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DE CIENCIA  
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**SUBPROGRAMA RAMON Y CAJAL  
CONVOCATORIA 2010**

**Nombre:** GLAMPEDAKIS , KONSTANTINOS

**Referencia:** RYC-2010-06608

**Area:** Física y Ciencias del Espacio

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**Título:**

Magnetic field dynamics and evolution in neutron stars

**Resumen de la Memoria:**

Since their discovery in 1967 neutron stars have played a central role in modern astrophysics. Neutron stars are kilometer-scale cosmic laboratories of exotic and exciting physics and their understanding requires a fusion of different fields of modern physics, ranging from relativistic gravity and nuclear physics of superdense matter to magnetohydrodynamics of superfluid/superconducting matter. Given the extreme conditions that prevail in the ultra-dense interior of neutron stars, their observation provides the means to test our understanding of the fundamental properties of matter under conditions inaccessible in the laboratory. In this decade, a new generation of radio, X-ray and gravitational-wave observatories will come into operation, leading to high precision multi-messenger astronomy. The forthcoming observations will probe the detailed physics of neutron stars, with the promise to bring about a significant change in our view of the Universe. In order to ensure that this programme will reach its ambitious goals we need to improve our level of theoretical modeling of realistic neutron stars. The proposed research programme aims at improving our theoretical understanding of the role played by the magnetic field in the dynamics and secular evolution of neutron stars. We will focus on three fundamental astrophysics questions with observational importance: (i) What can we learn from magnetar flares? (ii) How does the magnetic field evolve in neutron star cores? (iii) What is the role of the magnetic field in the thermal properties of neutron stars? The proposed project is highly interdisciplinary, combining magnetohydrodynamics of realistic neutron stars with superfluid components, elasticity theory for the description of the neutron star crust, relativistic gravity, and Fermi-liquid microphysics for the correct description of matter composition and transport properties. This proposal is highly relevant for multi-messenger astronomy. Satellites like RXTE, XMM-Newton, and future missions provide excellent quality data for flaring magnetars and thermally emitting neutron stars, Lofar and SKA will be able to resolve radio pulsar timing properties with unprecedented precision, and the network of ground-based gravitational wave detectors already places limits on the amount of gravitational radiation associated with neutron stars. When completed, the proposed programme will greatly enhance our ability to extract from the data valuable astrophysical information on neutron stars.

**Resumen del Curriculum Vitae:**

**RESEARCH PROFILE** I have a long track-record in the field of neutron star and black hole physics. I started working on black hole perturbation theory and gravitational wave sources during my PhD in Cardiff University (UK). Starting with my first full postdoc at the University of Southampton (UK) I expanded my research interests to include neutron star dynamics, magnetohydrodynamics, and superfluidity. At the same time I continued working on gravitational waves from binary black hole systems. During my second postdoc in SISSA (Italy) I worked almost exclusively on dynamics of neutron stars, focussing on superfluid hydrodynamics and magnetohydrodynamics, and making contact with neutron star observations. Subsequently, I was offered a postdoctoral position at the University of Tuebingen, Institute for Theoretical Astrophysics (Germany), which is the position I presently hold. I continue working on various aspects of neutron star dynamics, such as magnetic fields, superfluidity and, more recently, thermal properties of neutron stars. Recently, I was awarded an Alexander von Humboldt fellowship for experienced researchers to carry out a research project on neutron star dynamics with exotic matter phases. **PUBLICATIONS** In the last ten years I have published 26 papers in high profile international refereed journals, receiving more than 480 citations, and covering a wide range of topics from general relativity and black holes to dynamics of neutron stars (instabilities, pulsations, magnetic fields) and physics of superfluids and superconductors. I am the first author in 16 of these papers, including the most highly cited ones, and usually have 1-2 co-authors. My contribution to all these papers has been significant. **COLLABORATIONS AND PROJECTS** During the last ten years I have established strong collaborations with a number of world-leading experts in neutron star physics and gravitational wave theory. Currently I have an active collaboration with Prof. N. Andersson (Southampton) who is a world-leader in neutron star oscillations and superfluidity, with Dr. I. Jones (Southampton), an expert in pulsar physics and neutron star precession, with Dr. L. Samuelsson (Umea/Nordita), an expert in multifluids and elasticity theory, and with Prof. J. Pons (Alicante), a world-leading expert in thermal properties of neutron stars and magnetic fields. I also keep strong relations with experts in neutron star observations, most notably with Dr. A. Watts and Dr. A. Patruno in Amsterdam. In the past I collaborated with leading experts in gravitational wave source modelling, such as Prof. S. Hughes (MIT), Dr. D. Kennefick (Caltech, Arkansas), Dr. S. Babak (AEI), and Dr. J. Gair (Cambridge). Currently I am the PI in the two-year project "Modelling the dynamics of superfluid neutron stars" funded by the Alexander von Humboldt Foundation, taking place at the University of Tuebingen. Also, I am a co-PI in the project "Kerr black holes or other exotic objects?" funded by the German DAAD and the Greek IKY. **AWARDS** Recipient of the "Vrontoulakis" award for entering the University of Athens Physics Department with the highest exam score (1991). Recipient of a 4-year PhD scholarship (in the UK) from the Greek State Scholarships Foundation (IKY) (1997) Recipient of a 2-year Alexander von Humboldt fellowship for experienced researchers (2010)



**Nombre:** LOPEZ MOYA, MARCOS

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**Area:** Física y Ciencias del Espacio

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**Título:**

Exploración del Universo en Rayos Gamma con detectores actuales y futuros

**Resumen de la Memoria:**

El trabajo de investigación que proponemos persigue tanto objetivos científicos como tecnológicos. En primer lugar deseamos ahondar en el conocimiento del Universo de origen no-térmico mediante la utilización y desarrollo de telescopios de rayos gamma, tanto montados en satélites, como en tierra con los llamados telescopios de luz Cherenkov. Se pretende dar respuesta a preguntas candentes de la astrofísica contemporánea, tales como el origen de la emisión de radiación gamma de muy alta energía (entre 10 GeV y 100 TeV) en los núcleos de las galaxias activas, la naturaleza de las llamadas explosiones de rayos gamma, o la constatación de la existencia de materia oscura. Para ello participaremos en la explotación científica del satélite Fermi y del telescopio terrestre de rayos gamma más avanzado construido hasta la fecha, el telescopio MAGIC situado en la isla de La Palma, y en cuya construcción ha participado el grupo de altas energías de la Universidad Complutense de Madrid Y por otro lado, con el proyecto CTA perseguimos aumentar la capacidad actual de los telescopios Cherenkov, desarrollando nuevas tecnologías que permitan construir una nueva generación de telescopios con un bajo umbral de observación a la par de una alta sensibilidad. CTA es un proyecto internacional de desarrollo tecnológico que pretende instalar una red de hasta 100 telescopios Cherenkov. El proyecto CTA se beneficiará sin duda de la experiencia ganada con MAGIC en el dominio de decenas de GeV, tanto en la fase de desarrollo del detector, como en su puesta a punto y explotación científica, lo que nos permitirá por ejemplo realizar observaciones simultaneas con ambos experimentos.

**Resumen del Curriculum Vitae:**

Highlights of qualifications: Highly inquisitive, creative and resourceful. Experienced with the development of data analysis and monitoring tools for gamma-ray telescopes. Familiar with the technologies used in particle detectors, and specially with the ones used in Cherenkov and space telescopes, as the trigger and data acquisition systems. Expert in C++, ROOT, shell scripts, databases, and related software used in Astrophysics for data analysis and image processing. Excellent skills in communication and collaboration, with much experience working in international collaborations.

1 Education: Doctorate Ph.D. by the University Complutense of Madrid, 2006. Master thesis Master Degree by the University Complutense of Madrid, 2001. Degree Bachelor's degree in Physics, University Autónoma de Madrid, 1999.

2 Current position: Post-doctoral fellowship in the Istituto Nazionale di Fisica Nucleare (INFN), Padua section.

3 Research interests: Study of the gamma-ray Universe with space and ground-based telescopes.

4 Research experience: Member of the international experiments HEGRA (High Energy Gamma Ray Astronomy) and MAGIC (Major Atmospheric Gamma-ray Imaging Cherenkov Telescope), since 2000 and 2001 respectively. Both are experiments for the observation of the Universe in gamma-rays.

4.1 Post-doctoral research: My post-doctoral research has been focused on the study of gamma-ray pulsars, and in particular, in achieving the first detection ever of a gamma-ray pulsar with a Cherenkov Telescope. I was directly involved in the small team which achieved in 2008 the detection of the Crab pulsar above 25 GeV with the MAGIC telescope. Since February 2008 I am the convener of the MAGIC pulsar working group, being responsible of the coordination of all the efforts within the collaboration regarding the detection and study of pulsars. Since the beginning of my post-doct, I am the responsible person of the simulations of the MAGIC-I telescope, providing with new simulations to the collaboration every time that a major upgrade of the telescope is done.

Doctoral research: Development of analysis software and Monte-Carlo simulations for MAGIC, and analysis of the first data taken by the telescope. Development of different gamma/hadron separation methods and the optimization at low energies. I was also in charge of the development of the algorithms for the energy reconstruction and spectrum calculation. Regarding the analysis of the first data, I point out obtaining the first spectrum of the Crab nebula at energies below 100 GeV. Study of gamma-ray pulsars, from a theoretical and observational point of view. Development of a numerical code for simulating the physical processes taking place in the magnetosphere of neutron stars. Development of the full analysis chain for pulsar searches. Analysis of the Crab pulsar and PSR B1951+32. I have worked as well with EGRET data, for testing the developed timing analysis software. Technical activities. Development of a special photo-detector located at the MAGIC camera center to measure the Crab pulsar optical emission. I was also co-responsible of the installation and testing of the time acquisition system of MAGIC, based on an atomic clock synchronized with a GPS.



Nombre: **BORRÁS MARTOS, ANA ISABEL**

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Area: Ciencia y Tecnología de Materiales

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**Título:**

Development and Processing of Functional Nanostructured Surfaces and 1D Nanostructures by Vacuum and Plasma Technologies

**Resumen de la Memoria:**

The Main Research Line of the candidate can be summarized with the title Development and Processing of Functional Nanostructured Surfaces and 1D Nanostructures by Vacuum and Plasma Technologies. This line involves two different and broad research areas: processing of nanostructured functional coatings and the synthesis of supported 1D organic and inorganic nanostructures. Novel nanostructured functional coatings have been fabricated using plasma deposition techniques. The candidate activity in this area involves the fabrication of semiconducting oxide thin films and luminescent organic nanocomposites. The fabrication of semiconducting thin films with tailored properties (refractive index, surface wettability and photoactivity with visible light) has been reported have found direct applications of the thin films as optical coatings, UV protecting layers, photocatalyst and self-cleaning surfaces. A novel technique for the direct characterization of thin film porous structure recently patented is also a result of these studies. The luminescent nanocomposites are fabricated by a novel general process based on partial plasma polymerization of sublimable functional dye molecules. Photonic chips based in these luminescent nanocomposites are being evaluated as environmental sensors in collaboration with industrial and scientific partners in the frame of a European Project. The candidate has also developed two new unprecedented methodologies for the synthesis of inorganic and organic 1D nanostructures: a) supported Ag@MOx nanowires by plasma chemical vapour deposition, a reversible superhydrophobic-superhydrophilic material with promising applications in solar cells and microfluidic; and b) a one-step general method for the growth of supported single crystal organic nanowires by physical vapour deposition, this methodology provides the fabrication of novel 1D organic heterostructures such as the open core@shell nanofibers, the binary nanowires and 1D n-p heterojunctions. Furthermore, the applicant has recently published a straightforward method for the ohmic connection of organic nanowires through metal nanoparticles and studied their transport properties. Nowadays her interest is focused in the exploitation of these 1D organic and inorganic nanostructures for applications in different fields including organic electronic, OLEDs, microfluidic, photocatalysis, solar cells, phototransistors and nanosensors.

**Resumen del Curriculum Vitae:**

The candidate obtained a FPU grant in 2004 (formation for university professors) from the MEC in national competition for the execution of her Ph. D. Thesis: TiO<sub>2</sub> nanostructures deposited by plasma technologies (Special Ph. D. Thesis Award in Physics in the University of Seville (course 2006/2007), date of defense 04.09.2007). The Ph. D. Thesis was carried out in the group  $\zeta$ Surfaces, Interfaces and Thin Films $\zeta$  (Institute of Materials Science in Seville CSIC-U. Seville). In May 2007 the applicant started her postdoctoral contract in EMPA (Swiss Laboratories for Materials Testing and Research, and institution under the ETH-Zurich domain, in Switzerland) in the "Nanotech@surfaces" group under the supervision of Dr. Pierangelo Groening. At the beginning of this contract the full time occupation of the candidate was related to the European Project New PHOTonic Systems on a Chip based on DYE for Sensor Applications scalable at Wafer Fabrication (PHODYE). Currently, the candidate has published 23 articles in SCI, 14 as first author, 3 as second and 6 as third author. 22 articles (96%) were published in journals among the 25% of the highest impact index in the corresponding SCI scientific areas. Moreover, two of these articles have deserved the cover page in the Plasma Processes and Polymers Journal and one in Advanced Materials. The work of candidate during her Ph. D. Thesis and postdoctoral period has provided two new methodologies for the growth of 1D nanomaterials. In a general way, her CV is related to fundamental research areas. However, her scientific interest is also focused in technology transfer activities. Such interest is clearly manifested by the large number of collaboration with the Industry (INDO, EDP, ETRA I+D, Omicron Nanotechnology, CIBA, Multitel, Mantis) and in the development of a patent in the measurement of adsorption isotherms in thin films. The applicant is the first author in this patent. Selection of the more relevant publications: 1.  $\zeta$ Relationship between scaling behaviour and porosity of plasma-deposited TiO<sub>2</sub> thin films $\zeta$ , A. Borrás et al. Phys. Rev. B 76, 2007, 235303. 2.  $\zeta$ Supported Ag-TiO<sub>2</sub> core-shell nanofibres formed at low temperature by plasma deposition $\zeta$ , A. Borrás et al. Nanotechnology 17, 2006, 3518. 3.  $\zeta$ Factors contributing to the growth of Ag@TiO<sub>2</sub> composite nanofibers $\zeta$ , A. Borrás et al. Plasma Process. Polym. 4, 2007, 515 (Journal Cover Plasma Process. Polym. n° 5 Vol 4). 4.  $\zeta$ Reversible Superhydrophobic to Superhydrophilic Conversion of Ag@TiO<sub>2</sub> Composite Nanofiber Surfaces $\zeta$ , A. Borrás et al. Langmuir 24, 2008, 8021. 5.  $\zeta$ Luminescent and Optical Properties of Nanocomposite Thin Films by Glow Discharge Assisted Sublimation of Rhodamine 6G Laser Dye $\zeta$ , F. Aparicio, A. Borrás et al. Plasma Process. Polym. 6, 2009, 17 (Journal Cover Plasma Process. Polym. n° 1 Vol 6). 6.  $\zeta$ Synthesis of Supported Single-Crystalline Organic Nanowires by Physical Vapor Deposition $\zeta$ , A. Borrás et al. Chem. Mater. 20, 2008, 7371. 7.  $\zeta$ Connecting Organic Nanowires $\zeta$ , A. Borrás et al. Adv. Mater. 21, 2009, 4816 (Journal Cover Adv. Mater. n° 47 Vol 21).



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**SUBPROGRAMA RAMON Y CAJAL  
CONVOCATORIA 2010**

**Nombre:** CINACCHI, GIORGIO

**Referencia:** RYC-2010-07475

**Area:** Ciencia y Tecnología de Materiales

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**Título:**

materiales autoensamblados: teoría y simulación

**Resumen de la Memoria:**

The research project is in the field of soft materials. Two main research themes will be investigated, both dealing with self-assembling systems. (I) The design of novel semiconductor materials of the columnar discotic liquid-crystalline type for application in a series of electronic devices, by the synergy of high level quantum-mechanical calculations of intermolecular interactions and atomistic classical and quantum molecular dynamics computer simulations to predict structural properties, including structural fluctuations and defects, of these self-assembling materials and how these properties influence the one-dimensional charge transport characteristics. (II) The theory and computer simulation of the phase behaviour, structure and dynamics of colloidal suspensions. Emphasis will be given to the evaluation of depletion interactions between rod-like colloids induced by smaller particles constituent of the system, the prediction of phase diagrams of mixtures of model rod-like colloids, and the investigation of single-particle and collective dynamical quantities of such systems. In all these cases, both rigid and flexible particles will be considered, in order to keep investigating how particle internal flexibility influences the various condensed phase properties.

**Resumen del Curriculum Vitae:**

I obtained my degree in Chemistry in 2000 at the University of Pisa, as a student of the Scuola Normale Superiore (SNS) di Pisa. My thesis work was on computer simulation of liquid crystals, a large part of which was done at the University of Southampton, United Kingdom. In 2001, I also obtained the Diploma in Chemistry from the SNS. Since January 2001 till December 2003 I was a graduate student of the "Classe di Scienze" of the SNS. During these three years, while keeping investigating mesogenic materials by computer simulation, I have extended my activity toward the statistical-mechanical theories of soft matter systems and the analysis of nuclear magnetic resonance experimental data on liquid crystals. I obtained my Ph.D. degree in Chemistry in 2004, 70/70 cum laude. The title of my Ph.D. thesis was "Theory and Computer Simulation of Liquid Crystals". I then obtained a post-doctoral position at the Department of Chemistry, University of Pisa, from January 2004 till December 2007. From January till August 2008 I have been a post-doctoral fellow of the Advanced Research Center for Electronic Systems, University of Bologna. Since September 2008 to present, I am a Marie Curie Research fellow of the School of Chemistry, University of Bristol, a position awarded to me by the European Commission within the 7th Framework Program of Research and Development. During all these years, I have pursued my research on the chemical physics of soft condensed matter systems. I am author/co-author of 41 articles published in international refereed journals (including one very recent Phys. Rev. Lett. and one, also very recent, J. Phys. Chem. Lett.), and of 2 chapters in edited books. Among all these articles, I am the single author of 4, while I am the main author of the majority of them. Up to now, my works have been cited almost 250 times, with the number of citations increasing progressively during these years. My h-index is 9. The sum of impact factors is 118 and the average number of authors of my articles is 3. I have collaborated and/or am currently collaborating with a number of researchers across Europe. I have attended several scientific schools and presented results of my research at many international conferences. I have given 19 talks, either in the form of oral communications to conferences or as invited seminars. I am reviewer for the Journal of Chemical Physics, Chemical Physics Letters, Journal of Physical Chemistry, Langmuir and Journal of the American Chemical Society.



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**SUBPROGRAMA RAMON Y CAJAL  
CONVOCATORIA 2010**

**Nombre:** SANCHEZ BENITEZ, F. JAVIER

**Referencia:** RYC-2010-06276

**Area:** Ciencia y Tecnología de Materiales

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**Título:**

High Pressure behaviour of metastable transition metal oxides

**Resumen de la Memoria:**

The objective of this Project is twofold: In the first place I aim to synthesize, under high pressures, certain metastable materials which have been little studied, despite their interesting electronic and magnetic properties, such as the metallic behaviour or the presence of metal-insulator (M-I) transitions or charge disproportionation effects. They are oxides of transition metals either exhibiting unusual valence states ( $\text{Ni}^{3+}$ ,  $\text{Mn}^{4+}$ ,  $\text{Cr}^{4+}$ ,  $\text{Fe}^{4+}$ ,  $\text{Mo}^{5+}$ ...) or adopting very distorted structures, the stabilization of which must be achieved under high pressures. In the second hand, I am interested in studying the behaviour of condensed matter under high external pressures; a particular issue concerns the melting of charge ordering under pressure. Charge ordering in oxides drives many important phenomena. The melting of charge order often leads to exotic conduction phenomena near the insulator to metal boundary, such as colossal magnetoresistance in manganites (e.g.,  $\text{La}_{0.5}\text{Ca}_{0.5}\text{MnO}_3$ ) and superconductivity in K- and Pb-doped  $\text{BaBiO}_3$ ; a similar disproportionation effect of high transition-metal valence states is also known in  $\text{CaFeO}_3$  ( $\text{CaFe}_{3+0.5}\text{Fe}_{5+0.5}\text{O}_3$ ) and  $\text{RNiO}_3$  ( $\text{RNi}_{2+0.5}\text{Ni}_{4+0.5}\text{O}_3$ , for  $\text{R} = \text{Y, Pr-Lu}$ ), many of them previously stabilised under pressure. Recently, the high-pressure melting of  $\text{BiNiO}_3$  and  $\text{LaCu}_3\text{Fe}_4\text{O}_{12}$  offers novel examples of internal charge transfer induced by external pressure. My aim is to explore and enlarge some of these systems, describing new phases or going deeper into the comprehension of the mentioned phenomena. Among other systems, I would explore some families of perovskites for which charge disproportionation is envisaged, such as  $\text{R}(\text{Ni}_{0.5}\text{M}_{0.5})\text{O}_3$  ( $\text{R} =$  rare earths;  $\text{M} = 3d$  transition metals). I will also explore novel compositions containing p-block elements at the A sites of the  $\text{ABO}_3$  perovskite structure, susceptible to present charge separation at the A sublattice, such as the paradigmatic example of  $\text{BiNiO}_3$ . We can imagine innovative stoichiometries such as  $\text{PbFeO}_3$ ,  $\text{PbCrO}_3$ ,  $\text{PbVO}_3$  etc. where it is plausible the existence of the mentioned charge disproportionation phenomenon. Some derivatives of the  $\text{AA}'_3\text{B}_4\text{O}_{12}$  family also offer original options for investigating this issue. The synthesis will always be followed by a full characterization including neutron diffraction, magnetotransport properties, etc. in order to better understand the roles of the structural features, the exchange interactions and the electronic instability in these interesting perovskites. The in-situ application of high pressure on the previously synthesized materials would allow me to follow the evolution of different properties: in situ powder neutron diffraction will yield accurate atomic coordinates, from which the charge distribution in the high-pressure phases can be obtained, gathering information about the charge order melting and/or the charge transfer between the involved ions. High-pressure measurements in a diamond anvil cell (DAC) are also essential to learn about the evolution of the electrical, magnetic and optical properties. My final goal is to correlate the different properties under study and to obtain a better comprehension of the behaviour of matter under pressure.

**Resumen del Curriculum Vitae:**

1999, M.Sc. in Physics, Universidad Autónoma de Madrid, subject: Materials Science. 2000, Teaching assistant at the Department of Physics, Faculty of Chemistry, Universidad de Castilla la Mancha. 2001-2005, FPI predoctoral fellowship. January 2006, Ph.D. in Physics of Materials Science at Instituto de Ciencia de Materiales de Madrid (ICMM-CSIC), on subject  $\zeta$  Synthesis and characterization of the  $\text{CaCu}_3\text{Mn}_4\text{O}_{12}$  complex perovskites derivatives with magnetoresistance properties  $\zeta$ . Gained experience on preparation and characterization of new metal oxides. Specialized in synthesis of new transition metal oxides under high pressures. Acquired experience in structural characterization by x-ray and neutron diffraction; acquisition and interpretation of magnetic and transport properties; resolution of magnetic structures. During Ph.D. Stage, participated, among others, in three Projects (Spanish Ministry of Education and Science) on synthesis of metastable oxides containing transition metals in unusual oxidation states, and study and improvement of its magnetotransport properties. 2004, 4 months stay with Prof. Abd-Elmeguid, University of Köln (Germany): gained expertise in measurement of transport properties under high hydrostatic pressure in diamond-anvil cell. January 2006-December 2008, Postdoctoral contract at the Centre for Science at Extreme Conditions (CSEC), University of Edinburgh, under the supervision of Prof. Kamenev: Effect of High Pressure on Single Molecule Magnets: study of different properties (transport, magnetism) under high pressure, becoming specialist in this topic. Design, build and test of new high-pressure cells specially adapted for the measurement of magnetic properties within SQUID magnetometer, PPMS system: access to interesting magnetic behaviours of single molecular magnets based on transition metals within organic matrixes. Responsible of the Magnetism Laboratory at CSEC (3 years). January 2009, Juan de la Cierva contract at the ICMM (second position in the ranking of selected candidates); implementation of the expertise in the measurements of different physical properties under an applied external pressure; setting up the designed high-pressure cells to the available magnetometers in this Center. Currently, leader scientist at ICMM of Project of Comunidad de Madrid (Química a Alta Presión  $\zeta$  QUIMAPRES, S2009PPQ-1551, under the global leadership of Prof. Garcia-Baonza, Univ. Complutense Madrid): preparation and study under high pressures of new transition metal oxides with multiferroic properties. Habitual user of different Large European Installations (Neutrons and Synchrotron X-rays). SCIENTIFIC PUBLICATIONS: Author in 38 papers in journals from the JCR, in the following fields: Physics, Chemistry, Materials Science, Crystallography, and Engineering. Among them: 1 *Angewandte Chemie*, 1 *Physical Review Letters*, 3 *Chemistry of Materials*, 2 *Chemical Communications*, 2 *Applied Physics Letter*, 2 *Inorganic Chemistry*, 5 *Dalton Transactions*, 3 *Physical Review B*, 1 *Journal of Physical Chemistry A*. First author in 36%; average IMPACT FACTOR 3.097. CITED 208 times, H-INDEX of 9. PRESENTATIONS: 24 in international conferences, 7 of them as oral presentation. RESEARCH PROJECTS: 10 at National and European level. Habitual referee of different journals.



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**SUBPROGRAMA RAMON Y CAJAL  
CONVOCATORIA 2010**

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**Area:** Química

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**Título:**

Encoding strategies for exploring the chemical space and targeting biological systems

**Resumen de la Memoria:**

Peptide Nucleic Acid (PNA) technology will be used as an unique tool to investigate chemical reactions and discovery new catalysts in a way which has not been examined before. The encoding of both modified peptides and small molecules libraries using PNA as tags will be achieved either by traditional solid support chemistry or exploring different chemistries to ligate small molecules and peptides to PNA tags in a one-to-one bases. Once these libraries are synthesised DNA-templated synthesis will be used to investigate new reactions. Libraries of small molecules and peptides, tagged with PNA and containing most of the functional groups will be assayed using many different conditions and catalysts, such as metals, could be screened in a quick manner, as my previous work with PNA-encoding peptide libraries has demonstrated. In this way and using both fluorescence and mass spec-based detection techniques compounds formed could be identified. This technology will be also able to investigate catalyst-free reactions, click-chemistry type, as DNA strands will bring to close proximity functional groups, thanks to their hybridization to complementary PNA strands which bear different fragments, which could thus react each other. This strategy will not only have relevance within the organic chemistry area but also it will be applied to biological systems. In this case cellular DNA or RNA will act as the template and therefore the approach could be used to target cells containing mutated genetic material. PNA strands containing fragments which will react each other and form a drug just when there is mutated genetic material present in the cells. The final goal of the project will be to apply my expertise in the knowledge transfer area to exploit all the potential commercial opportunities that the project could offer.

**Resumen del Curriculum Vitae:**

Following my degree in Pharmacy I started my PhD in the Department of Medical Chemistry at the University of Granada. I was involved in the project entitled "Design, synthesis and biological assays of novel molecules that interact with Ras/Choline kinase pathway as potential antitumoral drugs" where I synthesised and screened a family of cationic and phopho compounds which target Chloine Kinase. During that time I had a short stay in Ferrara under the supervision of Professor Baraldi working in the project: "Design, Synthesis and Biological Evaluation of new adenosinic antagonist of A2B receptors". Finally and before moving to the UK I was involved in a project funded by FAES S.A. where I developed new COX-2 inhibitors. Then, I went to the UK to work with Prof. Bradley on combinatorial chemistry and high-throughput screening platforms. In that time I was in charge of bringing microarray facilities to the School of Chemistry at the University of Southampton allowing the group to develop in the field of DNA and material microarrays to be applied in Chemical Biology. While I was at Southampton I started to develop a unique PNA-encoded strategy which has been proven highly successful and has been used to profile kinase and protease. This technology is the backbone of many projects within the group and it is the key of current international collaborations, as one with the Dutch consortium CTMM in which I am Partner Coordinator. In 2005 I was appointed Senior PDRA and I coordinated the move of the whole group, 25 people, from Southampton to Edinburgh and then managed the lab in a daily basis. I worked on a variety of projects from cell-based microarrays, peptide chemistry and organic chemistry to high-throughput screening platforms with fairly good success as the number of published peer-reviewed articles shows. In 2008, following the filling of a UK patent, I was awarded a Scottish Enterprise Proof of Concept Project which final aim is to commercialise a scientific idea. This has given me the opportunity to get into the field of knowledge transfer, allowing me to develop my knowledge on areas such as marketing, intellectual property, finances and business development thanks to the extensive training courses that Scottish Enterprise offer to the PoPP holders. My idea of doing DNA sequencing and SNP analysis by just using chemical methods was patented by the University of Edinburgh being myself inventor and recently has been published in Angewandte Chemie, the premier chemical journal, in which I am corresponding author. This publication has generated a lot of media attention being featured in many of the UK media such as BBC, The Times and The Scotsman due to the potential applications that can offer to the society. Currently we are engage in building up our business plan and raising funds with the aim of spinning-off a company before the end of the year. This latter project has allowed me to get a full picture of how to get the most of research ideas through different ways of commercialisation. Finally a summary of my publication record: 28 peer-reviewed publications, 11 oral presentations, 11 poster communications 2 UK patents, 1 PCT patent (a second one will be filed within this month), H-index 11, Sum of the Times Cited 262.



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**Area:** Química

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**Título:**

Novel Technological Nanostructured Materials

**Resumen de la Memoria:**

My main research line would deal with the synthesis and structural and physical characterization of novel size and shape-controlled nanostructured materials. The ability of tailoring the dimensional regime of nanocrystals represents a landmark achievement in materials science, since at the nanoscale both size and shape dictate the peculiar properties of materials. However, the increasing technological demand is recently favouring the development of novel objects where two or more materials are combined in the single unit, without sacrificing the nanometer dimensions of the same. Consequently, the synthesis of complex nanocrystals, where at least two inorganic materials share a solely inorganic interface, is specially interesting and would be strongly addressed in my project. Several advantages can arise from such heterostructures, as for instance the improvement/tuning of their physical properties, the combination of different properties in single nanoparticles, or the possibility to offer two differentiated chemical surfaces that can be selectively and simultaneously exploited for different purposes. My previous experience in this field allows me to work with a vast range of materials (i.e. metals, oxides, semiconductors) that can be epitaxially combined to study highly complex structures with magnetic, optic, electric, electrochemical or catalytic properties for instance. The main goal of my project is to prepare and characterize new nanostructured systems, which offer innovative properties derived from both their size confinement, as well as from the physical coupling of different materials through a unique inorganic interface. Moreover, I would strongly encourage a multidisciplinary research in collaboration with other groups of my host institution or coming from my external collaborations, in which the novel materials obtained could also be tested in different technological fields such as in biomedicine, in photovoltaic or electronic devices or in the prominent energy storage field, depending on the specific focus of my research. My professional career allowed me to develop good skills in the colloidal preparation of a wide variety of materials at the nanoscale, both single and hybrid nanocrystals. I have proved a good experience in the synthesis and structural and physical characterization of mainly magnetic and optically active nanostructures. For these reasons I suggest three main research lines in which my previous experience would definitely be of interest, that are divided as follows: a) Development and characterization of new single and hybrid magnetic nanostructures designed for biomedical applications. b) Development and characterization of advanced hybrid semiconductor nanostructures for optical, electric or photovoltaic devices. c) Development and characterization of new single and hybrid electroactive nanostructures for improved Li-ion rechargeable batteries. These research lines, they all deal with the preparation of novel nanoparticulated materials with a high control over their size, shape and composition. My previous experience shows my competence in the materials science field in which my contribution could be of significant importance. The wide variety of applications in which such materials can find a place would definitely open the doors for a multidisciplinary research with collaborators from different fields.

**Resumen del Curriculum Vitae:**

My scientific career from 2000 until now covers several fields ranging from magnetic molecular-based materials to magnetic and optically active nanostructured materials. In September 2000 I was granted with a 4-year PhD fellowship from the Spanish Government with a project concerning the synthesis and structural characterization of mixed molecular compounds of transition metal (d) and lanthanide (f) ions and study of their magneto-structural correlations. The papers therefrom derived represented an interesting achievement in the field since it was the first time that a complete structural and magnetic characterization was performed for entire families of isostructural mixed d-f molecular compounds, where both ions showed spin-orbit coupling effects, increasing in this way the potentiality of the systems as molecular magnets. During my PhD I spent some periods in Molecular Magnetism-leading European research teams as the one from Prof. Dante Gatteschi in Florence (Italy) where I improved my skills in single crystal magnetic characterization of d-f compounds to quantify their crystal anisotropy. Some publications derived from this collaboration. During the last part of my PhD I had the chance to establish my first external collaboration working on triangular magnetic systems interesting for the study of spin-frustration phenomena. In some of the publications derived from it, I appear, for the first time, as corresponding author without the presence of my PhD supervisor. After completing my PhD in July 2005, I moved to the National Nanotechnology Laboratory (Lecce, Italy). From the end of 2006, I achieved a high level of experience in the size, shape and composition controlled colloidal synthesis of metallic, oxide and semiconductor nanocrystals with potential applications ranging from magnetic resonance imaging enhancers to solar cell energy conversion devices and light emitting diodes. These works led to the publication of two papers in internationally well recognized scientific journals and both manuscripts deal with the synthesis, structural and physical characterization of hybrid nanocrystals: highly luminescent CdSe@CdS core@shell rods in the first one, and bimagnetic FePt-iron oxide dimeric nanocrystals in the second one. In the latter, I am both first and corresponding author. After that, I kept on working with semiconductor materials but more focused in their organization or assembly for an easier fabrication of nanocrystal-based devices. My most remarkable contribution in this field is a general and simple approach for the assembly in a liquid solution of several shape-controlled semiconductor nanocrystals, such as rods and tetrapods that was also published in a journal with a high impact factor. When I joined the Istituto Italiano di Tecnologia as a Senior Postdoctoral researcher in 2010, I became the Scientific Leader for the IIT partner in the european MAGNIFYCO project, which deals with the synthesis of novel nanostructured magnetic materials for antitumoral hyperthermia and in which I supervise the experimental work concerning materials sciences research in this direction. During all my scientific career I developed good skills in different synthetic approaches of both molecular species and nanostructured materials as well as in the most important techniques for their structural and physical characterization.



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**Título:**

Integración de los bioinsecticidas BVs como componentes de sistemas de control integrado de plagas en cultivos hortícolas de invernadero

**Resumen de la Memoria:**

El desarrollo de resistencia por los insectos a los insecticidas químicos de síntesis más comúnmente utilizados, junto con la aprobación en la Unión Europea de una legislación muy restrictiva y la preocupación pública por la presencia de residuos tóxicos en los alimentos, han contribuido a que los horticultores de Almería adopten el control biológico, en los últimos años, como la principal estrategia de control de plagas de los cultivos de invernaderos. Actualmente se dispone de enemigos naturales (parasitoides y depredadores) muy efectivos para el control de muchas plagas de invernaderos; sin embargo, un número de especies de lepidópteros, específicamente *Spodoptera exigua*, *Helicoverpa armigera* y *Chrysodeixis chalcites*, son difíciles de controlar. A su vez, la presencia de enemigos naturales y polinizadores (ej. *Bombus* spp) en los invernaderos limita muy seriamente la utilización de todos los plaguicidas excepto la de aquellos productos fitosanitarios que son más selectivos. Los baculovirus (BVs) de insectos son bioinsecticidas muy selectivos y altamente efectivos para el control de plagas de lepidópteros. El objetivo general de este proyecto es entender las interacciones de los bioinsecticidas BVs con otros componentes biológicos y químicos que son claves para establecer sistemas de control integrado de plagas en los agroecosistemas de los invernaderos de Almería. Se trata de optimizar la utilización de dichos bioinsecticidas en programas efectivos y sostenibles de control de plagas. Para ello, se llevarán a cabo una serie de estudios en laboratorio y en cultivos de invernadero que nos permitan clonar genotipos e identificar genes que jueguen un papel clave en patogenicidad y virulencia del virus para el desarrollo de nuevos bioinsecticidas. Otros aspectos de interés serán: (1) la identificación de componentes (derivados del estilbeno, enhancinas, etc.) para la obtención de formulados que mejoren la eficacia y persistencia de los bioinsecticidas Bv, y 2) la identificación de análogos de la hormona juvenil y su utilización tecnológica para desarrollar efectivos sistemas in vivo de producción industrial del virus. Utilizando un modelo matemático simple, se estimarán los valores del umbral económico de daños y el umbral de tratamiento, para cada plaga de lepidóptero y su respectivo BV, con objeto de hacer el uso económicamente más rentable y ecológicamente más adecuado de los bioinsecticidas BV. Al mismo tiempo, se determinarán los efectos positivos y negativos que se derivan de las interacciones de los bioinsecticidas BVs con los enemigos naturales y con algunos de los productos fitosanitarios biorracionales (imidacloprid, indoxacarb, spinosad, avermectin, neem, *Bacillus thuringiensis*, etc.) más frecuentemente utilizados en la producción de cultivos en invernaderos. Los resultados de las interacciones de los bioinsecticidas BVs con los enemigos naturales y productos biorracionales serán explicitados en ensayos de invernaderos para definir importantes áreas de potencial incompatibilidad o mejora de la eficacia del control de plagas. Este conjunto de estudios tienen un gran potencial para hacer más extensivo el uso de sistemas de control integrado de plagas, el cual aportará un claro beneficio en la sostenibilidad de las estrategias de control y la reducción de residuos xenobióticos en los cultivos hortícolas de los invernaderos de Almería.

**Resumen del Curriculum Vitae:**

Comencé mis estudios en 1995 en la Universidad de Navarra, obteniendo mi título de licenciada en la especialidad en Biología Medioambiental y Agrícola en 1999. Posteriormente, me incorporé al Dpto. Producción Agraria de la Universidad Pública de Navarra (UPNA) y obtuve una beca predoctoral del MEC para realizar la tesis doctoral. En ella investigué la diversidad genética de los baculovirus y la importancia funcional de los genotipos individuales presentes en estas poblaciones virales, con el fin de desarrollarlos como bioinsecticidas. Durante este periodo realicé dos estancias, de 6 meses cada una, en el Institute National de la Recherche Agronomique (INRA), Francia, bajo la supervisión del Dr. M. López-Ferber, donde aprendí las distintas técnicas de biología molecular y celular aplicables a los microorganismos entomopatógenos. En 2004 obtuve el título de doctor con mención de doctorado europeo. En 2005 conseguí una beca postdoctoral del MEC, la cual me permitió incorporarme al Centre for Ecology and Hydrology, Oxford, Reino Unido, bajo la supervisión del Prof. R.D. Possee. En esta etapa me adentré en el campo de la ecología molecular de los baculovirus y sus aplicaciones. Aquí llevé a cabo, de manera exhaustiva, la caracterización de nuevos genes del virus e identifiqué el efecto de uno ellos en la transmisibilidad de los baculovirus y la causa molecular que lo determina. También investigué sobre las infecciones persistentes producidas por baculovirus. En 2007 me incorporé, como Prof. Ayudante Doctor, a la UPNA donde colaboré activamente en varias asignaturas de protección de cultivos impartidas en la titulación de Ingeniero Agrónomo e Ingeniero Técnico Agrícola. Al amparo de dos ayudas de movilidad del Programa José Castillejo, realicé sendas estancias en centros de alto prestigio internacional; Great Lakes Forestry Centre (Sault St Marie, Canadá) y Centre Nationale de la Recherche Scientifique (CNRS, Francia). En 2009 me incorporé al grupo de Bioinsecticidas Microbianos del Instituto de Agrobiotecnología (Universidad-CSIC, Pamplona) con un contrato JAE-DOC. Creo relevante destacar que mi retribución como investigadora ha sido siempre sufragada a partir de convocatorias de concurrencia competitiva de amplio espectro (becas y contratos pre y postdoctorales, ayudas de movilidad internacional, etc.). Tengo 13 publicaciones internacionales, en once de las cuales soy la primera autora, todas ellas incluidas en el ISI y algunas de éstas han acumulado más de 40 citas. He dirigido 9 tesis de máster, dirijo 2 tesis doctorales y colaboro en la docencia de dos asignaturas específicas del Máster Universitario en Agrobiotecnología el cual está acreditado con la Mención de Calidad del Ministerio (MCD 2003-00677). Durante estos años he participado en 6 proyectos de investigación competitivos financiados por convocatorias públicas, siendo el investigador principal de uno de ellos, y en otros 6 proyectos de especial relevancia con empresas. He realizado 26 comunicaciones en congresos internacionales y 13 en nacionales. Igualmente, he sido miembro de varios tribunales de tesis doctorales, varias comisiones de contratación, y de un jurado internacional para la evaluación de la mejor ponencia y póster de estudiantes en el 41th Annual Meeting SIP, 2008, Warwick, Reino Unido. Estoy en posesión de la Acreditación Positiva, por la ANECA, para la figura Profesor Contratado Doctor.



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**Título:**

Computational fluid dynamics applied to numerical weather forecast

**Resumen de la Memoria:**

Mesh generation Nowadays, the Delaunay and the advancing front methods are the most widely used. Both have reached a high level of maturity and robustness for isotropic meshes, where there is no special stretching direction. However it is easy to see with a simple plate law in laminar regime that a method like LES (Large Eddy Simulation) applied to a complex geometry like a plane requires a number of nodes much larger than what will be possible in the next 15 years. It is therefore necessary to use alternative methods like the RANS (Reynolds Average Navier-Stokes) method where the stretching is used to capture the boundary layer with a minimum number of elements. A modern mesh generator should be able to mesh or remesh boundary layers and shocks identified by the solver, with structured and unstructured areas, and use all these capabilities depending on the kind of problem at hand. Iterative solvers The incompressible Navier-Stokes equations have been studied from a theoretical point of view since a long time but its numerical resolution still represents a challenge. On one hand, the monolithic resolution of the velocity/pressure system is slow. On the other hand, iterative solvers based on the Uzawa method are fast but they do not respect well neither mass conservation nor boundary conditions. In both cases, iterative solvers are necessary in three dimensions to resolve at least the implicit pressure system. Compressible flow The compressible Navier-Stokes equations were studied first historically on a computational point of view. Numerous results were produced since the half of the last century. The author is currently investigating using them in a numerical weather prediction context to accelerate simulations and improve the scaling of the artificial dissipation models used. Historically, numerical weather forecast relies almost exclusively on finite differences where a special treatment is applied in the vertical and horizontal directions. Similar or better results should be obtained relying on linear algebra, as this kind of acceleration may be interpreted as a preconditioning of the global system, without the need to explicitly apply different treatments to the horizontal and vertical directions. Linelet preconditioning have been used steadily in compressible and incompressible solvers, and are an example of the benefits of applying CFD to numerical weather prediction. If numerical weather prediction methods and CFD have been up to now distinct areas of research, the computation of supersonic business jets in real atmosphere is today's reality. Parallelism The more the number of transistors is increasing, the more power resources are needed. Therefore constructors seem to move towards non homogeneous architectures where the responsibility of the programmer is more and more important. Therefore, the BSC is a very good place to know accurately what are the new tendencies in supercomputing. Shared memory architecture and renumbering has been recently intensively investigated by the author. The hybrid paradigm will be the next strategy studied.

**Resumen del Curriculum Vitae:**

During my PhD in Barcelona with advisers Prof. Oñate and Idelsohn, I focused on the study of incompressible flows with free surface and thermal coupling in a Lagrangian framework. The first difficulty when dealing with a Lagrangian formulation is the necessity to constantly remesh the volume under study at each time step, as the fluid suffers large deformations. After my PhD, I had a post doc status at George Mason University in Fairfax, Virginia, working with Professor Lohner. After having compared my PhD code with the one of Professor Lohner, I concentrated on the mesh generation for turbulent stationary flows simulations or RANS (Reynolds Average Navier-Stokes) with complicated geometries with ridges and corners. It relies on the introduction of degenerated triangles which will form well defined prisms during the extrusion of the boundary layer mesh. The main difficulty consists in recovering the triangulation conformity, which was lost during the insertion of the virtual triangles. The last year in United States was dedicated to study ways to accelerate the resolution of Poisson solvers, which are classically associated with the incompressibility constrain. The CPU time associated with the solver resolution accounts for the main part in the whole solver. The experience I had during my PhD on incompressible flows helped me in this task. The CFD group at George Mason University is specialized in particular with hemodynamic for patient specific applications in real time. Therefore, a deflated iterative solver was implemented in this context, which provided added robustness and speed, which allowed solving geometries until then intractable. Since April 2008, I am a researcher at the Barcelona Supercomputing Center (BSC), in the CASE (Computer Applications in Sciences and Engineering) department. The center is divided in four departments, one of which is Earth Sciences where one of the main research lines is numerical weather forecast. Numerical methods used in numerical weather forecast rely mainly on high order finite difference. One of its main weaknesses is that the stencil used to reach high order impedes an efficient parallelization, where the ratio between computation and communication between processors must be taken into account. My job consists in developing a highly scalable fully compressible three dimensional unstructured solver to run as efficiently on PCs as in modern supercomputers. In order to keep a general framework and take advantage of unstructured meshes, the real domain is studied where the anisotropy arises in the mesh. My experience in United States on anisotropic mesh generations was instrumental to generate efficiently these meshes. On the other hand, the department is constituted by young researchers in computational fluid dynamics. My other task consists in improving various numerical aspects of an in house code where my experience could help. One of the first problems in CFD appears when importing a geometry. Furthermore, extensions of the deflated solver to parallel shared and distributed machines have been conducted. Finally, various strategies to efficiently parallelize a generic edge based solver on shared memory machines have been investigated through extensive numerical computations and timings.



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**Título:**

Nanoingeniería de interfaces para la optimización de generadores termoeléctricos avanzados

**Resumen de la Memoria:**

La necesidad de utilizar las fuentes de energía en forma más eficiente atemperando el impacto del uso de los combustibles fósiles por el cambio climático inducido sobre el medio ambiente, se está convirtiendo en un problema para la humanidad. Actualmente, la mayor cantidad de energía se desperdicia en forma de calor. En este contexto, los materiales termoeléctricos, que son los que generan electricidad a partir del calor desperdiciado o de la radiación solar concentrada, podrían tener un lugar preponderante en la solución sostenible a la demanda energética. Los materiales termoeléctricos clásicos usados hasta ahora son semiconductores que contienen Pb, Te, Bi, Sb, pero la implementación a alta temperatura es difícil debido a su toxicidad, escasez y a su pobre estabilidad química a alta temperatura. El uso de intermetálicos y óxidos como materiales termoeléctricos a diferentes rangos de temperatura manifiesta un enorme potencial para resolver estos problemas. Estos materiales son muy atractivos y a la vez ambientalmente limpios porque permiten generar potencia eléctrica libre de CO<sub>2</sub>. Su implementación en dispositivos depende de la creación de nuevos materiales con alta eficiencia termoeléctrica con respecto a los disponibles actualmente. Un buen material termoeléctrico tiene que exhibir alta estabilidad, alto coeficiente Seebeck (S), buena conductividad eléctrica (s) y baja conductividad térmica (k) con el mayor gradiente de temperatura posible. La obtención y combinación de dichas propiedades suponen, a día de hoy, un verdadero desafío científico y tecnológico. Este proyecto tiene como objetivo mejorar la eficiencia en la conversión calor-electricidad por medio de la obtención de superredes, nanopartículas, los cuales reducen la conductividad térmica optimizando la dispersión de fonones en las intercaras. Los compuestos a desarrollar serán intermetálicos, óxidos tipo perovskitas y óxidos binarios que sean semiconductores tipo p o tipo n. El método experimental para dicho desarrollo constará de: i) métodos modernos de síntesis: como por ejemplo la deposición de capas atómicas (ALD) o deposición química en fase vapor aumentada por plasma (PECVD) para obtener materiales en 2D, y métodos de química suave para obtener nanopartículas; ii) caracterización de los materiales por técnicas diversas que son particularmente útiles para materiales a nano-escala: microscopía electrónica de transmisión en ultra alta resolución (UHRTEM) y con barrido (STEM) y espectroscopia de pérdida de energía electrónica (EELS) o estructura de borde de absorción en pérdida de energía electrónica (ELNES); iii) caracterización de propiedades de transporte: se emplearán medidas Hall, Seebeck y conductividad eléctrica por medio de 4 puntas también como método de termoreflectancia para la conductividad térmica. Finalmente, los dispositivos termoeléctricos se fabricarán con los materiales, semiconductores tipo p y tipo n, que muestren las mejores figuras de mérito para cada rango de temperatura mejorando así la eficiencia del sistema.

**Resumen del Curriculum Vitae:**

Myriam Haydee Aguirre se doctoró en Diciembre del 2001 en Ciencias Físicas en la Universidad de Buenos Aires-Argentina. Su tesis titulada: ¿Estudio de los defectos producidos por implantación iónica en el proceso de obtención de la unión p/n en HgCdTe¿ recibió la nota máxima (10 sobresaliente). Este trabajo fue realizado en colaboración con la Universidad Complutense de Madrid (UCM) donde realizó una estancia de aproximadamente 2 años con la financiación del Programa Europeo Alfa para el estudio de materiales por microscopía electrónica de transmisión. El eje principal de investigación fue el estudio de la estructura y microestructura de los materiales II-VI correlacionada con sus propiedades eléctricas para la detección infrarroja y uso en detectores fotovoltaicos. Tras su doctorado se incorporó al Dept. de Química Inorgánica I-UCM como Becario Postdoctoral CAM (2002-2004) para el estudio de materiales cerámicos superconductores de alta temperatura crítica por medio de síntesis de alta presión y caracterizándolo con microscopías electrónicas avanzadas. Fue investigador visitante (1/2/2003-1/5/2004) en la Universidad de St. Andrews-School of Chemistry and Materials, en Escocia, financiado con una ¿Research Visit Fellowship¿ otorgada por la Royal Society of Chemistry-UK para establecer una activa colaboración entre el Laboratorio de altas presiones-UCM y la escuela de materiales de la Universidad de St. Andrews en la síntesis y caracterización de perovskitas. Fue investigador y profesor asistente (1/6/2004-31/12/2005) en el Instituto de Física Aplicada del ETH (Eidgenössische Technische Hochschule) Zürich, Suiza. Es investigador (1/1/2006-actualidad) del Grupo de Química de estado sólido y Catálisis del EMPA-Material Science and Technology, perteneciente al ETH. Sus principales líneas de investigación son los materiales termoeléctricos para su aplicación a dispositivos de conversión en energía (>25 publicaciones) y materiales que presentan la propiedad de cambio brusco de la resistividad (¿resistivity switching¿) para su aplicación en memorias (> 8 publicaciones). Tiene varias participaciones en contratos de investigación y transferencia de tecnología de especial relevancia con empresas (Balzers AG, Daimler AG, Novatlantis AG). Posee 76 publicaciones (3 enviadas, 9 aceptadas, 64 publicadas) de las cuales 7 corresponden a informes a compañías, 2 capítulos de libro, 3 en revistas de divulgación científica, 7 proceedings con Science Citation Index, 5 proceeding sin SCI, 52 peer review papers (Chemistry of Materials, Acta Materialia, Inorganic Chemistry, Applied Physics Letters, Journal of Applied Physics, Advanced Functional Materials, Journal of Material Chemistry, Applied Catalysis B, entre otras). Dirigió varias Tesis de Master en ETH (S. Wenger y N. Schäuble) y actualmente codirige la tesis doctoral de Nina Schäuble en films termoeléctricos y Andrey Shkabko. Tiene más de 10 años de experiencia docente y 12 años de experiencia en TEM. Tiene cerca de 40 contribuciones a congresos nacionales e internacionales. Es revisor habitual de las revistas científicas Chemistry of Materials, Material Chemistry & Physics, Inorganic Chemistry, Journal of Solid State Science, Physica Status Solidi, Micron, Journal of Alloys and Compounds, Journal of Crystal Growth, Applied Energy, Solid State Science, Material Science and Engineering B.



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**Título:**

Translational regulation of connexins and functional consequences during human tumour progression

**Resumen de la Memoria:**

Connexins, structural proteins of gap junctions allowing direct intercellular communication, can act as tumour suppressors and the principal investigator and others have demonstrated reduced or aberrant connexin expression in many tumours and tumour cell lines. It is becoming clear however, that the function of connexins is isoform-specific, tissue and tumour stage specific, and in part due to non-gap junctional properties. Indeed, overexpression of connexins have also in cases been shown to promote invasion and metastasis, and clinical studies have correlated increased connexin expression with tumour aggressiveness and reduced prognosis. Connexins form part of a small number of genes that contain internal ribosome entry site (IRES) elements allowing cap-independent mRNA translation, typically activated during cellular stress including hypoxia, radiation, starvation, and during programmed cell death and differentiation. In recent years, cap-independent translation has emerged as a major and important pathway activated during tumour progression and is associated with poor prognosis. Restoration of connexin expression and gap junctions through cap-independent translation has been described as a mechanism for density-inhibition of cancer cells. However, it is conceivable that in certain circumstances such as metastasis, increased cap-independent translation of connexins may instead promote tumourigenesis. Thus, although connexins have been proposed as potential pharmacological targets, mechanistic data of how connexins are regulated during tumour progression, and further functional consequences of this, needs to be addressed. We aim to characterize connexin expression in various human tumours and correlate this with tumour stage and the expression and phosphorylation status of key mediators of cap-independent translation. We will modulate the cap-independent translation machinery in vitro in tumour cell lines and correlate this with connexin expression, cell communication, and assay the functional consequences including proliferation, tumourigenicity and epithelial-to-mesenchymal transition. Direct modulation of connexins (by overexpression and RNAi approaches) will be used in complement to identify connexin-specific effects. Our results should gain mechanistical insight into the regulation of connexins, identify possible functional consequences during cancer progression, and shed light on how activation of the cap-independent translational machinery may regulate this process.

**Resumen del Curriculum Vitae:**

TRAINING: PhD: 1999-2002 University of Glasgow, Scotland, UK (Gap junctions and connexins in squamous epithelial differentiation and HPV-associated carcinogenesis). Postdoctoral: 2003 Institute of Cancer Research, London, UK (Fumarate Hydratase in Tumour Development). 2004-07 Centre for Cutaneous Research, Institute of Cell and Molecular Science, Queen Mary University of London, UK (Cell Biology of Gap Junctions). 2007-10 Center for Regenerative Medicine in Barcelona, Spain (Gap Junctions in Human Embryonic Stem Cells / Induced Pluripotent Stem Cells). KEY AWARDS: British Society for Investigative Dermatology Young Investigator 2005. Wellcome Trust Value in People (VIP) award 2005. FRONT COVERS: Nature Biotechnology 2008, Nature Protocols 2010. KEY PUBLICATIONS: Aasen T 5(2):371-82. Giorgetti A, et al. Generation of induced pluripotent stem cells from human cord blood using OCT4 and SOX2. Cell Stem Cell. 2009 Oct 2;5(4):353-7. Raya A, et al. Disease-corrected haematopoietic progenitors from Fanconi anaemia induced pluripotent stem cells. Nature. 2009 Jul 2;460(7251):53-9. Aasen T, et al. Efficient and rapid generation of induced pluripotent stem cells from human keratinocytes. Nature Biotechnology. 2008. 26(11):1276-84. Matos TD, et al. A novel M163L mutation in connexin 26 causing cell death and associated with autosomal dominant hearing loss. Hearing Research. 2008 Jun;240(1-2):87-92. Matos TD, et al. A novel hearing loss related mutation occurring in the GJB2 basal promoter. Journal of Medical Genetics. 2007 Nov;44(11):721-5. Unsmoth H\*, Aasen T \*, et al. Tissue specific effects of wildtype and mutant Connexin 31: a role in neurite outgrowth. Human Molecular Genetics. 2007 Jan 15;16(2):165-72. Aasen T, et al. Reduced expression of multiple gap junction proteins, including connexin 26, is a feature of cervical dysplasia. Molecular Cancer, 2005, 9;4(31):1-5 (Corresponding author). Di WL, et al. Connexin interaction patterns in keratinocytes revealed morphologically and by FRET analysis. Journal of Cell Science 2005 April 1;118 (Pt 7):1505-14. Aasen T, et al. The relationship between connexins, gap junctions, tissue architecture and tumour invasion, as studied in a novel in vitro model of HPV-16-associated cervical cancer progression. Oncogene 2003. 22 (39): 7969-7980. Bakirtzis G, et al. Targeted epidermal expression of mutant Connexin 26(D66H) mimics true Vohwinkel syndrome and provides a model for the pathogenesis of dominant connexin disorders. Human Molecular Genetics. 2003. 12 (14): 1737-1744. Thomas T, et al. Transport and function of cx26 mutants involved in skin and deafness disorders. Cell Communication and Adhesion 2003. 10(4-6): 353-358. Bakirtzis G, et al. The effects of a mutant connexin 26 on epidermal differentiation. Cell Communication and Adhesion 2003. 10(4-6): 359-364. BOOK REVIEWS: Aasen T & Belmonte JCI. Keratinocyte induced pluripotent stem cells: from hair to where? Springer Press (accepted). Aasen T & Kelsell DK. The role of connexins in skin biology. Connexins: A Guide. Humana Press 2009, ISBN: 978-1-934115-46-6. Aasen T & Houlston SR. Mitochondria and cancer: more to life than death. Research Advances in Cancer, 2003 vol. 3, pp. 283-294.



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**Título:**

Identification of diagnostic, prognostic markers and new therapeutic targets in liver cancer

**Resumen de la Memoria:**

The hepatoblastoma (HB) and the hepatocellular carcinoma (HCC) are the main liver tumors that appear in the childhood and in adults, respectively. Although chemotherapy and surgery has improved the survival of the patient with HB, a quarter of these patients does not respond to chemotherapy and does not survive. On his part, HCC is the third cause of cancer-related death and the success of the treatment depends on its early diagnosis. The early HCC detection is possible by developing surveillance programs in the cirrhotic population by means of imaging techniques but the lack of effective serum markers prevents its detection at earlier phases. Recently, cancer stem cells have been identified in different neoplasms including liver cancer as responsible of tumorigenesis, failure to current anti-tumoral therapies and impaired long-term patients' survival. A new subclass of HCC with hepatic stem cell features has been identified by microarray (Lee JS et al, Nature Med, 2006). Similarly in HB, we have identified a new subclass of aggressive tumors with a hepatic progenitor phenotype and we have defined a 16-gene signature that allows the identification of the group of HBs and HCCs with poor prognosis (Cairo-Armengol et al, Cancer Cell, 2008). The study of both tumor types could offer a new sight to better understand the underlying mechanisms of hepatocarcinogenesis and could help in the management of patients with liver cancer. The first aim of this project is to identify diagnostic markers of HCC by analyzing the protein profile of the plasma of 200 cirrhotic patients with or without the neoplasm by using mass spectrometry. The protein expression of candidate markers will be validated in an independent training set of 200 additional samples by mass spectrometry. Immunostaining (IHC) and Western Blot will be used to study the expression of the identified markers in tumor specimens. The second aim is to perform a high-throughput proteomic screening by 2-D Fluorescence Difference Gel Electrophoresis (DIGE) and mass spectrometry of the 2 recently identified HB subclasses (Cairo-Armengol et al, Cancer Cell, 2008) in order to better understand the molecular pathways of HB oncogenesis. The obtained proteomic findings together with the 16-gene expression signature previously published will be used as the basis to develop a new protein prognostic signature for HB patients in order to facilitate its application in the clinical practice by replacing Real-Time PCR for a simple IHC. The study of the candidate protein markers will be evaluated in 100 paraffin-embedded HBs in a Tissue Microarray (TMA) that is being developed. Once the protein signature is defined, its application in HCC patients will be also evaluated by TMA. Finally, with the aim to identify new therapeutic anti-tumoral targets we will done functional studies of the proteins identified to identify which of them are initiating or promoting the neoplastic process. To accomplish this we will establish cell lines derived from liver tumors as well as mouse models by subcutaneous cell line injection and we will use RNA interference technology. This project aimed to identify new diagnostic markers for early detection of HCC in cirrhotic patients, to define a prognostic signature at protein level for patients with liver cancer to facilitate its application in the clinical practice and to identify therapeutic targets based on proteomic studies to develop new drugs for HB and HCC patients.

**Resumen del Curriculum Vitae:**

Degree in Biology by the Universidad de Girona (1996) and Degree in Biochemistry by the Universidad Autónoma de Barcelona (1998). PhD thesis in Biochemistry by the University of Barcelona (2004), directors: J Bruix, MD and O Bachs, PhD. During my PhD on liver cancer, I have published 2 papers as first author in first quartile journals (Clin Cancer Res, 2004 and J Hepatol, 2003), I took part actively in 2 public projects financed by the Instituto de Salud Carlos III and the Comisión Interministerial de Ciencia y Tecnología, I was awarded with the price for younger researchers of Rius i Virgili Foundation (1998) and I obtained a pre-doctoral FPI grant for the researchers formation of Spanish Ministry of Education (1999-2002). In my 3-year post-doctoral training (2004-2007) in the Institut Pasteur (Paris) supervised by MA Buendia PhD, I obtained a post-doctoral grant from the European Association for the Study of the Liver and another post-doctoral grant from the French Medical Research Foundation, I started a new research line on genome-wide studies of liver cancer by microarrays and a paper as first-author in Cancer Cell in Dec 2008 (IF: 24.962) summarizes the main findings. Moreover, I have published as first author a book chapter in *Genetics in Liver Diseases* (2007) and I am co-author of 3 other papers in first quartile journals (J Biol Chem, 2008; PlosOne, 2008; Cancer Res, 2007). Moreover, I am co-discovered of one patent (Registry N: 08290628.0), I actively participated as principal investigator in projects financed by the French National Institute of Health and Medical Research and by the Institut Pasteur for a total amount of 200.000€. In 2008, I have started a research line focused on liver cancer in the Institute of Biomedical Investigation of Girona and since 2009 I am continuing it in the Health Science Research Institute Germans Trias i Pujol of Badalona. Nowadays, I am a post-doctoral researcher of the Biomedical Research Center Network in Liver and Digestive Diseases authorized by the ISCIII to be Principal Investigator, I am member of the International Liver Cancer Association and of the Evaluation Committee of the French National Cancer Institute and I am referee of several high-impact international journals (J Hepatol, Liver Intern, Hepatol and Clin Cancer Res). Importantly, I have boosted the first research line on childhood liver tumors in Spain with the support of the Childhood Liver Tumours Study Group (SIOPEL) and the Society of Pediatric Hematology and Oncology (SEHOP) and I have started a project aimed to identify new diagnostic factors for hepatocellular carcinoma recently financed by the ISCIII (104.060 euros, 2010-2013), I have created the first National Biobank of Childhood liver tumors, I am directing one PhD thesis, I am tutor of a student of Biology, I have recently written 2 reviews (Armengol et al, Int J Biochem Cell Biol, 2009 and Cairo, Armengol et al Front Biosc, in press) and I have 3 manuscripts under preparation. I keep active scientific collaboration with several Spanish and International teams of Institut Pasteur; Hospital Clinic and University of Barcelona; H Bicêtre; CICBioGUNE; H. Vall Hebron of Barcelona; European SIOPEL group; University of Hong Kong) and in total I have actively participated in 25 meetings (18 oral communication).



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**Area:** Biomedicina

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**Título:**

A genetic dissection of tumour progression and invasion in the context of a living epithelium

**Resumen de la Memoria:**

I will characterise the very first steps in tumour progression and invasion within a living animal. Using state-of-the-art live cell imaging and Drosophila genetics, I will follow transformed epithelial cells as they grow and invade surrounding tissue, and will identify the genes involved as targets for future therapeutic intervention. I have recently established a system that enables me to visualise the behaviour of individual mutant epithelial cells in a living tissue in the fly. In the proposed project I will use this as an animal model in which to study the very early events in tumour development. This is significant because although tumour development, from cell over-proliferation to metastasis, are the leading cause of death in the majority of human tumours, little work has been done to study these processes in an in vivo context or to identify the genes involved. Using GFP to label cancerous epithelial cells, I aim to image the very first cell biological events that underlie over-proliferation, invasion and metastasis within a living animal. I will then use a combination of classical fly genetics and RNAi to identify the key molecules involved and characterise how these genes may promote or inhibit tumour progression. Using the Drosophila notum as a model system I will characterise the critical events that underlie tumour cell invasion using the following research plan: 1st) I will describe the behaviour of GFP-labelled epithelial cells live in the intact animal during each step in the process of tumour cell invasion. Additionally, I will compare how cells with different genetic backgrounds behave following transformation. 2nd) I will identify novel genes that promote or inhibit tumour progression and invasion through the use of an unbiased RNAi screen. 3rd) I will characterise the molecular events that control invasion in this system. If novel conserved genes are identified that inhibit tumour progression in this Drosophila system, they may prove to be good targets for the development of anti-cancer therapies. To take this further the role of homologous genes would be tested in mammalian cell culture models of metastasis and in mouse models. In this way, novel cancer therapies could arise directly or indirectly from this research.

**Resumen del Curriculum Vitae:**

Throughout my career I have maintained a broad interest in science, but have focused the vast majority of my research in Cell and Developmental Biology. Following early laboratory training in Spain, I developed an interest in Neurobiology, moving to the fruit fly as a model system. I initially focused on neuron-glia interactions during the development of the CNS in the Drosophila embryo, with Alicia Hidalgo at the University of Cambridge. I then worked on axon guidance at the midline of the Drosophila embryo with Guy Tear at King's College, London. On receiving my PhD with Guy Tear, I wanted to focus my research more on cell morphology and on the molecular mechanisms that lead to the generation of distinct complex morphologies, obtaining an EMBO long-term fellowship to work in Barry Dickson's laboratory in Vienna to study neuronal cell morphology within the Drosophila visual system. For the past few years I have been working as a post-doctoral fellow in the laboratory of Buzz Baum at the LMCB. In that time I have developed a novel in vivo system in Drosophila that allows me to study epithelial cell and tissue morphogenesis in real time. This system has proven to be highly productive as it has not only led to the recent publication of a study investigating the role of the polarity complex Cdc42-Par6-aPKC in local adherens junction remodelling and in the maintenance of junction integrity, but has also led to further insights into epithelial cell morphology and Delta-Notch signalling in the fly notum. In work currently in press, I have shown how polarity determinants and Rho-GTPases cooperate to form and position distinct classes of dynamic protrusions within a tissue. Additionally, a third paper from work over the past 3 years is currently under review. In this study I investigated how cell shape and dynamic protrusions function to regulate patterning in the developing fly. I have extensive experience in training students and in collaborating with colleagues. I have written several publications and project proposals, acquiring an EMBO long-term fellowship and additionally obtaining funding from Cancer Research UK for my post-doctoral position with Buzz Baum. I am accomplished at communicating my research to colleagues, collaborators and at international scientific meetings. I have had numerous successful collaborations, ranging from working with Electron Microscopists to Physicists and Mathematicians. I am very excited by the prospect of using this assay as a Drosophila model for tumourigenesis and metastasis. Significantly, this is one of the few model systems in which it is possible to characterise the precise molecular and cell biological events that lead to the development of a malignant tumour. Therefore I hope and expect this project to provide important information both in the fields of Cell and Developmental Biology and Cancer Research. My work over the past few years has been at the interface of Cell and Cancer Biology, specifically addressing fundamental processes such as the regulation of the actin cytoskeleton, cell polarity, cell morphology, cell adhesion, endocytosis, trafficking, tissue architecture, signal transduction and cell signalling. I am confident that my extensive research experience in the fields of Cell, Developmental and Cancer Biology will allow me to establish exceptional independent research.



MINISTERIO  
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**SUBPROGRAMA RAMON Y CAJAL  
CONVOCATORIA 2010**

**Nombre:** JIMÉNEZ DÍAZ, LYDIA

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**Area:** Biomedicina

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**Título:**

Molecular basis of cognitive impairment in Alzheimer's disease early stages

**Resumen de la Memoria:**

Early Alzheimer's disease (AD) manifests as an inability to form new memories. Amyloid plaques and neurofibrillary tangles, formed by deposits of amyloid-beta (AB) peptide and microtubule-binding protein tau respectively, represent the two neuropathological hallmarks of AD. Increasing evidence supports the new concept that early soluble forms of AB produce an initial stage of synaptic dysfunction that underlies the early learning deficits observed in AD patients. The proposed research will focus on the molecular bases of synaptic dysfunction and cognitive impairment in the early stages of AD. In the search for a convergent intracellular pathway underlying these deficits, PKC signalling pathways seem to emerge as a pivotal finely tuned system capable of coupling many aspects of AB function. PKC regulates important molecular events in the neurodegenerative pathophysiology of AD and plays a crucial role in associative memory. This parallel involvement of PKC in both memory and neurodegeneration indicates a common basis for the origins of both the memory loss and the pathology of AD. To test the working hypothesis that, in AD early stages, the mechanisms underlying cognitive impairment imply synaptic dysfunction through PKC-dependent signalling pathways, I will use in vitro and in vivo AD models. As Juan de la Cierva postdoctoral fellow, I started a new line of investigation to analyze AB-induced synaptic dysfunction in two in vitro models of AD early stages. I have implemented single cell quantitative RT-PCR coupled to patch-clamp recordings to measure mRNA expression, synaptic transmission and plasticity on individual hippocampal neurons. I will take advantage of this technology to further investigate whether PKC modulation (with inhibitors and potent, anti-tumorigenic PKC activators) modifies or prevents AB-induced neuronal changes. Relevant glutamic/muscarinic receptors and PKC downstream targets ERK 1/2 and Arc (both strongly related to memory processes and AD) will be analyzed. For the in vivo studies I will first establish a clinically-relevant mouse model in which natural human soluble synaptotoxic AB species (obtained from cortical tissue of AD patients from the Neurology Unit, Clinical Hospital, Granada) will be injected i.c.v. to mimic the early phase of AD. Relevant behavioural tests to determine AB-induced cognitive deficits (such as Morris Water Maze, fear conditioning and object recognition) will be combined with protein/mRNA analysis of activity-related products (Arc, p-ERK, Fos, etc) to determine altered synaptic function in the hippocampus and amygdala. PKC modulation will be tested before and after AB injections. Finally, our study will be extended to a triple transgenic mouse model of AD (3xTg-AD) with plaques and tangles relevant the proposal aim. PKC has a crucial role in both the amyloid and tau processing. Soluble tau in 3xTg-AD mice has been shown to play a role in the cognitive decline in the presence of concomitant AB pathology. Results of PKC modulation on 3xTg-AD mice will therefore inform of the effects of simultaneous PKC-mediated tau and AB function interference and extend our knowledge of tau contribution to the cognitive impairment in the initial phases of AD. In summary, the results of this proposal will shed a light on the role of PKC in memory loss triggered by AD pathophysiology.

**Resumen del Curriculum Vitae:**

Licenciada en Farmacia 1998 por la Univ. Granada obtuve un Premio Nacional Fin de carrera del MEC con un expediente de 3.86 sobre 4. Fui becaria de pregrado (96-98) en el Dep de Bioquímica y Biología Molecular (becas Iniciación Investigación Plan Propio Univ. Granada y Colaboración del MEC). En nov 98 me incorporé al Laboratorio de Neurociencia del Dr Delgado-García (1º en la Univ Sevilla y luego en la Univ. Pablo de Olavide (UPO)) para realizar mi tesis doctoral sobre las bases neuronales del aprendizaje motor asociativo. Disfrute de una beca predoctoral FPU del MEC (99-02) y beca de Formación en Investigación FIS (02-05) defendiendo mi tesis en dic 03 y desarrollando un año de investigación post-doctoral en el mismo laboratorio. Para completar mi tesis realicé 6 estancias, financiadas en convocatorias competitivas del MEC, en las Universidades de Valencia (Biología Celular, Dr López), UNED (Madrid, Psicobiología, Dra Sandi) y en el Hospital Valme Sevilla (Farmacología, Dr Miñano). Los resultados de esta labor investigadora se han publicado en 7 artículos del 1er cuartil, siendo 1ª autora en 4 (ejem. JNeurosci.) y en 2 capítulos de libro. En 2005 desarrollé mi segundo posdoc en el Centro Regional de Investigaciones Biomédicas de la Univ Castilla-La-Mancha, estudiando los cambios moleculares asociados a un modelo de plasticidad sináptica en la vía auditiva. Posteriormente me uní al grupo del Dr Hunt en el University College London primero con un contrato de Reseach Fellow del UCL y posteriormente con una beca postdoc del MEC además de ser Honorary Research Fellow del UCL. Inicié y desarrollé una línea investigadora novedosa sobre el papel de la traducción axonal de mRNA en modelos de plasticidad sináptica a largo plazo (dolor persistente) en el sistema sensorial nociceptivo, publicando 2 artículos de alta repercusión como primera autora y autora para la correspondencia (PLoS One, JNeurosci.) y una revisión. Finalmente en 2007 me incorporé al Instituto de Neurociencias de Castilla y León con un contrato Juan de la Cierva. Soy responsable de los experimentos conductuales y moleculares en las líneas existentes en el laboratorio (3 artículos y 1 capítulo de libro) sobre trasplantes neuronales y sistema oculomotor. Además inicié una nueva línea sobre el estudio de las bases moleculares y electrofisiológicas que subyacen a la disfunción sináptica temprana observada en la enfermedad de Alzheimer, que me permite aplicar toda mi experiencia en abordajes multidisciplinares usando técnicas electrofisiológicas, de biología molecular y celular, y de microscopía. He presentado mi resultados pre y postdoctorales en más de 35 congresos obteniendo numerosas ayudas de asistencia. He sido investigadora principal de varios proyectos a nivel nacional y coaplicante en un proyecto en Reino Unido, además de haber participado en más de 20 proyectos de investigación. He dirigido 8 trabajos de investigación fin de carrera, master y doctorado. He asistido a más de 30 cursos de especialización y formación docente. Soy referee en revistas como The Journal of Neuroscience, European Journal of Pain o Behavioural Neuroscience. Soy codirectora de dos tesis doctorales sobre regiones cerebrales relacionadas con el almacenamiento de memoria y la enfermedad de Alzheimer. Siempre he simultaneado mi formación y actividad investigadora con la docencia de pre y posgrado.



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**Título:**

Role of Fc receptors in generating immune protection in vivo against Vaccinia virus

**Resumen de la Memoria:**

The smallpox vaccine, live vaccinia virus (VACV) has been enormously effective in preventing smallpox disease. Poxviruses have two distinct virion forms, intracellular mature virions (MV) and extracellular enveloped virions (EV), each with unique biology. Antibodies against of VACV are an important component of protective immunity in animal models and likely contribute to the protection of immunized humans against poxviruses. A complete understanding of virus neutralization by antibodies still remains challenging, and several models for different viruses have been proposed. We have recently reported, using murine or human monoclonal antibodies, that neutralization of vaccinia EV virions is not simply dependent on antigen binding but is actually heavily dependent on antibody effector functions and complement (Rafii-El-idrissi Benhnia M. et al., 2009). Furthermore, Complement-depleted mice given mAbs were still partially protected from disease, and that protection was substantially greater with the IgG2a than the IgG1 MABs, and may likely due to enhanced Fcγ receptors (FcγRs). Three subtypes of FcγRs have been described in mice and humans: FcγRI (CD64), FcγRII (CD32), and FcγRIII (CD16). Therefore, FcγRs are an important link between humoral immunity and cellular immunity and the role of FcγRs in generating immune protection in vivo against VACV remain unclear. The goals of my project is to study (i) the phagocytic activity, destroying infected cells, of macrophage or neutrophil upon binding to IgG2a MAB by FcγRs (ii) NK cell Fcγ-mediated ADCC (antibody dependent cell mediated cytotoxicity) activity in an IgG-dependent manner (iii) the role of FcγRs to facilitate neutralizing antibody-mediated protection in vivo against VACV via intranasal challenge using WT, FcγR -/- mice (deficient in functional FcγRII and FcγRIII) and FcγRIIB-/- mice. Understanding the role of FcγR and immunoglobulin-mediated protection in vivo against other pathogens will lead ultimately to more-effective vaccines.

**Resumen del Curriculum Vitae:**

I earned my Bachelor's degree (1992) in Biology from School of Science, University Moulay Ismail in Meknes (Morocco). I joined as graduate student the University of Seville (Spain) and I received my Master Degree in Clinical Biochemistry (1995) from the School of Medicine. In addition, I was named as collaborator honors during the academic years: 1993/94, 1995/96, and 1997/98. I also, received my CAP in 2001 (Certificated of Pedagogic Aptitude). My first discoveries in the field of Neuro-Immunology were published in the best journals in the field of neuro-immunology (8 papers, 1 review and 1 book chapter). As first author, I published 3 papers, and as co-authors I published 5 papers, one review and one book chapter. I received my Ph.D degree in Biology (2002) with distinction "Excellent Cum Laude with Unanimity". The title of my thesis is: "Characterization of melatonin receptor in rat immune system and mechanisms of regulation". As a postdoctoral fellow at Albany Medical College (2003-2006), Center of Microbial Disease and Immunology (New York), I was studying the role of CD14 engagement in protecting the host against chronic inflammation and persistent bacterial infection and elucidate the mechanism(s) by which this modulation of host defenses occurs. I publish, as first author, my finding in Journal of Immunology. In collaboration with Dr Kronenberg (President Rafii-El-idrissi Benhnia M. et al., Journal of Virology Dec vol. 83(23) 2009; Rafii-El-idrissi Benhnia M. et al., Journal of Virology, Feb vol. 83(3) 2009; Tupin E\*, Rafii-El-Idrissi Benhnia M\*, Kinjo Y\* et al., PNAS vol.105 (2008); Alessandro Sette et al., Immunity Jun 28 (2008); Rafii-El-idrissi Benhnia M. et al., Journal of Virology vol. 82 (2008); Kinjo Y et al., Nature Immunology, Sep 9 (2006); Rafii-El-idrissi Benhnia M. et al., Journal of Immunology, Feb 174 (2005); Garcia Pergñeda A. et al., Journal of Neuroimmunology, 86 (1998); Rafii-El-idrissi M. et al., Journal of Neuroimmunology, 86 (1998); Garcia-Maurino S. et al., Journal of Immunology, 159 (1997); Harmouch A. et al., Journal of Endocrinology, 155 (1997); Harmouch A. et al., Bioscience report, vol.16(5) 1996; J. M. Guerrero et al., Microscopy Research and technique, 34 (1996); Rafii-El-idrissi Benhnia M. et al., Journal Pineal Research, 20 (1996); Rafii-El-idrissi Benhnia M. et al., Journal of Neuroimmunology, 57 (1995); J. R. Calvo, et al., Journal Pineal Research, 18 (1995).



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**Area:** Biomedicina

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**Título:**

Deciphering the roles of microtubule networks during neuronal growth and maintenance

**Resumen de la Memoria:**

Los microtúbulos (MTs) son componentes esenciales del citoesqueleto. En el sistema nervioso aseguran la arquitectura neuronal, controlan cambios morfológicos, regulan el transporte intracelular y la transmisión de señales celulares, lo que hace de los MTs elementos esenciales para el correcto funcionamiento, desarrollo, morfología y plasticidad del sistema nervioso. No es sorprendente por lo tanto que la pérdida o mala regulación de los mismos resulte en un número elevado de patologías neuronales, por esto mismo, los MT representan un gran potencial como dianas de fármacos. La regulación de los MTs implica procesos tales como polimerización, estabilización y transporte, pero como se controlan tales procesos, y como éstos contribuyen al crecimiento y mantenimiento de neuronas, sigue siendo una laguna importante en nuestro conocimiento. Mi línea de investigación tiene el objetivo de comprender los mecanismos que regulan los MTs durante la formación y el mantenimiento de las redes neuronales, utilizando un modelo que ha demostrado ser extremadamente similar al de mamíferos, con todas las ventajas de manipulación genética, tiempo de investigación y coste de los invertebrados, como es el que ofrece *Drosophila melanogaster*. Con este modelo investigo una serie de proteínas asociadas a MTs, Tau, MAP1B, EB1, Clasp, Clip, APC y Spectraplakins, determino su función en la organización de redes de MTs, su influencia en el crecimiento axonal y como interaccionan entre sí para regular este proceso. Empleo mutaciones que afectan la función de las proteínas asociadas a MTs combinado con técnicas para el estudio del citoesqueleto de neuronas in vitro e in vivo. Mi proyecto también pretende determinar como los MTs y sus procesos reguladores median en los procesos de degeneración neuronal. Varias cascadas de señalización que incluyen JNK, PKA, MAPK, GSK y Toll-interleukin se encuentran implicadas en enfermedades neurodegenerativas tales como Alzheimer, y se ha sugerido que las proteínas asociadas a MTs podrían ser las dianas de tales procesos de señalización. Con el fin de elucidar la relación entre estas cascadas de señalización y los mecanismos reguladores de MTs, propongo la modificación genética y/o a través de fármacos de los componentes de las cascadas de señalización y de los mecanismos reguladores de MTs, seguido por el estudio de los efectos de tales modificaciones en la organización, polimerización, estabilización y transporte de MTs y en procesos neurodegenerativos. En suma, los hallazgos de este estudio podrán ser utilizados como paradigma para descifrar los mecanismos moleculares reguladores de MTs alterados en diferentes enfermedades neurodegenerativas así como facilitar su diagnosis y más adelante su cura.

**Resumen del Curriculum Vitae:**

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**Título:**

Coordination of cell movement during eye morphogenesis in development and disease

**Resumen de la Memoria:**

Congenital malformations of the eye, such as anophthalmia, microphthalmia and cyclopia are amongst the most severe defects associated with blindness. These malformations arise very early during embryonic development, and in order to fully understand the morphogenetic and developmental defects underlying them we need a thorough understanding of the early stages of eye development. The primordium of the eyes is specified at early stages of embryogenesis as a single domain, the eye field, which is subsequently split in two primordia, the optic vesicles (OVs), by extensive morphogenetic movements. Despite significant advance in last years to identify the molecular mechanisms underlying early eye development, we know virtually nothing about the morphogenetic movements involved in OV evagination and the signals that regulate them. During OV evagination the eye field cells reorganise in a highly dynamic way. Similar tissue remodeling processes in other morphogenetic contexts require extensive reorganisation of cell polarity and cell-cell adhesive contacts, which are likely to be important for OV evagination as well. I will make use of advanced imaging techniques in the living zebrafish embryo to follow cell behaviour and analyse the distribution of adhesion molecules and apical-basal cell polarity components during OV evagination. I will combine this *in vivo* approach with well established *in vitro* approaches that will allow us to determine whether eye field cells are intrinsically able to migrate and polarise, or require the interaction with the surrounding tissues. The Wnt and Ephrin signalling pathways regulate cell polarity and adhesion in other tissues, and our preliminary analyses suggest they may be important to maintain eye field cells segregated from the surrounding tissues and regulate cell polarity remodeling during OV evagination. I will manipulate the activity of these pathways and analyse cell behaviour, polarity and adhesion during eye morphogenesis in these conditions. This combination of approaches will contribute to the understanding of a poorly analysed morphogenetic process and will set the basis to understand how defects in cell behaviour may lead to absence of OV evagination in cyclopia and micro/anophthalmia associated conditions.

**Resumen del Curriculum Vitae:**

My interest in becoming a Researcher drove me to join Prof. Modolell's group when I was still an undergraduate student. After graduating I was awarded a Studentship to develop my PhD project under his supervision, which allowed me to acquire extensive training on Developmental Biology, Genetics and Molecular Biology studying pattern formation in *Drosophila*. During my stay at Prof. Modolell's group, my studies focused on the role of a group of homeodomain transcription factors, the *iroquois* genes, in the patterning of various regions of the body of the adult fruit fly, and resulted in several publications (Diez del Corral et al., 1999; Cavodeassi et al., 1999; Cavodeassi et al., 2000; Cavodeassi et al., 2002) The expertise I acquired in Prof. Modolell's group has been complemented in recent years with my training on zebrafish embryo manipulation and imaging techniques at Prof. Wilson's group. My research in Prof. Wilson's group has contributed to the understanding of both eye induction and how this process is coordinated with morphogenesis during the early stages of eye formation (Cavodeassi et al., 2005). In recent years my research interests have focused on eye morphogenesis, and this has already resulted in a collaborative publication where we show for the first time by *in vivo* analysis, how fate specification and morphogenesis are coordinated during maturation of the eye (Picker, Cavodeassi et al., 2009). In addition to this line of research, I closely collaborate with other colleagues in Prof. Wilson's lab and outside it, and this is reflected in my participation in a number of projects aimed at understanding different aspects of optic cup morphogenesis and retinal differentiation (<http://www.ucl.ac.uk/zebrafish-group/research/eye.php> for more information on our research). My active involvement in the design and direction of the eye development research program in the lab resulted in my co-application with Prof. Wilson for an MRC Research Grant, which was successfully awarded in 2006. The administration of this grant has been an excellent source of experience that has helped me to develop my organisational skills and my abilities in people and project management. In Prof. Wilson's lab I am involved in the teaching and mentoring of students in their final year B.Sc. Project and in the first year of their Ph.D. Programme. This supervision has been an important source of experience. It has also been particularly rewarding as two of the students supervised by me have subsequently chosen to join our group. One of them is pursuing his Ph.D. Project under my supervision. The expertise I have gained at Prof. Wilson's lab, not only technical and intellectual, but also in other aspects of lab management and resource administration, has prepared me to to successfully undertake this project as an independent researcher. By combining the amenability of the zebrafish for the analysis of developmental processes in living embryos, with well-established cell biology approaches and the analysis of cell polarity and cell adhesion properties during early eye morphogenesis, this program of research will make major contributions to the understanding of a poorly analysed morphogenetic process and will set the basis to understand how defects in eye morphogenesis may result in cyclopia and micro/anophthalmia associated conditions.



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**Título:**

Evolution and transgenerational inheritance of chromatin states.

**Resumen de la Memoria:**

Chromatin structure is important for the packaging of DNA in the nucleus and for faithful gene expression during development. For example, DNA tightly wrapped around nucleosomes is less likely to engage in promiscuous interactions with DNA-binding proteins. Mainly from studies in yeast, it is known that nucleosome positioning is affected by genomic characteristics, such as DNA sequence composition and short sequence motifs. There is now an increasing amount of genomewide nucleosome positioning and histone modification data for many different organisms including human. I propose to use this data to investigate the impact that genome evolution has on chromatin structure and vice versa. Understanding the impact that sequence changes have on chromatin will help us understand the effects of mutations in human disease. In addition, I would like to understand how chromatin is transmitted from one generation to the next. It is not clear the extent to which epigenetic information can be inherited across generations and what mechanisms can achieve this. I propose to study this systematically using *C. elegans* as a model system. Understanding how chromatin state can be inherited between generations could have great implications on predicting phenotypic variation and disease risk.

**Resumen del Curriculum Vitae:**

I obtained my PhD from the University of Cambridge in 2007. Having worked in Dr. Greg Elgar's group at the MRC HGMP-RC in Hinxton, Cambridge, UK for two years as a bioinformatics specialist on the assembly of the *Fugu rubripes* genome I decided to embark on my own predoctoral research to study the evolution and mechanisms of action of highly conserved noncoding elements (CNEs) in metazoan genomes. In 2003 I was awarded a highly prestigious MRC Predoctoral Fellowship and under the supervision of Dr. Elgar and Professor Walter R. Gilks I spent the first year of my PhD at the MRC HGMP-RC in Hinxton, Cambridge and the next two years at the Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK. I then moved to Dr. Ben Lehner's lab at the EMBL/CRG Systems Biology Unit in Barcelona, Spain to study the evolution and mechanisms of robustness to genetic mutation using a combined computational and experimental approach. My postdoctoral research was funded by a Marie-Curie Intra-European Postdoctoral Fellowship. The three main research lines I have pursued so far in Dr. Lehner's lab are (1) the evolutionary conservation of functional redundancy between duplicated genes (published in *Trends in Genetics*), (2) the mechanisms underlying the robustness to genetic mutations that lead to increases in gene expression (published in *Cell*) and (3) how functional probabilistic networks can predict genetic interactions (manuscript currently under review). I am currently studying the determinants of histone retention in human sperm, as a mechanism of inheritance of epigenetic information. Throughout my research career I have been successful in receiving funding from prestigious funding bodies (including BBSRC, MRC and European Commission, Framework FP7), my research has been published in high-impact journals, my articles have often been recommended for reading by Faculty of 1000 Biology and have been highly cited: T. Vavouri, G. Elgar, *Curr Opin Genet Dev* 15, 395 (2005); A. Woolfe, M. Goodson, D. K. Goode, P. Snell, G. K. McEwen, T. Vavouri et al., *PLoS Biol* 3, e7 (2005); G. K. McEwen, A. Woolfe, D. Goode, T. Vavouri, H. Callaway, G. Elgar, *Genome Res* 16, 451 (2006); T. Vavouri, G. K. McEwen, A. Woolfe, W. R. Gilks, G. Elgar, *Trends Genet* 22, 5 (2006); T. Vavouri, K. Walter, W. R. Gilks, B. Lehner, G. Elgar, *Genome Biol* 8, R15 (2007); G. Elgar, T. Vavouri, *Trends Genet* 24, 344 (2008); J. I. Semple, T. Vavouri, B. Lehner, *BMC Syst Biol* 2, 1 (2008); T. Vavouri, J. I. Semple, B. Lehner, *Trends Genet* 24, 485 (2008); T. Vavouri, B. Lehner, *Bioessays* 31, 727 (2009); T. Vavouri, J. I. Semple, R. Garcia-Verdugo, B. Lehner, *Cell* 138, 198 (2009).



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**Título:**

Characterization of the molecular machinery required for protein trafficking to the plant storage vacuole

**Resumen de la Memoria:**

The protein storage vacuole is an organelle unique to plants. The machinery responsible for delivery of storage cargo proteins still remains largely unknown. Even though storage protein sorting pathway is predominant in storage tissues as seeds, it is also fully functional in vegetative tissues and therefore, mature plants can be successfully used for genetic screens to identify novel components of this pathway. A genetic system that employs a vacuolar storage cargo marker that when secreted, causes a visible phenotype in mutant plants has been developed recently. Using this screening methodology, we have recently identified several proteins that participate in this pathway, including proteins that serve as receptors for cargo proteins or regulate vesicular fusion (Zouhar et al., *Plant Physiology* 2009), proving a reliability and robustness of the genetic screen. Once we identify novel mutations that modify or block storage protein trafficking, we will perform a functional characterization of the corresponding genes. The utilized techniques will include an analysis of the mutation effect on the plant endomembrane system using markers of different subcellular compartments and a proteomics analysis of the vacuoles in mutant plants, which may yield novel storage cargo. Using fluorescent protein fusions, prepared antibodies and subsequent immunoassays, we will analyze molecular activity and subcellular localization of the corresponding proteins. To further characterize a molecular environment of the identified trafficking components, we will perform two-hybrid screens for their regulators and effectors and try to isolate their binding partners using TAP-TAG strategies. Understanding the machinery responsible for delivery of the storage proteins to the specialized vacuoles is of a great importance not only for plant cell biology and biotechnology, but also for a growing human population in general, as we can expect that knowledge in this area can lead to greatly improved nutritional values of many commercially utilized grains.

**Resumen del Curriculum Vitae:**

From September 1992 to August 1997 I attended MSc. studies at the Dept. of Biochemistry, Masaryk University, the Czech Republic. My thesis focused on fungal nitrogen metabolism, particularly on a glutamate synthase. To characterize its biochemical and structural properties, a multistep purification protocol to isolate native enzyme from fungal cultures was designed. From September 1997 to September 2000 I attended PhD studies at the Laboratory of Plant Molecular Physiology and the Dept. of Biochemistry, Masaryk University. My thesis focused on a structure-function relationship of a maize cytokinin-O-glucoside-specific beta-glucosidase Zm-p60. The recombinant wild type protein was crystallized and analyzed by X-ray crystallography and molecular modelling/docking techniques, resulting in identification of amino acid residues responsible for substrate recognition and catalysis. The catalytic competence and the substrate affinity of corresponding point mutant proteins was subsequently analyzed. Unexpectedly, we identified an active-site glutamate residue to be essential not only for catalysis but also for the formation of a catalysis-competent homodimer (Zouhar et al., *Plant Physiol.* 2001). The insoluble Zm-p60 point mutants were subjected to protein renaturation and assisted refolding. From September 2000 to January 2001 I briefly continued on this project as a postdoctoral fellow in the Institute of Biophysics, Academy of Sciences of the Czech Republic, studying the Zm-p60 enzyme affinity towards phytohormone conjugates and artificial substrates under various chemical conditions using ELISA techniques. From February 2001 to December 2001 I worked as a Research Associate at the MSU-DOE Plant Research Laboratory in East Lansing, USA, focusing mainly on vacuolar biogenesis and protein trafficking to the lytic vacuoles, using forward genetics and high-throughput confocal microscopy. From January 2002 to August 2006, I worked as a PG Research Plant Biochemist at the Center for Plant Cell Biology, University of California in Riverside, USA, studying protein processing and degradation in the vacuole, implementing organelle proteomics and genomics methods. In 2003, we pioneered a high-throughput drug discovery and chemical genomics in plant systems, resulting in identification of unique chemical compounds that affect vacuolar protein sorting in both plants and yeast (Zouhar et al., *Proc Natl Acad Sci U S A.* 2004). In September 2006 I joined the Centro Nacional de Biotecnología CSIC, Madrid, Spain to study protein trafficking to the plant storage vacuole, an organelle unique to plants with an enormous biotechnological potential. We have identified several novel components of this plant-specific pathway, including vacuolar sorting receptors and factors directly involved in vesicular fusion (Zouhar et al., *Plant Physiol.* 2009).