANDOMNESS IN PHYSICS, CHEMISTRY AND BIOLOGY

- J.M.G. Vilar “Submicron-scale statistical thermodynamics in living systems”

Sitges, Barcelona, Spain,  
4-8 June, 2012

INTERNATIONAL CONGRESS OF THE SPANISH BIOPHYSICAL SOCIETY

- Xabier Contreras “Molecular recognition of a single sphingolipid species by a protein’s transmembrane domain”

- J.M.G. Vilar. “Computational biophysics of cellular processes in health and disease” (Werfen award conference)

Barcelona, Spain  
3-6 July, 2012

MM4TB FP7 MEETING

- D. Albesa-Jové “Crystal structure of Rv2436 from Mycobacterium tuberculosis”

Tällberg, Sweden  
5-6 July, 2012

MYCOSPAIN

- M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”

Madrid, Spain  
9-10 July, 2012

INTERNATIONAL GLYCOMICS SYMPOSIUM

- M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”

San Sebastian, Spain  
19-21 July, 2012

26<sup>TH</sup> INTERNATIONAL CARBOHYDRATE SYMPOSIUM, ICS

- M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”

Madrid, Spain  
22-27 July, 2012

GLAXOSMITHKLINE, GSK

- M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”

Tres Cantos, Madrid, Spain  
27 July, 2012



WORKSHOP ON ORIGINS, EVOLUTION AND FUTURE OF THE BIOSPHERE.

- K. Ruiz-Mirazo “From protocells to minimal cells: models and experimental vesicle systems”

Banyuls, France  
20-31 August 2012

31<sup>ST</sup> EUROPEAN CONGRESS ON MOLECULAR SPECTROSCOPY

- J.L.R. Arrondo “Amyloid Formation Studied by IR 2DCOS-Moving Lapse”

Cluj-Napoca, Romania  
26, August, 2012

INTERNATIONAL INTERDISCIPLINARY SYMPOSIUM “THE EMERGING SCIENCE OF GASTROPHYSICS”

- F.M. Goñi “A biophysicist in the kitchen”

Copenhagen, Denmark  
27-28 August, 2012



ICPOC'21 (21<sup>ST</sup> INTERNATIONAL CONFERENCE ON PHYSICAL ORGANIC CHEMISTRY)

- K. Ruiz-Mirazo “Self-assembly, stability and permeability of precursor cellular membranes”

Durham, UK  
9-13 September, 2012

TUBERCULOSIS, BIOLOGY, PATHOGENESIS, INTERVENTION STRATEGIES

- M.E. Guerin “Conformational changes as key factors in glycosyltransferases mediated reactions”

Institut Pasteur, Paris, France,  
11-15 September, 2012

II INTERNATIONAL WORKSHOP ON CHAGAS DISEASE, TRIATOMINES, T. CRUZI, AND TRIATOMA VIRUS

- D.M.A. Guérin “Advances in structural studies on TrV: Capsid Disassembly and RNA Release”

Cochabamba, Bolivia  
17-20 September, 2012

11<sup>TH</sup> GRETA PIFAT INTERNATIONAL SCHOOL OF BIOPHYSICS

- J.L.R. Arrondo “Infrared Spectroscopy of Lipoproteins”
- J.L.R. Arrondo “Infrared Spectroscopy: A Tool in the Study of Biomolecules”

Primošten, Croatia,  
30 Sept. - 9 October, 2012

X INTERNATIONAL ONTOLOGY CONGRESS “PHYSIS, FROM ELEMENTARY PARTICLES TO HUMAN NATURE”

- F.M. Goñi “Genetics and Humanism: a tribute to Francisco J. Ayala” Round table.

Donostia-San Sebastián, Gipuzkoa, Spain  
1 October, 2012

XXXV REUNIÓN ANUAL SOCIEDAD DE BIOQUÍMICA Y BIOLOGÍA MOLECULAR DE CHILE

- F.M. Goñi “Novel concepts in the structure and dynamics of cell membranes”

Puerto Varas, Chile  
2-5 October, 2012

ENCUENTRO INTERNACIONAL DE TECNOLOGÍAS Y METODOLOGÍAS PARA LA COLABORACIÓN (COLLAB EDUCACIÓN 2012)

- F.M. Goñi “Eficiencia, calidad y educación”

Donostia-San Sebastián, Gipuzkoa, Spain  
10-11 October, 2012

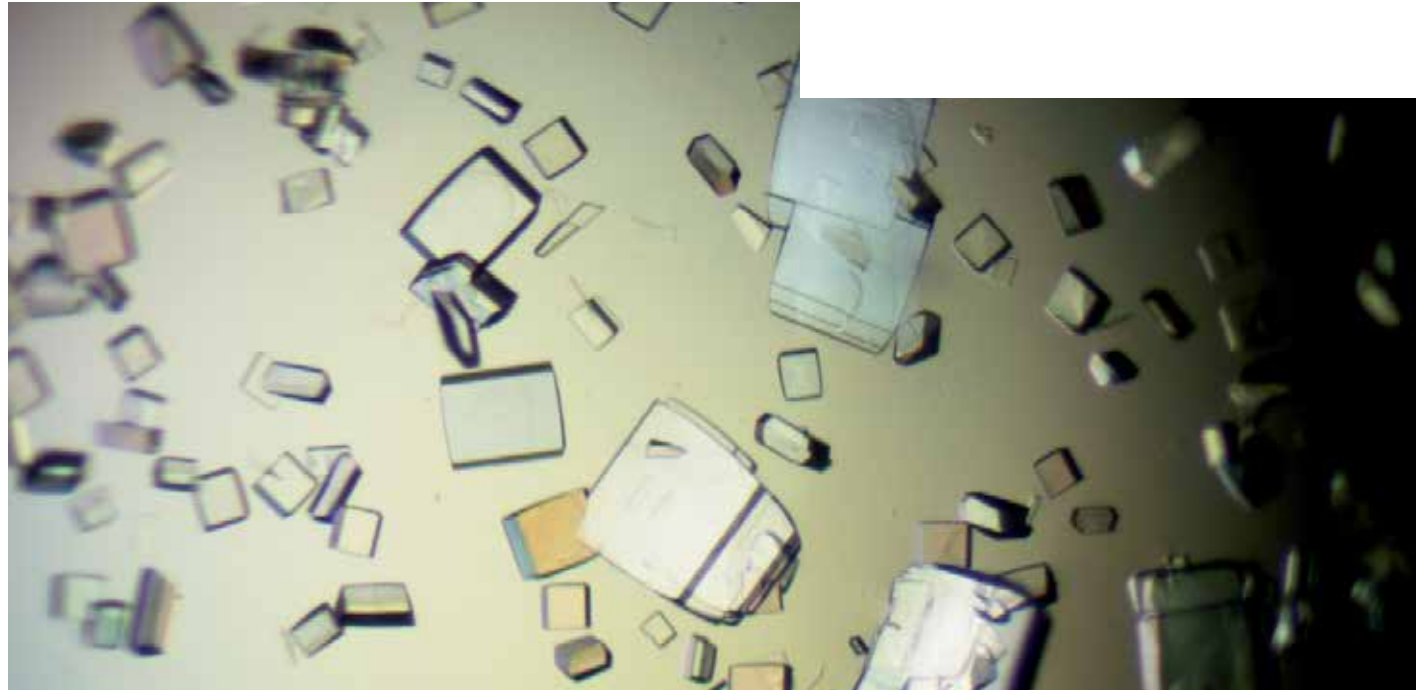
- D.M.A. Guérin “El talento foráneo en Euskadi. Razones para elegir Euskadi” Round table.

Palacio Euskalduna, Bilbao, Bizkaia, Spain  
5 November, 2012

I CONGRESO DE LA AIFIBI (ASOCIACIÓN IBERO-AMERICANA DE FILOSOFÍA DE LA BIOLOGÍA)

- K. Ruiz-Mirazo “On the origin of self-constructing functional protocells: the lipid-peptide model”

Valencia, Spain  
28-30 November, 2012



## Free Communications

Members of the Biophysics Unit have presented communications at conferences, **41** at international and **10** at national events, among which we should highlight contributions to the **56<sup>th</sup>** Annual Meeting of the Biophysical Society, San Diego, California (USA), and the **XXXV** Congress of the Spanish Society for Biochemistry and Molecular Biology, SEBBM held in Sevilla, Spain.

# Bilbao Advanced Courses on Biophysics 2012

COORDINATOR: ITZIAR ALKORTA

[www.fundacionbiofiscabizkaia.org/bilbaobiophysics/](http://www.fundacionbiofiscabizkaia.org/bilbaobiophysics/)

ADVANCED COURSE:

“Biophysical aspects of Type IV secretion”

September 17-22, 2012

The aim of the course is to introduce students to Type IV Secretion Systems (T4SS) from a multidisciplinary point of view. Cellular, genetic, biochemical, structural, and functional approaches to the study of T4SS will be presented. The course is mainly addressed to PhD students and PostDocs in the field of T4SS.

HEAD:

Prof. Peter J. Christie (University of Texas-Houston Medical School, USA)

**ORGANIZERS:**

Dr. Itziar Alkorta (Biophysics Unit, University of the Basque Country, Spain)

Dr. Elisabeth Grohmann (University Medical Centre Freiburg, Germany)

**INVITED SPEAKERS:**

Itziar Alkorta (University of the Basque Country, Spain)

Steffen Backert (UCD, Dublin, Ireland)

Christian Baron (Université de Montreal, Canada)

Peter J. Christie (University of Texas-Houston Medical School, USA)

Fernando de la Cruz (Universidad de Cantabria, Spain)

Christoph Dehio (Biozentrum, University of Basel, Switzerland)

Manolo Espinosa (CIB CSIC, Spain)

Bruno González-Zorn (Universidad Complutense, Spain)

Elisabeth Grohmann (University Medical Centre Freiburg, Germany)

Matxalen Llosa (Universidad de Cantabria, Spain)

Craig Roy (Yale School of Medicine, USA)

Renée Tsois (School of Medicine, UC Davis, USA)

Gabriel Waksman (Institute of Structural and Molecular Biology, London, England)

Ellen Zechner (IMB, University of Graz, Austria)

**The course was attended by 43 students, from 10 different countries.**

# Science Communication

A Lecture Series on **Enfermedades asociadas al envejecimiento** was organised by the BBVA Foundation and CIC bioGUNE in collaboration with the **Biophysics Unit**, the British Council, the Regional Government of Biscay, CSIC-UPV/EHU and Government of the Basque Country (Bilbao, February-May 2012). The speakers included M. Serrano, A. Vidal-Puig, S.C. Lu, E. Villa, S. Moncada and A. López de Munain.

**Darwin Day** was organised by the UPV/EHU in collaboration with the CIC bioGUNE, **Biophysics Unit**, Círculo escéptico and Center for inquiry (Bilbao, February 14 2012). The speakers included K. Altonaga (UPV) and J.M. Bermúdez de Castro Centro Nacional de Investigación sobre la Evolución Humana y Co-director de Atapuerca).

With the title: **“Scientific institutions: production and communication of science”**, the fourth seminar of scientific communication organized by **Biophysics Bizkaia Foundation** was held on 26th April 2012. This seminar aims to spread knowledge about Science and cooperate with professionals in the field of scientific communication. In the present edition, as well as in the previous ones, the Chair of Scientific Culture of the UPV/EHU was also involved.

**A. Alonso** has organised the fourth series of BioForo Lectures at the Faculty of Science through 2012 with participation of the following researchers:

**Jordi Hernandez Borrell**, Dpto. Fisicoquímica, Univ. de Barcelona "Selectividad lipídica y distribución de lactosa permeasa de *Escherichia coli* en bicapas: estudios comparados de microscopia de fuerza atómica y espectroscopia de fluorescencia".

**Patricia Bassereau**, Institut Curie, Paris "How Lipids and Proteins Sense Membrane Curvature".

**Keith Suckling**, GlaxoSmithKline, UK "Molecular biology in drug discovery – examples from atherosclerosis".

**Ina Vorberg**, Bonn, Germany "Prions and prion-like aggregates: Insights into their replication mechanisms".

**Hartmut Luecke**, Depts. Of Biochemistry, Biophysics & Computer Science, University of California, "Crystal structure of the urea channel from the human gastric carcinogen *Helicobacter pylori*".

**Irina Kratchmarova**, Odense, Dinamarca, "Quantitative proteomic analysis of the secretome during myogenesis".

**Isabel Varela- Nieto**, Centro Investigaciones Biomédicas CSIC, Madrid "Autofagia, apoptosis y proliferación celular durante el desarrollo auditivo: regulación diferencial e implicaciones en el diseño de nuevas terapias".

**Michael P Cummings**, University of Maryland, Dept. Biology, USA "Quantifying lineage divergence: the genealogical sorting index".

**Ana Sánchez**, Instituto de Biología y Genética Molecular, CSIC-Universidad de Valladolid, "Células Madre: Origen, tipos y aplicaciones clínicas".

**Javier García-Sancho**, Instituto de Biología y Genética Molecular, CSIC- Universidad de Valladolid "Aplicación de la terapia celular a la enfermedad degenerativa discal".

**Enrique Pérez-Paya**, Centro de Investigación Príncipe Felipe, Valencia "Charting apoptosis regulatory pathways using chemical biology".

**Maria Pia Cosma**, CRG Barcelona "Dissecting functions of Wnt signalling in cell reprogramming and regeneration".

**Rosa Planells-Cases**, Centro de Investigación Príncipe Felipe, Valencia "Pain transduction: Mechanisms of

cellular TRPV1 traffick and surface expression".

**Alfred L. Goldberg**, Harvard Medical School, Boston "New Insights into Proteasome Function".

**José Luis García Pérez**, Center for Genomics and Oncological Research Granada "Control Epigenético de los elementos móviles de ADN humanos LINE-1".

**Peter J Christie**, Dept. Microbiology and Molecular Genetics University of Texas Medical School at Houston "The Structural and Biological Diversity of Bacterial Type IV Secretion Systems".

**Onetsine Arrizabalaga**, GSI Helmholtzzentrum für Schwerionenforschung GmbH, Biophysics division, Darmstadt, Germany "Radiobiological studies using embryonic stem cells related to ion beam therapy".

**José Manuel Andreu**, Centro de Investigaciones Biológicas (CIB) CSIC "Targeting the assembly of cell division protein FtsZ with small antibacterial molecules".

**Ignacio Varela**, IBBTEC y Universidad de Cantabria "Nuevas tecnologías en Genómica del cáncer".

**Arcadi Navarro**, Institut de Biologia Evolutiva, Barcelona "The truth under GWAS. Are they the major contributors to genomic risk for complex disease common to all humankind?".

**Antonio Zorzano**, IRB Institut de Recerca Biomedica, Barcelona "Mitochondrial dynamics, metabolism and disease".

**Francisco Ciruela**, Universidad de Barcelona "Lighting up multiprotein complexes functioning: lessons from G protein-coupled receptor oligomerization".

**Udo Bläsi**, Max F. Perutz Laboratories (MFL), University of Vienna, Austria "Regulation by RNAs and Hfq in microbes: From stress response to virulence".

## Third Alumni Research Meeting (2012/12/19)

**Miguel Andrade**, Max Delbrück Center for Molecular Medicine, Berlin "Data and text mining for the analysis of protein-protein interaction networks".

**Unai Silván**, Uniklinik Balgrist, Institute für Biomechanics, ETH and University of Zürich, Switzerland "The organization of actin cytoskeleton".

**María Soledad Santisteban**, University of North Carolina at Pembroke, USA "Histone variant H2A.Z role in transcription".

**Eduardo Rial**, CIB Centro Investigaciones Biológicas - CSIC, Madrid "Oxidative stress, thermogenesis and evolution of the uncoupling proteins".

**Guillermo Montoya**, CNIO Centro Nacional Investigaciones Oncológicas, Madrid "Molecular machines involved in protein folding and DNA unwinding or how to spend ATP for a good cause".

## Governing Bodies and Academic Committees

**I. Alkorta** continued to serve as Vice-Dean of the Facultad de Ciencia y Tecnología, in charge of Science Communication.

**J.L. Nieva** continued to serve as Head of the Department of Biochemistry and Molecular Biology.

**H. Ostolaza** continued to serve as the Academic Secretary of the Department of Biochemistry and Molecular Biology.

**F.M. Goñi** continued as Coordinator of the Ph D Programme in Molecular Biology and Biomedicine (until June 2012).

**A. Alonso** continued as a Member of the Commission for Teaching Evaluation of the Spanish National Evaluation Agency ANECA in the area of Health.

**I. Alkorta** continued to serve as a Member of the Academic Affairs and of the Academic Exchange Committees of the Facultad de Ciencia y Tecnología.

## Scientific Societies

**A. Alonso** continued as VicePresident for International Affairs of the Spanish Society for Biochemistry and Molecular Biology (SEBBM).

**A. Alonso** continued to serve as member of the Spanish Committee of the International Union of Pure and Applied Biophysics (IUPAB).

**A. Alonso** continued to serve as a member of the Executive Committee of the International Union for Pure and Applied Biophysics (IUPAB). <http://iupab.org/about/officers-and-council/>

**F.M. Goñi** continued as Chair of the International Relations Committee of the Biophysical Society (USA) for a three-year term (July 1, 2010 - June 30, 2013).

**I. Alkorta** continued as Consul for the Basque Country of the Spanish Society of Biochemistry and Molecular Biology (SEBBM).

**I. Alkorta** continued as ordinary member of the Admissions Committee of the Spanish Society of Biochemistry and Molecular Biology (SEBBM) for a four-year term (September 1, 2010 - September 30, 2014).

**I. Alkorta** was the Representative of the Biophysics Unit at the Plataforma Española de Nanomedicina.



## Scientific Journals

**F.M. Goñi** continued to serve as a member of the Editorial Advisory Board of Chemistry and Physics of Lipids (Elsevier), the Journal of Chemical Biology, (Springer) and of the scientific magazine CIC-Network.

**A. Alonso** continued to serve as a member of the Editorial Committee of Biophysical Reviews.

**J.M.G. Vilar** continued to serve as Associate Editor of BMC Systems Biology.

## Other Activities

**F.M. Goñi** was a member of the Evaluation Committee for Fundamental Research of the Iñigo Alvarez de Toledo Renal Foundation. (21 September 2012).

**J.L.R. Arrondo** continued to serve as a member of the ESF Pool of Reviewers of the European Science Foundation.

**F.M. Goñi** continued as evaluator of international scientific and technical projects by the Agency for Quality Assurance in Higher Education and Research of Andalusia (Department of Innovation, Science and Business).

**D.M.A. Guérin** continued to serve as remote referee of the Ideas Specific Programme, European Research Council.

**F.M. Goñi** continued to serve at INBIOMED Scientific Advisory Board.

# Visitors Programme

COORDINATOR: I. ALKORTA

**Stefka G. Taneva** from the Institute of Biophysics, Bulgarian Academy of Sciences, Sofia, Bulgaria, as an Fundaci Visiting Fellow, Dec. 2012.

**Jorge Navaza** from the Institut de Biologie Structurale Jean-Pierre Ebel (IBS), Grenoble, France, is an Ikerbasque Visiting Fellow, Oct. 2011-May. 2012.

**Elisabeth Grohmann**, University Hospital Freiburg, Germany, is a Biofisika Bizkaia Foundation Visiting Fellow, January 2012-June 2012.

**Dov Lichtenberg** from the Tel-Aviv University, Jerusalem, Israel, stayed with us in October 2012-December 2012.

During brief visits, the following researchers gave seminars:

**Jordi Hernandez Borrell**, Dpto. de Fisicoquímica, Universidad de Barcelona "Selectividad lipídica y distribución de lactosa permeasa de *Escherichia coli* en bicapas: estudios comparados de microscopia de fuerza atómica y espectroscopia de fluorescencia".

**Luis M. Liz-Marzan**, Dpto. de Química Física, Universidad de Vigo "Shape controlled metal nanoparticles and their application for SERS detection and imaging".

**Veronique Calleja**, Cell Biophysics Laboratory, Cancer Research UK, Londres "PKB/Akt and PDK1 activation dynamics in cells by FRET/FLIM".

**Hartmut Luecke**, Depts. of Biochemistry, Biophysics & Computer Science, University of California, USA "Crystal structure of the urea channel from the human gastric carcinogen *Helicobacter pylori*".

**Dominique Gagnon**, University of Chicago, USA "Potassium channel function with a single voltage-sensing gate-keeper".

**Pablo Artigas**, Texas Tech University Health Sciences Center, USA "Selectividad y transporte iónico por la bomba de Na/K".

**Nikita Gamper**, Faculty of Biological Sciences - University of Leeds, UK "TMEM16A: Ca<sup>2+</sup> activated Cl<sup>-</sup> channel of epithelia, smooth muscle and sensory neurons".

**Raúl Estevez**, Laboratory Neurophysiology, Department Physiological Sciences I, School of Medicine, University of Barcelona-IDIBAPS "Mecanismos moleculares implicados en la homeostasis iónica y del agua por las células gliales".

**Enrique Pérez-Payá**, Centro de Investigación Príncipe Felipe, Valencia "Charting apoptosis regulatory pathways using chemical biology".

**Ismael Igartua**, GALBAIAN Intellectual Property "Propiedad Intelectual".

**Rosa Planells-Cases**, Centro de Investigación Príncipe Felipe (CIPF), Valencia "Pain transduction: Mechanisms of cellular TRPV1 traffic and surface expression".

**José F. Rodríguez**, Departamento de Biología Molecular y Celular. Centro Nacional de Biotecnología-(CSIC), Madrid "Biología molecular y estructural del virus de la bursitis infecciosa".

**Martín G. Míguez**, Biotechnology, Spain & Portugal "Infrared Based Methods for Protein Quantitation and in-Vivo Target Identification".

**Cristina Sánchez**, INBIOMED "Plataforma de vectores virales de Inbiomed: producción, desarrollo y aplicaciones".

**Jorge Navaza**, Laboratoire de Microscopie Electronique Structurale, Institut de Biologie Structurale Jean-Pierre Ebel, Grenoble, France "Microscopia electrónica en transmisión: metodología, alta resolución, uso combinado con radiocristalografía. Ejemplos ilustrativos".

**Ulf Radler**, Ibidi GmbH Munich, Germany "Cells in focus - new ways in cell microscopy".

**Martin Ulmschneider**, Center for Biomembrane Systems, Depts. of Biochemistry, Biophysics & Computer Science, University of California "The mechanisms of solute flux through membrane channels from multi-microsecond equilibrium simulations".

# PhD Theses from the Biophysics Unit

(Until 1999, Biomembrane Group of the  
Department of Biochemistry, UPV/EHU)

- José Ignacio García Gurtubay (1979)
- Alicia Alonso Izquierdo (1981)
- M<sup>a</sup> Carmen Barbero González (1981)
- M<sup>a</sup> Angeles Urbaneja Arrúe (1984)
- José María Valpuesta Moralejo (1985)
- Arturo Muga Villate (1988)
- Juan Manuel González Mañas (1989)
- María Aránzazu Partearroyo (1989)
- José Luis Nieva Escandón (1991)
- Ana Rosa Viguera Rincón (1992)
- José Castresana Villamor (1992)
- Helena Ostolaza Echabe (1992)
- Sonia Bañuelos Rodríguez (1995)
- M<sup>a</sup> Asunción Requero Zabala (1995)
- Gorka Basañez Asua (1996)
- Fernando Moro Pérez (1996)
- Ana Soloaga Villoch (1997)
- Susana Rivas Cacho (1997)

- Izaskun Echabe Pérez (1997)
- Francisca Pereira Rios (1997)
- M<sup>a</sup> Begoña Ruiz-Argüello (1998)
- José Manuel Martínez Caaveiro (1999)
- M<sup>a</sup> Pilar Veiga Alameda (1999)
- Ana V. Villar Ramos (2000)
- Tatiana Suárez Cortés (2000)
- Asier Sáez Cirión (2001)
- Aitor Hierro Ayuela (2002)
- Aitziber López Cortajarena (2002)
- Aitziber Agirre Ruiz de Arkaute (2003)
- Asier Galán Cousillas (2003)
- Ion Gutiérrez Aguirre (2003)
- Itsaso Hormaeche Berciano (2003)
- Begoña Sot Sanz (2003)
- Ibon Iloro Manzano (2004)
- Xabier Coto Revuelta (2004)
- Jesús Sot Sanz (2005)
- Ruth Montes Burgos (2005)
- Vanesa Fernández Sáiz (2006)
- Isbaal Ramos Hernández (2006)
- Maier Lorizate Nogales (2006)
- Francesc-Xabier Contreras Gómez (2006)
- Silvia Sánchez Martínez (2007)
- Lisete Sánchez Magraner (2007)
- Marcos García Pacios (2007)
- Oihana Terrones Urio (2007)
- Aintzane Cabo Bilbao (2008)

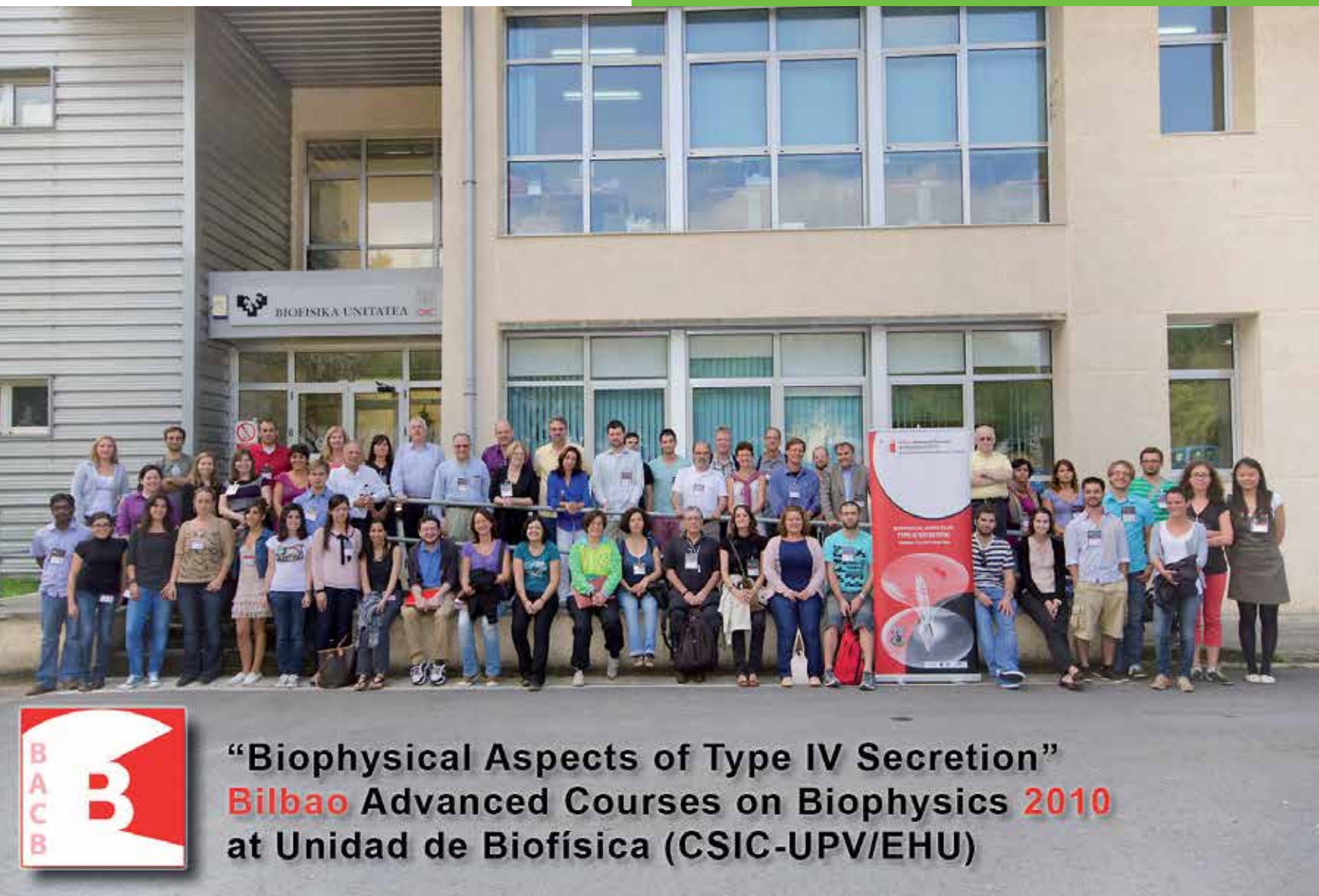
- José Ángel Fernández Higuero (2008)
- Paloma Aivar Mateo (2008)
- Sergio Pérez Acebrón (2008)
- Nerea Huarte Arrayago (2008)
- Aitor Etxebarria Gallego (2009)
- David López Jiménez (2009)
- Patricia Urbina Fernández (2009)
- Jon Agirre Hernández (2009)
- Geraxane Gómez Bilbao (2009)
- Ariel E. Mechaly García (2009)
- Maitane Ibarguren Aizpitarte (2009)
- Igor de la Arada Etxebarria (2009)
- Ana Julia Vecino Ortega (2009)
- Jon Busto Vega (2009)
- Igor Arregi Vado (2010)
- Juan Camilo Gómez Posada (2010)
- Urko del Castillo Rojo (2010)
- Alessandro Alaimo Campi (2010)
- Alain Ibañez de Opakua López de Abetxuko (2011)
- Rubén Maeso Gallego (2011)
- Judit Perales Calvo (2012)
- Begoña Ugarte Uribe (2012)
- Beatriz Apellaniz Unzalu (2012)
- Koldobika Morante Sagasti (2012)
- Juncal Fernández Orth (2012)
- Jorge Falces Ramos (2012)
- Iván Bermejo Luhía (2012)



## Fundación Biofísica Bizkaia Biofisika Bizkaia Fundazioa

**FBB** is a foundation created in 2007, focused on developing and optimizing the activities of Unidad de Biofísica. Both management and scientific areas in the Unidad have been catalysed by FBB.

Since 2009, FBB is listed as a Basque Excellence Research Centre (BERC) by the Department of Education of the Basque Government with the aim of promoting research in the area of biophysics.



## FBB Board Members

### **BASQUE GOVERNMENT**

Department of Education, Universities and Research

**Begoña Ochoa Olagasco**  
(Director of Science Policy)

Department of Industry, Innovation, Commerce and Tourism

**Juan Goicolea Ruigómez**  
(Deputy Minister of Innovation and Technology)

### **PROVINCIAL AUTHORITY OF BIZKAIA**

**Izaskun Artetxe García** (Department of Economic Promotion)

### **UNIVERSITY OF THE BASQUE COUNTRY**

**Iñaki Goirizelaia Ordorika** (Rector)

**Félix M. Goñi Urcelay** (President)

**José Luis Rodríguez Arrondo** (Treasurer)

**Jon Arrieta Mardaras** (Vice-President)

# Funding

In 2012, the Biophysics Unit received funding from the following institutions (listed alphabetically).



The Unit wishes to thank to all of these sponsors for their generous funding and ongoing support.