



Red Aragón 7PM:

Research lines and competences for participating in FP7 Health

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Dra. Pilar Giraldo – Research on Rare Diseases

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THE RESEARCH PROGRAM ON RARE DISEASES (Keywords: Nanoparticles, LSDs, macrophages, microRNAs, enzymes, chemical chaperones)

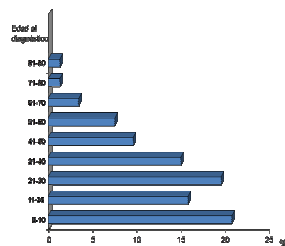
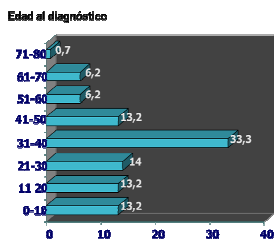
Dr. Giraldo's multidisciplinary group studies different diseases of the lysosomal deposit. It examines new therapies for Gaucher disease, and strategies for application of substitution enzyme therapies and the influence of genetic factors on their effectiveness. Search for other genes of influence in the clinical variability of the disease. Furthermore it examines procedures for evaluation of bone and neurological disease. Dr. Giraldo's group on Gaucher disease was integrated in the Cooperative Research Network of the Carlos III Institute as a number 11 node of Metabolism Inherited Diseases Network (REDEMETH) Ref 03/054 and it also participates in the Network of Epidemiology of Rare Diseases REpIER and the Network of Epidemiology and Public Health Centres RCESP. Our scientific activity has National and International recognition. The group usually collaborates with the Spanish National Association of Patients and Relatives of Gaucher Disease (AEEFEG).

Specific Research Lines:

- Gaucher disease epidemiology, in Spain: National Registry accredited by ISO 9001 (Num EC2751/07)
- Genetic analysis and search of genes related to clinical heterogeneity. Directed mutagenesis. DNA, serum, plasma and leukocyte patient samples biobank.
- Study of biomarkers and inflammatory cytokines and its relationship with response to treatment.
- Study of bone disease by imaging techniques and its relationship with plasma biomarkers.
- Neurological disease evaluation by clinical, neurophysiological and imaging methods.
- Clinical research of new drugs on clinical trials (OGT-011, TKT034, TKT039, Protalix). Independent clinical trial.
- Epidemiology of hematological neoplasias. Gene expression marker study and search of polymorphisms accounting for familial aggregations.

POSSIBLE CONTRIBUTIONS:

- The biobank of the Translational Research Unit Laboratory contains monocyte cell lines from control and patients with Gaucher disease, Nienman-Pick disease, Fabry disease and MPS1-Schie disease
- Member of the European Working Group on Gaucher Disease (EWGGD)



SCIENTIFIC CO-ORDINATOR:

Dr. Pilar Giraldo: MD PhD has more than 25 years of research experience in the academic-hospital field, of which she concentrated 15 years of research of the Gaucher disease.

She is founder member of the Spanish Gaucher Foundation (FEETEG) and member of the European Working Group on Gaucher Disease (EWGGD)

Dr. Pilar Giraldo is the co-coordinator of the Spanish Gaucher Registry since 1993. She is the editor of Guidelines for Gaucher Disease Management and of the web site of the Spanish Gaucher Foundation (www.feeteg.org), which contains information, recommendations and new knowledge for patients and researcher regarding this disease. She is also editor of the periodical edition of the Gaucher Disease Bulletin (Noticias FEETEG) with the most recent and relevant news related to Gaucher disease.

Dr. Pilar Giraldo is member of the Cooperative Research Network, and coordinator of the 11th node of Metabolism Inherited Diseases Network (REDEMETH) Ref 03/054 and participates in the Network of Epidemiology of Rare Diseases (REpIER) in addition to the Network of Epidemiology and Public Health Centers (RCESP).

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The **Technical Scientific Services** offer a broad portfolio of services at the molecular, cellular and animal experimental models, in order to respond to the needs of all research groups of the I+CS. Other groups and entities may also request these services. The SCT are equipped with specialized facilities and equipment and a qualified team provides advice and technical and scientific support.

EXPERIMENTAL RESOURCES

Unit	Equipment / capacities
Genomics Unit	<ul style="list-style-type: none"> • Automatic extraction of DNA • Detection of mutations and/or polymorphisms • DNA methylation analysis • Analysis of gene expression
Proteomics Unit	<ul style="list-style-type: none"> • Protein separation by 1D and 2D electrophoresis • Differential expression of proteins by DIGE and iTRAQ • Protein identification by MALDI-TOF MS and MS / M • Separation and identification of proteins by MALDI-TOF LC-MSMS • Quantification of metabolites and proteins (HPLC-4000QTRAP)
Cell Separation and Cytometry Unit	<ul style="list-style-type: none"> • Flow cytometry • Cell sorting by flow cytometry • Magnetic cell separation • Multiplex analysis
Cell Culture Unit	<ul style="list-style-type: none"> • Obtaining Primary Cultures • Cultivation and differentiation of adult and embryonic human and animal stem cells • IPS cell generation • Analysis of mycoplasma contamination of crops • Genetic engineering techniques for modifying and labeling of cell lines
Microscopy and Imaging Unit	<ul style="list-style-type: none"> • Conventional microscopy (Halogen and Fluorescent Light) • Confocal Microscopy • Monitoring ex vivo cell in real-time • Immunocytochemistry and Image Analysis
Pathology Unit	<ul style="list-style-type: none"> • Tissue processing, staining and immunohistochemistry preparations • Laser microdissection • Scanning of preparations • EXAKT system processing of hard materials • Tissue matrix production (Tissue microarray) • Reporting and graphical documentation
Functional Assessment Unit	<ul style="list-style-type: none"> • Optical Image • Telemetry • Metabolism • Evaluation of the Sensory-Motor System • Projects with rodents
Transgenic Unit	<ul style="list-style-type: none"> • Generation of transgenic mice by microinjection of DNA into pronucleus • Production of mouse chimeric in order to generate knockout mouse lines and KI and chimerism studies • Preimplantation embryo development studies • Rederivation of mouse lines • Cryopreservation of mouse lines • Studies and assistance in mouse breeding • Temporary housing of experimental animals (rabbit, pig, sheep and rat) • Surgery and microsurgery techniques in clinical conditions
SAI Biomedicine and Biomaterials. Experimental Surgery	<ul style="list-style-type: none"> • Housing of experimental animals (mouse, rat and rabbit) in accordance with current legislation. • Management of rodent colonies
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Dr. Luis Pablo Júlvez, Department of Ophthalmology, Miguel Servet University Hospital, Zaragoza, Spain

2012-1.2-1. Development of technologies with a view to patient group stratification for personalised medicine applications.

Contact: Luis Pablo Júlvez, **Department of Ophthalmology**, Miguel Servet University Hospital. Email: lpablo@unizar.es; please also send a copy of your message to mkoelling@redaragon7pm.eu

THE RESEARCH PROGRAM Early prevention and diagnosis of blindness:

The Department of Ophthalmology at the Miguel Servet University Hospital has a long tradition in computerized analysis of vascular images, and a substantial body of research on 2D retinal imaging has been published by the members of the group. The research group under the coordination of Luis Pablo Júlvez is nowadays an international recognized player in the field of retinal imaging and measurement; 3D Vascular Imaging and research on hemodynamic flow. The research group focuses on the utility of applying a mass screening in primary care visits based on automatic classifications generated from fast functional tests and imaging devices. The studied technologies include frequency-doubling perimetry, new vision function tests conducted on laptop computers, optical coherence tomography and confocal scanning laser ophthalmoscopy. The Group attempts to develop algorithms and functions, obtained from one test or by combining the outcomes of different equipments, to improve early glaucoma diagnosis and evaluate the cost-effectiveness of applying them in a primary care environment or as a telemedicine program.

SPECIFIC RESEARCH LINES:

- Bio availability and penetration of neuro-protectors
- Developing new tools for early diagnosis and monitoring glaucoma progression
- Early prevention and diagnosis of glaucoma
- Alternatives to the medical surgery treatment of the optic neuropathy with origin in glaucoma and other optic diseases
- Neuroprotection in the degenerative retinal pathology
- Structural and functional Evaluation of the retinal nerve fiber layer
- Imaging of the Retinal Nerve Fibre Layer with Spectral-domain Optical Coherence Tomography in Patients with Glaucoma
- Study of the Embryo and fetal neurodevelopment through the optic nerve

POSSIBLE CONTRIBUTIONS TO ONGOING PROYECTS:

- Retinal Imaging and measurement –
- 3D Vascular Imaging,
- Industrial collaborators - long-term relationship with the market leader Heidelberg Engineering GMBH and Carl Zeiss Meditec.
- International contacts:

University of Thessaloniki, Greece (Assist Prof Fotis Topouzis; Dr Panayiota Founti)
University of Mainz, Germany (Dr Franz Grus)
University of Aberdeen (Prof Augusto Azuara-Blanco)
University of Genoa, Italy (Prof Michele Iester)
City University London, UK (Prof David Crabb)
Bietti Foundation, Rome (Dr Francesco Oddone)
University Eye Hospital, Wurtzburg, Germany (Dr Marc Schargus)
University Complutense Madrid, Spain (Prof Julián García-Feijoo, Dr José María Martínez de la Casa)

DIAGNOSTIC AND MEASUREMENT SYSTEMS AVAILABLE AT THE DEPARTMENT OF OPHTHALMOLOGY:

- Optic nerve head stereophotography
- Monochromatic fundus photographs
- Heidelberg confocal scanning tomography (HRT 3)
- Spectral-domain optical coherence tomography (Cirrus HD, Spectralis)
- Scanning laser polarimetry (GDx VCC)
- Heidelberg edge perimetry (HEP)
- Humphrey Field Analyzer (HFA)
- Frequency-doubling perimetry (FDT)
- Ocular blood flow (doppler ultrasound)

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THE BARBASTRO HEALTH CARE AREA (BHCA)

Contact: mkoelling@redaragon7pm.eu

The **Aragon Health Sciences Institute (I+CS)** is a public institution dependent on the Government of Aragon devoted to Health Sciences development. It was created by the Regional Health Law (6/2002) and its objective is to generate knowledge in order to fulfil the main needs in health, producing scientific results capable of raising resources and promoting research amongst the public hospitals and health services in the Region of Aragon. In order to fulfil its aims, and according to the framework agreement signed between the Regional Health System of Aragón (owner of the hospitals) and the I+CS, all the research groups and infrastructures from public hospitals and health centres are managed by I+CS, besides their structural dependence.

THE BARBASTRO HEALTH CARE AREA (BHCA)

The BHCA is responsible for the public health care services in the eastern half of the Spanish province of Huesca, one of the three regions which are part of Aragón. It covers **all assistance levels**: primary, specialized, socio sanitary and mental and provides health care services to 110.000 inhabitants within a geographic area of ca. 7.500 km². **Population density is very low** standing at 13.75 inhab/km² being one of the lowest in Spain and in the whole EU. The elderly people rate (aged more than 65) stands at 28.3%.

The BHCA is divided in fifteen geographic areas called "zonas de salud" (literally "health care zones"). In each of such "health care zones" there is one health care centre along with several local offices that provide ongoing primary health care services. (136 offices in all health care zones). Second level (specialized) health care services are provided by the General Hospital, placed in the geographical centre of the geographic area, Barbastro. The **hospital has 160 beds available in the hospitalization area**. Surgical area has 5 operating theatres. Furthermore, it counts with a **recent built intensive care unit** provided with the highest technical equipment. Ambulatory care is provided by offices in the hospital itself as well as in two specialized delegations, located 17 and 75 km away from the main site, respectively. Besides there is a socio sanitary centre located in the far south of the territory.

The objective is to provide an **"end to end" health care service** to the citizens and residents within the BHCA geographical area, by ensuring their easy and quick access to the service, understood as: promotion of healthy ways of life; prevention and protection against physical, environmental and biologic factors; provision of any care required in an illness situation; whilst keeping the highest degree of autonomy and insertion of patients in their environment and in the society in order to meet all his/her needs and expectations in terms of personal health.

The BHCA heads on towards a scenario where an outstanding health care service is provided through the optimum management of public resources allocated whilst reaching a high level of customer satisfaction, fully backed by the citizens. Besides, professionals working for the BHCA are motivated and highly involved in achieving this objective.

The health care sector has made a revolution in the way of managing the gap between the two levels of health care assistance, primary assistance and specialized assistance, through the deployment of two strategic projects that now the Aragon's Health Service (Servicio Aragonés de la Salud) is replicating through the rest of the organization. The first project consisted on the development of a powerful intranet for the sanitary sector allowing the integration of the different IT systems available in the two levels of health care assistance (primary and specialized), which has been the starting point for the existence of the single record for patient shared among primary, specialized and sociosanitary healthcare. This approach has improved the availability and **accessibility of the clinic data** and improving consequently the assistance quality.

Also, a **telemedicine system** has been deployed allowing the daily contact and the **sharing of knowledge among the different professionals** in the health care area (practitioners, specialist, nurses, etc.)

EXPERIENCE IN EUROPEAN PROJECTS:

HEALTH OPTIMUM (eTEN) Telemedicine Project approved and co-funded by the European Commission within the eTEN programme. It ended on June 2009 with the following results:

- **Telecounseling and virtual teleconsultation**, Objective: to make virtual consultations to patients and internal consultations between professionals by means of videoconferencing facilities.
- **Tele-retinography**, Objective: to store screening images of diabetic retinopathy in the corporate PACS system and access through the own viewer to the Intranet, being part of the clinical shared record of the patient. The screening tests will delay or avoid the appearance of 40,000 blindness in Aragón within the next 5 years.
- **Tele-dermatology**, Objective: to make asynchronous internal consultations between primary care and dermatology. Data and medical images are obtained in primary care and the diagnosed and therapeutic advice is given by the dermatologist.

- **Tele-ictus, Objective:** to drop mortality and the effects of sick people of ictus. At this moment, we are at the end of Spain in mortality and more than 300 patients could benefit annually.

EUROGENE (eTEN) The project's aim was to create a medical nutrigenetic portal as a reference in Europe. The project ended on 2009 with the following results:

- **Web portal:** it allows to give advice to patients about their living habits and healthy dietetics according to their genetic characteristics in order to prevent chronic diseases
- The "**usability**" has been validated by healthcare professionals and patients. The validation of the effectiveness of measurements is still pending by a case-control study.

DREAMING (CIP-PSP) Project funded by the European Commission under the new Competitiveness and Innovation Programme. It intends to pilot a new, economically sustainable home assistance and inclusion services able to both extend the independent living of elderly people and reduce their social exclusion. The home monitoring and the assistance is guaranteed by the use of privacy respecting and user-friendly technologies: self-operated medical monitors, environmental sensors and TV based videoconferencing. The project will measure the impact of monitoring of elderly people considering the following important aspects, such as:

- The quality of life of the elderly people themselves and of their formal and informal caregivers
- Elder's health conditions
- The costs elders generate to the health system

The project started on May 2008 and will last until 2012.

RESATER (Interreg) Aragon's Healthcare System (SALUD), represented by Barbastro's Health Care Area is now participating as a collaborating public entity in this project, whose main objective is to create a telemedicine model able to connect the elderly nursing homes with the public healthcare body.

EXPERIENCE IN NATIONAL PROJECTS

ISPAMAT (PLAN AVANZA) Public Services Integration. This Project belongs to Plan AVANZA@ 2006-2010 by Spanish Ministry of Industry, Tourism and Commerce. This project integrates four pilot sites with different experiences. These pilot sites are located in Aragon, and each one refers to a different field: Education (Graus), Health (Fraga), Tourism (Jaca) and Electronic Administration (Barbastro). The whole project goal is to integrate different devices and access networks in order to offer and guaranteed public services for whole citizens. These technologies are: internet, TDT (Digital Television), third generation mobile networks, and so on. In this way we are feeling the real digital citizenship.

REALTH (PLAN AVANZA) is a scientific-technologic Singular and Strategic Project co-funded by Spanish Plan AVANZA@ 2006-2010 by the Spanish Ministry of Industry, Tourism and Commerce. The Project's objective is reaching a social welfare by means of sanitary services and sanitary resources management.

PITES T-AYUDA Project founded by the Health Insititut Carlos III, which intends to create a technological platform in order to combine healthcare and social services for chronic frail elderly people. At this moment, the project is in the initial phase and will last 36 months.

CENTRO DE SALUD VIRTUAL Project funded by the national program INNPACTO. It aims to provide a healthcare centre in the patients' homes by means of a TV interactive decoder and biomedical sensors.

Aragon Workers Health Study (AWHS)

Contact: **Dra. Montse León**, mleon.iacs@aragon.es (mkoelling@redaragon7pm.eu)

THE CARDIOVASCULAR RESEARCH PROGRAM

The **PRICA (Cardiovascular Research Program)** was created within the I+CS with the objective of stimulating new initiatives of interdisciplinary research in lines related to cardiovascular pathology, such in epidemiological, as in etiopathogenic, diagnostic and therapeutic aspects. This program pretends also to improve the knowledge in cardiovascular area and its subsequent application to the diffusion of the knowledge and the rapid translation to the clinical practice.

One of the main projects within PRICA is **AWHS (Aragon Workers Health Study)**, carried out in collaboration with the “Health and Safety at Work” Service and the workers of the General Motors Factory (Zaragoza) and the Centro Nacional de Investigaciones Cardiovasculares (CNIC). The project includes the annual (during a period of 6 years) monitoring and collection of anthropometric, clinical, analytical and metabolic data and habits related to diet, life style and physical activity of 6000 volunteers within the staff of the factory. Its goal is to evaluate young middle age men and women (30 - 55 years of age), a key age range in the onset of metabolic syndrome but still largely without clinical manifestations. In addition, a biological sample (blood, serum, DNA, urine) has been created in order to identify genetic determinants and life style habits that favor the appearance of cardiovascular disease and the progression of cardiovascular risk factors. Furthermore the cohort morbidity-mortality and subclinic arteriosclerosis and their relationship with the above risk factors will be studied through image diagnosis tests with special emphasis on overweight-obesity. The study provides an infrastructure for the investigation of genetic, psychosocial, and established risk factors that determine: a) the trajectories of metabolic and cardiovascular risk factors over time (overweight and obesity, blood pressure, lipid profile, lipoproteins, glucose abnormalities and diabetes, smoking habits, and non-traditional risk factors); b) the presence and development of subclinical atherosclerosis; and c) the development of clinical cardiovascular and other disease endpoints. Specific aims pertaining to this project are the identification of genetic biomarkers associated to insulin resistance, dislipemia, high blood pressure and MetS progression.

POSSIBLE CONTRIBUTIONS:

- Biobank Samples: Blood samples; serum samples; plasma EDTA samples; urine samples; DNA samples
- ISO 9001/2008 - quality management system for the recompilation and the treatment of the biological sample

EXPERIENCE IN EUROPEAN PROJECTS:

The research group participates in the ENIAC Joint Undertaking project- CAJAL4EU - <http://cajal4eu.com/>. The objective of the CAJAL4EU project is to develop nanoelectronics-based biosensor technology platforms enabling in-vitro diagnostic test manufacturers to rapidly build a variety of new multi-parameter test applications in a robust, user-friendly and cost-effective way.

STAFF SCIENTISTS INVOLVED:

Prof. Fernando Civeira is professor of Internal Medicine at Zaragoza University School of Medicine, chief of the Lipid Clinic at Miguel Servet Hospital University and Director of the Lipid Metabolism Research group at Aragon Institute of Health Sciences (I+CS) in Zaragoza, Spain. His research group includes 9 people who are involved in a number of studies on new genes causing dyslipidemias and in the relationship between genotype and phenotype in dyslipidemias

He has published 88 works in international journals in different fields of lipid metabolism. Dr Civeira is member of several scientific societies. He has been the principal investigator of over 20 research projects supported by public and private grants.

Dr. Jose Antonio Casasnovas Ienguas Director of a cardiovascular research program of the Aragon Institute of Health Sciences of the Aragon Government and professor of Cardiology at the University of Zaragoza. He directed MESYAS study about metabolic syndrome and cardiovascular risk in cohorts of Spanish workers until 2008 and has been the promoter and chairman of the Working Group on Metabolic Syndrome of the Spanish Society of Cardiology.

He is co-coordinator and member of the scientific committee of Aragon Workers' Health Study (AWHS), that will provide the infrastructure to identify the genetic and environmental factors that determine the development and progression of cardiovascular and metabolic risk factors.

Dra. Monserrat Leon Latre Physician doctor. Family doctor. Coordinator of the Working Group on Metabolic Syndrome of the Spanish Society of Cardiology. Clinical-coordinator of AWHS (Aragon Workers' Health Study)

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Dr. Pilar Martin-Duque - Research on Gene and Cell Therapy for cancer and regenerative medicine

2012-1.4-1: Innovative approaches to solid organ transplantation.
2012-1.4-2: Medical technology for the transplantation sector and bioartificial organs.
2012-1.4-3: Innovative strategies for translation of stem cell based therapies in regenerative medicine
2012-1.4-4: Targeted nucleic acid delivery as an innovative therapeutic or prophylactic approach

Contact: Email: mpmartind.iacs@aragon.es (mkoelling@redaragon7pm.eu)

THE RESEARCH PROGRAM ON GENE AND CELL THERAPY FOR CANCER AND REGENERATIVE MEDICINE

The research group of Dr. Pilar Martin-Duque works on regenerative medicine for cancer from the very different aspects of regeneration at the genetic, cellular or tissular levels. The group recently submitted the first few papers and it is expect that in few years the group will be a referenced group in the field. The international collaborations started with Dr Tristan Rodriguez (Imperial College School of Medicine).

STAFF SCIENTISTS INVOLVED:

The research group is built of a senior researcher, a post-doctoral researcher and four PhD students. It has obtained 6 grants to perform its work from regional and national funding.

RECENT PUBLICATIONS:

- **2010:** Merron Andrew; Baril Patrick; Martin-Duque Pilar; de la Vieja Antonio; Tran Lucile; Briat Arnaud; Harrington Kevin J; McNeish Iain A; Vassaux Georges Assessment of the Na/I symporter as a reporter gene to visualize oncolytic adenovirus propagation in peritoneal tumours. European journal of nuclear medicine and molecular imaging 2010; 37(7):1377-85.
- **2010:** Baril Patrick; Martin-Duque Pilar; Vassaux Georges Visualization of gene expression in the live subject using the Na/I symporter as a reporter gene: applications in biotherapy. British journal of pharmacology 2010; 159(4):761-71.
- **2009:** Peerlinck Inge; Merron Andrew; Baril Patrick; Conchon Sophie; Martin-Duque Pilar; Hindorf Cécilia; Burnet Jerome; Quintanilla Miguel; Hingorani Mohan; Iggo Richard; Lemoine Nick R; Harrington Kevin; Vassaux Georges Targeted radionuclide therapy using a Wnt-targeted replicating adenovirus encoding the Na/I symporter. Clinical cancer research : an official journal of the American Association for Cancer Research 2009;15(21):6595-601.
- **2009:** Chisholm Edward J; Vassaux Georges; Martin-Duque Pilar; Chevre Raphael; Lambert Olivier; Pitard Bruno; Merron Andrew; Weeks Mark; Burnet Jerome; Peerlinck Inge; Dai Ming-Shen; Alusi Ghassan; Mather Stephen J; Bolton Katherine; Uchegbu Ijeoma F; Schatzlein Andreas G; Baril Patrick Cancer-specific transgene expression mediated by systemic injection of nanoparticles. Cancer research 2009;69(6):2655-62.
- **2008:** Belmar-Lopez Carolina; Mancheno-Corvo Pablo; Saornil Maria Antonia; Baril Patrick; Vassaux Georges; Quintanilla Miguel; Martin-Duque Pilar Uveal vs. cutaneous melanoma. Origins and causes of the differences. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico 2008;10(3):137-42.
- **2008:** Lomas Jesus; Martin-Duque Pilar; Pons Mar; Quintanilla Miguel The genetics of malignant melanoma. Frontiers in bioscience : a journal and virtual library 2008;13():5071-93.

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EXPERIMENTAL RESOURCES

Unit	Equipment / capacities
Genomics Unit	<ul style="list-style-type: none"> Automatic extraction of DNA Detection of mutations and/or polymorphisms DNA methylation analysis Analysis of gene expression
Proteomics Unit	<ul style="list-style-type: none"> Protein separation by 1D and 2D electrophoresis Differential expression of proteins by DIGE and iTRAQ Protein identification by MALDI-TOF MS and MS / M Separation and identification of proteins by MALDI-TOF LC-MSMS Quantification of metabolites and proteins (HPLC-4000QTRAP)
Cell Separation and Cytometry Unit	<ul style="list-style-type: none"> Flow cytometry Cell sorting by flow cytometry Magnetic cell separation Multiplex analysis
Cell Culture Unit	<ul style="list-style-type: none"> Obtaining Primary Cultures Cultivation and differentiation of adult and embryonic human and animal stem cells IPS cell generation Analysis of mycoplasma contamination of crops Genetic engineering techniques for modifying and labeling of cell lines
Microscopy and Imaging Unit	<ul style="list-style-type: none"> Conventional microscopy (Halogen and Fluorescent Light) Confocal Microscopy Monitoring ex vivo cell in real-time Immunocytochemistry and Image Analysis
Pathology Unit	<ul style="list-style-type: none"> Tissue processing, staining and immunohistochemistry preparations Laser microdissection Scanning of preparations EXAKT system processing of hard materials Tissue matrix production (Tissue microarray) Reporting and graphical documentation
Functional Assessment Unit	<ul style="list-style-type: none"> Optical Image Telemetry Metabolism Evaluation of the Sensory-Motor System Projects with rodents
Transgenic Unit	<ul style="list-style-type: none"> Generation of transgenic mice by microinjection of DNA into pronucleus Production of mouse chimeric in order to generate knockout mouse lines and KI and chimerism studies Preimplantation embryo development studies Rederivation of mouse lines Cryopreservation of mouse lines Studies and assistance in mouse breeding Temporary housing of experimental animals (rabbit, pig, sheep and rat) Surgery and microsurgery techniques in clinical conditions
SAI Biomedicine and Biomaterials. Experimental Surgery	<ul style="list-style-type: none"> Housing of experimental animals (mouse, rat and rabbit) in accordance with current legislation. Management of rodent colonies
SAI Biomedicine and Biomaterials. Animal Housing	
SAI Cell Sorting and Sequencing.	<p>DNA Sequencing Area</p> <ul style="list-style-type: none"> Automatic DNA sequencing RFLP analysis Detection of mutations by SSCP technique Real-time quantitative PCR (RT-PCR) <p>Cell Separation Area</p> <ul style="list-style-type: none"> Cell sorting by flow cytometry Cellular characterization cytometry techniques

Sofia Samper

HEALTH.2012.2.3.2-1: Co-infection of HIV/AIDS, malaria, tuberculosis and/or hepatitis

HEALTH.2012.2.3.2-2: Co-morbidity between infectious and non-communicable diseases

Contact: Sofia Samper: samper@unizar.es

➤ **RESEARCH LINES**

- Molecular Epidemiology of Tuberculosis in ARAGON: A population study carried out in Aragón which includes the total of the tuberculosis cases, is proposed in order to achieve the decrease of the rates of tuberculosis in Aragon by the implementation of effectiveness TB control measures. This line include the objectives of developing new method to rapid identify the prevalent strains. The study of a strain causing near 20% of the cases in 2001 to 2004 is also fitted. Impact of immigration.
- Molecular Epidemiology of Multidrug-Resistant Tuberculosis in Spain, analyse systematically MDR and XDR tuberculosis isolates in Spain in order to identify the strains that are being transmitted, how are they evolving and the mechanisms of transmission for these strains. Impact of immigration.
- Genomic studies. Studies of the genome of the most transmitted susceptible and MDR strains. Studies of clonality. It has been demonstrated that some strains may differ in virulence, pathogenesis, and epidemiologic characteristics. This line increase awareness about the insertion sequence IS6110.

➤ **POSSIBLE CONTRIBUTIONS**

- Network of European, Latin American and Mediterranean Countries.
- population study carried out in Aragón

➤ **EXPERIENCE IN RESEARCH PROJECTS**

EUMEDNETvsTB—Building a cooperative strategy between Europe and Mediterranean Countries for upgrading tuberculosis research and control, Call (part) identifier FP7-REGPOT-2009-2

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Cell Separation and Cytometry Unit	<ul style="list-style-type: none"> • Flow cytometry • Cell sorting by flow cytometry • Magnetic cell separation • Multiplex analysis
Cell Culture Unit	<ul style="list-style-type: none"> • Obtaining Primary Cultures • Cultivation and differentiation of adult and embryonic human and animal stem cells • IPS cell generation • Analysis of mycoplasma contamination of crops • Genetic engineering techniques for modifying and labeling of cell lines
Microscopy and Imaging Unit	<ul style="list-style-type: none"> • Conventional microscopy (Halogen and Fluorescent Light) • Confocal Microscopy • Monitoring ex vivo cell in real-time • Immunocytochemistry and Image Analysis
Pathology Unit	<ul style="list-style-type: none"> • Tissue processing, staining and immunohistochemistry preparations • Laser microdissection • Scanning of preparations • EXAKT system processing of hard materials • Tissue matrix production (Tissue microarray) • Reporting and graphical documentation
Functional Assessment Unit	<ul style="list-style-type: none"> • Optical Image • Telemetry • Metabolism • Evaluation of the Sensory-Motor System • Projects with rodents
Transgenic Unit	<ul style="list-style-type: none"> • Generation of transgenic mice by microinjection of DNA into pronucleus • Production of mouse chimeric in order to generate knockout mouse lines and KI and chimerism studies • Preimplantation embryo development studies • Rederivation of mouse lines • Cryopreservation of mouse lines • Studies and assistance in mouse breeding • Temporary housing of experimental animals (rabbit, pig, sheep and rat) • Surgery and microsurgery techniques in clinical conditions
SAI Biomedicine and Biomaterials. Experimental Surgery	
SAI Biomedicine and Biomaterials. Animal Housing	<ul style="list-style-type: none"> • Housing of experimental animals (mouse, rat and rabbit) in accordance with current legislation. • Management of rodent colonies
SAI Cell Sorting and Sequencing.	<p>DNA Sequencing Area</p> <ul style="list-style-type: none"> • Automatic DNA sequencing • RFLP analysis • Detection of mutations by SSCP technique • Real-time quantitative PCR (RT-PCR) <p>Cell Separation Area</p> <ul style="list-style-type: none"> • Cell sorting by flow cytometry • Cellular characterization cytometry techniques

Jose Miguel Arbones Mainar

HEALTH.2011.2.1.1-2: Proteins and their interactions in health and disease.

HEALTH.2011.2.1.1.-4: Population genetics studies on cardio-metabolic disorders in EU/AC and EECA populations.

HEALTH.2011.2.4.3-1: Investigator-driven clinical trials³⁷ to reduce diabetes complications.

HEALTH.2011.2.4.3-2 Development of novel treatment strategies based on knowledge of cellular dysfunction.

HEALTH.2011.2.4.3-3: Molecular and physiological effects of lifestyle factors on diabetes/obesity.

Contact: jmarbones.iacs@aragon.es

➤ KEYWORDS

Apolipoprotein E, Metabolic Syndrome, Diabetes, Obesity, Health sciences, Endocrinology, Metabolism, Insulin Resistance

➤ RESEARCH LINES

- Adipose tissue biology
- Role of the human Apolipoprotein E isoforms in the Metabolic Syndrome

➤ POSSIBLE CONTRIBUTIONS

- international collaborations with Dr. Osada at Zaragoza University, Dr. Maeda at the University of North Carolina, Dr. de Roos at the Rowett Institute as well as Dr. Newgard at Duke Metabolism Center.
- the DNA and plasma samples from a large-scale cohort study, in which individuals are followed over the time periods and assessed for the development of MetS. (healthy middle-age individuals, representatives of the general European population, within the key age range in the onset of MetS - 30-55 years of age). The study includes a longitudinal component, with repeated application of imaging techniques (aortic CT-Scan and echography) and dietary follow-up.

➤ EXPERIENCE IN RESEARCH PROJECTS

Jose Miguel Arbones-Mainar currently holds a 6-year “Miguel Servet” fellowship funded by the Health Institute Carlos III (Madrid, Spain). His research takes place in the Translational Research Unit at the Aragonian Health Science Institute (Zaragoza, Spain). As doctoral candidate, he performed several intervention studies assessing the effects of different dietary fatty acids and drugs on atherosclerosis, fatty liver and glucose intolerance development in transgenic mouse models. Subsequently, in his stay with Dr. de Roos in the Rowett Research Institute, UK, he was trained in the proteomics and systems biology fields. All these skills were complemented in the Nobuyo Maeda/ Oliver Smithies lab at the University of North Carolina with a further training in state-of-the-art metabolic profiling techniques, such as radio-tracers, in vitro assays and indirect calorimetry.

He continues actively collaborating with their former mentors Drs. Osada and deRoos, in addition during his stay in the University of North Carolina he has established fruitful relations with Dr. Newgard in the Sarah W. Stedman Nutrition and Metabolism Center at Duke University and Dr. Mazzone at the University of Illinois at Chicago.

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Dr. Alexandra Prados-Torres

2012-3.2-1 Improving the organisation of health service delivery.

2012-2.2.2.2. Investigator-driven clinical trials²⁶ for optimisation of management of elderly patients with multiple diseases.

Contact: Alexandra Prados Torres, Aragon Health Sciences Institute. Email: sprados.iacs@aragon.es (please also send a copy of your message to mkoelling@redaragon7pm.eu)

THE RESEARCH PROGRAM

The aim of Dr. Alexandra Prados-Torres's multidisciplinary group is to increase understanding of the broader healthcare needs of the population and to study the coherence between these needs and the organisation and provision of healthcare. This implies developing methods and tools that characterize the morbidity burden of the population from a clinical, societal and epidemiological perspective so as to define and categorize the comprehensive healthcare needs of the population. It also involves identifying elements and features of health systems and other sectors that successfully meet the newly defined and categorized healthcare needs of the population.

KEYWORDS

burden of morbidity, continuity of care, efficiency, equity, healthcare provision, healthcare needs, health information systems, health policy, health systems, methods, optimization, patient classification systems, primary health care, quality, solidarity, wellbeing

SPECIFIC RESEARCH LINES

- Determinants and patterns of health services utilization.
- Healthcare quality and outcomes evaluation.
- High-risk populations with intense health services utilization.
- Patient classification systems in primary care.
- Epidemiology of multimorbidity.
- Functionality of health information systems.

POSSIBLE CONTRIBUTIONS

- Management, processing and integration of extensive population-based Administrative databases from the primary care, hospital and emergency settings and the pharmacy database.
- Management, processing and integration of census-derived socio-economic data.
- Methodological and statistical developments for the study of healthcare resource consumption variables.
- Expertise in the study of multimorbidity and the use of patient classification systems.
- International contacts:
 - Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health (USA)
 - NIVEL, the Netherlands Institute for Health Services Research (Netherlands)
 - Department of Neurobiology, Care Sciences and Society, Karolinska Institute (Sweden)
 - Department of Primary Care and Public Health, Imperial College Faculty of Medicine (UK)
 - Academic Unit of Primary Health Care, University of Bristol (UK)
 - Division of Public Health and Primary Health Care, University of Oxford (UK)
 - Public Health Department, Faculty of Health Sciences, Klaipeda University (Lithuania)
 - Research Unit for General Practice, Aarhus University (Denmark)
 - Faculty of Social Welfare and Health Sciences, Haifa University (Israel)

EXPERIENCE IN RESEARCH PROJECTS

In the last years, Dr. Alexandra Prados-Torres has coordinated two consecutive 3-year multicentre funded by the Ministry of Science and Innovation and focused on the classification of health problems, predictive modelling of health resource use and the relationship between morbidity, health costs and clinical effectiveness.

Dr. Alexandra Prados-Torres's research group is also part of the Aragon Health Services Research Group, funded by the Regional Government of Aragón from 2006 until 2013, which includes members of the Department of Preventive Medicine and Public Health of the University of Zaragoza. The group formally collaborates with researchers from the Department of Primary Care and Public Health of Imperial College London and the ACG Team of Johns Hopkins Bloomberg School of Public Health.

STAFF SCIENTISTS INVOLVED

Dr. Alexandra Prados-Torres is the Scientific Director of the Aragon Institute of Health Sciences (I+CS) and has more than 10 years of experience in the field of health services research. Her research group includes 9 people with complimentary knowledge and experience in the fields of health services research methodology, data mining of clinical and administrative databases, statistical analysis and clinical practice.

RECENT PUBLICATIONS

- 2011** González F, Calderón A, Poblador B, Navarro C, López A, Prados A. Under-reporting of recognized adverse drug reactions by primary care physicians: an exploratory study. Accepted for its publication in *Pharmacoepidemiol Drug Saf*.
- 2011** Calderón A, Gimeno L, Macipe R, Poblador B, Bordonaba D, Prados A. Primary care utilisation patterns among the urban immigrant population in the context of a national health system. Accepted for its publication in *BMC Public Health*.
- 2011** Calderón A, Carney L, Soljak M, Bottle A, Partridge M, Bell D, Abi-Aad G, Aylin P, Majeed A. Association of population and primary healthcare factors with hospital admission rates for chronic obstructive pulmonary disease in England: national cross-sectional study. *Thorax* 2011;66(3):191-6.
- 2010** Calderón A, Poblador B, López A, Alcalá JT, Abad JM, Bordonaba D, Prados A. Does the pharmacy expenditure of patients always correspond with their morbidity burden? Exploring new approaches in the interpretation of pharmacy expenditure. *BMC Public Health* 2010 May 11;10(1):244.
- 2010** Calderón A, Abrams C, Poblador B, Weiner J, Prados A. Applying diagnosis and pharmacy based risk models to predict pharmacy use in Aragon Spain: The impact of a local calibration. *BMC Health Serv Res*. 2010;10:22.
- 2010** Sicras A, Pané O, Martínez T, Fernández JL, Prats J, Santafé L, Navarro R, Prados A, Estelrich J. Adjusted clinical groups use at a Spanish primary care center: a retrospective, population-based study. *Rev Panam Salud Publica*. 2010;27(1):49-55.
- 2009** Prados A, Calderón A, Sicras A, March S, Oliván B. Pharmaceutical Cost Control in Primary Care: Opinion and Contributions by Healthcare Professionals. *BMC Health Serv Res* 2009;9:209.
- 2009** Sicras A, Navarro R, Blanca M, Velasco S, Escribano E, Llopart JR, Violan C, Vilaseca JM, Sanchez E, Benavent J, Flor F, Aguado A, Rodríguez D, Prados A, Estelrich J. The relationship between effectiveness and costs measured by a risk-adjusted case-mix system: multicentre study of Catalonian population data bases. *BMC Public Health* 2009;9:202.
- 2009** Prados A, Sicras A, Estelrich J, Calderón A, Rabanaque MJ, López A. Identification of pharmacy cost outliers in primary care. *Aten Primaria* 2009;41(8):453-459.

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Unit	Equipment / capacities
Methodological support	<ul style="list-style-type: none"> • Methodological support research groups in the genesis of the idea of research and writing of protocols • Statistical support • Development of the research training • Development of scientific and technical feasibility reports for projects • Monitoring annual scientific reports and end of project • Building the relationship of groups and formation of the same
Management databases	<ul style="list-style-type: none"> • Management of administrative databases
Documentalist	<ul style="list-style-type: none"> • Scientific production measurement

Olga Abian - Drug Delivery systems and Diagnosis methods

NMP 2012.1.3-1 Systematic investigations of mechanism and effects of nanomaterials with living systems

Contact: Olga Abian (oabifra@unizar.es)

➤ PREVIOUS EXPERTISE

Olga Abian is a biochemical and molecular biologist from the Instituto Investigación Sanitaria de Aragón (IIS) and member of the Institute of Biocomputation and Physics of Complex Systems (BIFI). He works with the HCV NS3 protease viral protein searching for inhibitors and new drug delivery systems based in nanotechnology.

She uses several spectroscopic (Fluorescence, Circular Dichroism an Absorbance), biophysical techniques (Isothermal Titration Calorimetry (ITC), Differential Scanning Calorimetry (DSC) and Surface Plasmon Resonance) and performs High Throughput Screening experiments using chemical libraries. She also has already optimized cellular cultures for cell viability studies of drugs and nanoparticles and for testing the HCV antiviral activity of drugs.

Currently she is working on developing new drug delivery systems for hepatitis C infection treatment and new diagnosis methods for gastrointestinal diseases related with cancer.

➤ POSSIBLE CONTRIBUTIONS

- Biophysical characterisation of proteins/enzymes at atomic level complemented with solution studies
- Functional screening of chemical libraries
- Searching for chaperones and inhibitors of proteins involved in human diseases
- Drug delivery using nanoparticles
- Biotechnological and therapeutic applications
- Cell culture
- Fluorescence
- Circular Dichroism
- Calorimetry
- SPR

➤ EXPERIENCE IN RESEARCH PROJECTS

Olga Abian has participated in several research projects related to medical applications on a regional and national basis. She is leader of the project entitled: "Adapted Nanoparticles for transport and specific release of drugs against hepatitis C virus (VHC)" from the Instituto de Salud Carlos III.

The researcher also collaborates in other regional projects related with structural studies of Hepatitis C NS3 protease and the rational design of bioactive compounds.

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Microscopy and Imaging Unit	<ul style="list-style-type: none"> • Conventional microscopy (Halogen and Fluorescent Light) • Confocal Microscopy • Monitoring ex vivo cell in real-time • Immunocytochemistry and Image Analysis

BIFI – Institute for Biocomputation and Physics of Complex Systems

BIFI is a research institute that promotes interdisciplinarity to face the big challenges of innovation and development. BIFI's main research areas are: Biochemistry, Biophysics, Physics and Computing. BIFI hosts both fundamental and applied research, applying common techniques and multidisciplinary approaches to complex problems. It hosts researchers from the Universidad de Zaragoza and other Spanish and foreign universities and aims at developing a competitive research in computation applied to physics of complex systems and biological systems.

Equipment	Description
Spectroscopy Laboratory	Spectropolarimeter Fluorescence Spectrophotometer UV/visible Spectrophotometer Light scattering Dynapro
Calorimetry and SPR Laboratory	Differential Scanning Calorimeter Isothermal Titration Calorimeter Surface Plasmon Resonance Equipment
Microscopy and Chromatography Laboratory	Inverted microscope with Differential Interference Contrast HPLC (High performance liquid chromatography) FPLC (Fast protein liquid chromatography)
Molecular Biology Laboratory	PCR thermal cyclers DNA and protein electrophoresis system. 2D electrophoresis system Protein immunoblot system Electroporator Purification and Ultrapurification water system Manipulation yeast cabin. Safety chemistry cabin
Cristallography Laboratory	Thermostatic chamber at 18°C with anaerobic system Cold room at 4°C

Nanostructured Films and Particles (University of Zaragoza, Spain)

Contact: Prof. Jesus Santamaria (Jesus.Santamaria@unizar.es)

HEALTH-FP7. 1.4 INNOVATIVE THERAPEUTIC APPROACHES AND INTERVENTIONS

HEALTH.2012.1.4-4: Targeted nucleic acid delivery as an innovative therapeutic or prophylactic approach

➤ **PREVIOUS EXPERTISE:** The Nanostructured porous Films and Particles (NFP) group is composed of 12 doctors (8 are teaching staff at the University of Zaragoza), 17 Ph.D. students, and one laboratory technician. In the last 5 years they have published 115 refereed papers and presented 11 patents, two of them extended internationally. Particularly, the 4 NFP doctors that present this project have co-authored in the last 5 years (2006-2011) 74 papers and book chapters and 3 patents.

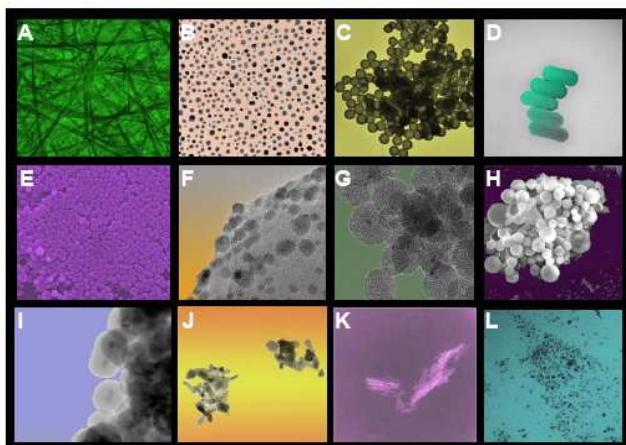
➤ The NFP Group was created in 2007 by researchers from different backgrounds, with the aim of concentrating efforts in the development and application of nanostructured materials, with an emphasis on nanoporous and hybrid systems. In our different group research lines we use of nanoporous and hybrid (porous/nonporous) materials as: i) individual nanoparticles, ii) surface coatings and iii) nano-fillers. We are interested in developing methods that allow us to carry out nanomaterials synthesis with a good control of size and shape, and also in methods that facilitate the assembly of these nanomaterials in structures that are useful on a variety of scenarios. One example is the use of nanoporous films as targets (or as barriers) to boost the selectivity of chemical sensors; in another, nanoporous coatings are employed to increase interphase contact area in structured microreactors. **We also investigate medical applications where our nanostructured materials can be employed to provide drug release or enhanced image (nano-diagnosis) features.** In other scenarios, nanostructured fillers provide outstanding (mechanical, magnetic, bactericidal...) properties to polymer-based nanocomposites. Finally, we are also concerned with nano-safety aspects, and we actively investigate the safe handling of nanomaterials. Currently, there are 4 main areas, which have been strongly developed by the creation of the Aragon Nanoscience Institute (INA), with state-of-the-art equipment, of which the NFP is one of the founding groups. The current research areas are:

- Chemical sensors
 - Structured reactors and microreactors
 - **Biomedical applications of nanoparticles**
 - Nanosafety
- As external indicators of the quality of the research carried out by the NFP the following can be quoted: i) it has been awarded the maximum research-quality grade “Excellence research group” by the State (Aragon) Government, after an external evaluation in which only about 15% of the research groups achieved this distinction; ii) NFP is among the 40 research groups that make up the highly selective CIBER BBN (Bioengineering, Biomaterials and Nanomedicine), selected in a national evaluation process that rejected nearly 90% of applicants; iii) the group has participated or is currently participating in numerous European research projects (i.e., Zeocell, Tecna, Cost, etc.) including two networks of Excellence in the VI Framework Program (“Nanomempro” and “InsidePores”). The Head of the Research group (Prof. Jesus Santamaria) is one of the recipients of the prestigious ERC (European Research Council) Advanced Grant.

➤ POSSIBLE CONTRIBUTIONS:

- Synthesis of engineered nanoparticles including iron oxides, silica, and gold for transfection applications.
- Surface functionalization of the different nanomaterials with metals (hybrid core/shell nanoparticles), polymers (including PEG, PEI, DMSA, etc.)
- Nanoparticle tagging to allow cellular trafficking.
- Large-scale production of engineered nanomaterials by using laser pyrolysis reactors.
- Complete physicochemical characterization of the synthesized nanoparticles by using:
 - HRTEM (including the atomic-scale resolution FEI Titan™ Instruments)
 - SEM
 - Colloidal stability studies by means of DLS
 - Protein adsorption studies by colorimetric analysis
 - Thermogravimetric analysis (TGA, DSC)
 - Surface area determination (BET area) and Hg porosimetry
 - Magnetic measurements (SQUID)
 - Atomic composition (AA) and XPS (surface)
 - X-Ray diffraction (crystallinity)
 - Chemical structure (FTIR and RMN)

Examples of our engineered nanoparticles are shown below (colour is computer added):



- A) Silver nanowires
- B) Gold nanoparticles
- C) SiO₂/Au nanoparticles
- D) Gold nanorods
- E) SiO₂ nanoparticles
- F) Supported gold nanoparticles
- G) Mesoporous SiO₂

➤ **Examples of our scientific publications in this field include:** On the role of the colloidal stability of mesoporous silica nanoparticles for gene delivery applications (accepted for publication in Journal of Nanoparticle Research, 2011); Therapeutic transgene delivery into human cells by using gold capped nanoparticles (submitted to Acta Biomaterialia)

➤ **EXPERIENCE IN RESEARCH PROJECTS:** Our Group is and has been involved both in national and European research projects and in research networks:

- FP7-(2011-2014): Large-scale integrating Collaborative Project with 35 partners: NANOVALID: DEVELOPMENT OF REFERENCE METHODS FOR HAZARD IDENTIFICATION, RISK ASSESSMENT AND LCA OF ENGINEERED NANOMATERIALS
- ERC-AG-PE8 ERC Advanced Grant (2011-2015) MICROWAVE-ASSISTED MICROREACTORS: DEVELOPMENT OF A HIGHLY EFFICIENT GAS PHASE CONTACTOR WITH DIRECT CATALYST HEATING (HECTOR)
- FP7-(2008-2010) NANOSTRUCTURED ELECTROLYTE MEMBRANES BASED ON POLYMER-IONIC LIQUIDS-ZEOLITE COMPOSITES FOR HIGH TEMPERATURE PEM FUEL CELL (ZEOCELL)
- Interreg Sudoe, EU, SOE1/P1/E184. TECNA: COOPERATIVE INTEGRATION OF TECHNOLOGICAL AND RESEARCH CENTRES IN THE SUDOE FOR THE PROMOTION OF THE NEW MATERIALS BASED ON THERMOPLASTIC NANOCOMPOSITES 2009-2011.
- FP-7 COST: COINAPO: MPNS Action MP0902. COMPOSITES OF INORGANIC NANOTUBES AND POLYMERS (COINAPO) (2010-2013)

ARAGON NANOSCIENCE INSTITUTE (INA) is one of the five Research Institutes of UNIZAR.

The Institute of Nanoscience of Aragon is an interdisciplinary research institute of the University of Zaragoza, created in 2003. Our activity is focused on R+D in nanoscience and nanotechnology, based on the processing and fabrication of structures at the nanoscale and the study of their applications, in collaboration with companies and technological institutes from different areas.

The Institute has high-level experts of different disciplines: Physics, Chemistry, Engineering, Biochemistry and Medicine, which allows us performing multidisciplinary research using different fields of knowledge to address Nanoscience.

Our aims are to:

Set the INA as a reference in nanotechnology-based research, both at national and international levels; Develop new research lines; Train new scientists and technologists in our field; Offer our experience and services to Research Centres and Companies; Support and encourage innovation and technological transfer through contracts with companies and the creation of new Spin-offs; Disseminate the research results and promote nanoscience among the general public.

A staff of 126 researchers (64 PhDs) and 17 qualified technicians are currently working at INA. Thanks to our qualified staff and our advanced instruments and infrastructures INA is a benchmark in Europe in the fields of: Physics of Nanosystems; Nanobiomedicine and Nanomaterials.

We have last cutting-edge equipment located in different labs including: Thin films growth: plasma PLD-Sputtering, PECVD, and Molecular Beam Epitaxy (MBE). Optical lithography. Clean rooms. Dual Beam Microscopy: Nanolithography. (Nanolab NOVA™ 200) Local probe microscopy: Atomic force microscope (AFM), Scanning tunnelling microscope (STM). Electronic microscopy: scanning electron microscopes (FEI FEG250; FEI Inspect F); High resolution electronic transmission microscopes (HRTEM; TECNAI T20; TECNAI F30, TITAN 60-300 and TITAN³). Characterization of nanostructures: XPS-Auger, XRD, VSM, and SQUID and so on.

<http://www.unizar.es/ina/index.php>

Apoptosis, Immunity and Cancer Team
Cell death during the control of pathogen infection and tumour development

Contact: Julian Pardo (pardojim@unizar.es)

TOPICS:	2012-2.3.0-1 Diagnostics for infectious diseases. 2012-2.3.2-1 Co-infection of HIV/AIDS, malaria, tuberculosis and/or hepatitis. 012-2.4.5.2 Biomarkers and diagnostics for chronic inflammatory diseases of the joints and digestive system
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➤ **PREVIOUS EXPERTISE**

Cell death by apoptosis is one of the major mechanisms of multicellular organisms to fight against pathogen infection as well as tumour development. Julian Pardo's team is interested in understanding the role of cell death during the host defense response (immune system) against tumour development and pathogen infection and, on the other hand, how pathogens manipulate cell death to promote persistence and infection. NK and Tc cells are the main cells of the host immune system involved in the elimination of pathogen infected or tumor cells. The two main mechanisms involved in this action are the granule exocytosis (perforin and granzymes) and the death receptor system (FasL, TRAIL, TNF).

The team studies the relevance of perforin, granzymes and death ligands in the elimination of tumour, bacterial and viral infections *in vivo* by using knock out mouse models. In addition, the Apoptosis, Immunity and Cancer group studies the molecular mechanisms of cell death induced by perforin and granzymes on tumor or virus infected cells by using *ex vivo* and *in vivo* biological relevant models based on intact NK or Tc cells. Their major objective is to explore the ability of specific grms to kill virus or tumour cells highly resistant to classical therapeutic treatments in order to design therapies that are able to overcome tumour or virus resistance. In addition, they are interested in finding out the biological role of perforin and granzymes in inflammatory and autoimmunity processes.

Our group also study the relation between cell death and pathogen virulence using models of virus (*Mousepox*), fungal (*Aspergillus*) and bacterial (*Mycobacterium tuberculosis* and *Brucella spp*) infections.

➤ **POSSIBLE CONTRIBUTIONS**

- Role of the effector molecules (Perforin, Granzymes and Death Ligands) of cytotoxic T (Tc) and Natural Killer (NK) cells in the elimination of tumor and pathogen infected cells.
 - *In vivo* and *ex vivo* models (Tc and NK cells) to analyse cell death induced by perforin and granzymes as well as death ligands in tumor cells.
 - Knock-out mouse colony to analyse the biological relevance of perforin, granzymes and death receptors in tumor and pathogen elimination.
 - Human models to analyse cell death induced by Tc and NK cells on tumor cell lines as well as in cells from patients with hematological neoplasias.
- Role of the effector molecules (Perforin, Granzymes and Death Ligands) of cytotoxic T (Tc) and Natural Killer (NK) cells in autoimmune diseases.
- Mouse *in vivo* models (KO) to study the mechanisms (perforin, granzymes, FasL, etc.) of tumor or anti-viral immunotherapies as mAb.
- Development of human NK cell immunotherapies to kill tumor cells highly resistant to apoptotic stimuli.
- Mouse *in vivo* and *in vitro* models to study cell death induced by fungal, viral or bacterial pathogens.

➤ **EXPERIENCE IN RESEARCH PROJECTS**

The team led by Dr Pardo has participated in several projects on a regional, national and international basis. The results of the group have appeared in highly ranked journals and they have had a great impact. Moreover, his group holds a research contract with Max-Planck Innovation through the company Lead Discovery Center in Germany).

Dr Pardo is co-inventor of two different patents which are currently active. They are called "Inhibition of gliotoxin" and "Use de SS'-dimetil-gliotoxin as diagnostic biomarker in pathologies caused by gliotoxin- or its derivates-producing fungus".

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APOPTOSIS, IMMUNITY AND CANCER GROUP

The group "Apoptosis, immunity and cancer" has been awarded in 2009 as "Group of Excellence in Research" by the Government of Aragón, indicating that its activity is between the upper 10% in their thematic areas of research in Spain.

Their main scientific achievements during the last 5 years include:

- More than 40 papers in international journals including Nature Immunology, Trends in Immunology, Immunity or the Journal of Cell Biology.
- More than 25 national projects, 3 EU projects and several research contracts with national and European companies.
- 3 national and 1 European patent are holded by members of the group.
- 10 PhD theses have been finished (four of them awarded with the Extraordinary PhD prize of the University of Zaragoza).

The following equipments are available at the Department of Biochemistry and Cellular and Molecular Biology:

- Flow cytometer FACSCalibur,
- Gel electrophoresis and blotting equipment,
- Nucleofector for cell transfection from Amaxa,
- NanoDrop spectrophotometer for protein and nucleic acid quantification, luminometer, thermocyclers,
- Fluorescence and light microscope,
- Light cycler for real time PCR and S2 level installation of cell culture with laminar flow hood and incubators
- LEICA SP2 confocal microscope,
- FACS Aria sorter, small animal living imaging system (Biophotonic Imaging) IVIS® Lumina (Xenogen-Caliper), anatomical pathology and DNA or protein sequencing services.
- A new animal facility is presently being established at the University of Zaragoza where the last technological advances to perform animal models will be incorporated.

Apoptosis, Immunity and Cancer Team New Diagnosis markers of invasive fungal infections

Contact: Julian Pardo (pardojim@unizar.es)

TOPIC :	2012-2.3.0-1 Diagnostics for infectious diseases
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➤ PREVIOUS EXPERTISE

The saprophytic fungus *Aspergillus fumigatus*, an opportunistic fungal human pathogen with a high presence in air, is responsible for more than 90% of invasive aspergillosis (IA) cases in patients suffering from AIDS, tuberculosis, cancer or are undergoing organ transplants, resulting in higher than 80% mortality. One of the major problems concerning IA is that the disease is only definitively identified at a late stage when it is already too severe and treatments have become ineffective. This is due in large part because current techniques for early diagnosis are not very specific. In fact, the diagnosis can only be classified as possible or probable and can only be confirmed after death or by highly invasive techniques as lung biopsy.

Our group is trying to establish new diagnosis markers of IA such a detection of secondary metabolites produced by *Aspergillus* spp as gliotoxin (GT) or its derivative SS⁻-dimethylgliotoxin (Bismethylgliotoxin, bmGT), which maybe able to identify fungal presence faster than current markers as galactomannan and fungal DNA. During the last year, we have established a cheap, fast, sensitive and minimally invasive technique to detect and quantify the secondary metabolite GT and its inactive derivative bmGT in serum from patients at risk of IA.

POSSIBLE CONTRIBUTIONS

- Samples of patients at risk of IA (collaboration with Miguel Servet Hospital)
- Technology (chromatography, ELISA, blot, etc) to detect and quantify secondary metabolites from *Aspergillus* spp as gliotoxin and Bismethylgliotoxin in humans, animals and other sources (soil, food, etc).

➤ EXPERIENCE IN RESEARCH PROJECTS

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- A new animal facility is presently being established at the University of Zaragoza where the last technological advances to perform animal models will be incorporated.

Psychogeriatrics, Psychosomatics and Liaison Psychiatry

Contact: Antonio Lobo Satué (alobo@unizar.es)

TOPIC :	
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➤ KEYWORDS

Neurodegenerative disorders, dementia, vascular dementia, Alzheimer Disease; neuroinflammation, vascular disease, cardiovascular disease, cerebrovascular disease, myocardial infarction, diabetes mellitus, stroke; Affective disorders, depression, consultation-liaison; Health services research.

➤ RESEARCH LINES

The Psychosomatics and Liaison Psychiatry Unit has two principal lines of research (basically focused in clinical psychiatric epidemiology), where four “generations” of increasing complexity have been developed. It is now involved in the fifth “generation” of studies, which include translational research, with recent involvement in studies incorporating biological parameters, including inflammatory biomarkers and genetic assessment.

Line I is devoted to psychiatric aspects of the aging process, and includes the study of dementia and depression in the elderly, with special emphasis in aspects relevant for the present study, such as vascular depression, vascular dementia, post-stroke depression, co-morbidity medical-psychiatric, etc. Some international reports in Line I, including studies of multimorbidity in the elderly population, of depression in medical diseases, are directly inter-connected with Line II.

Line II is devoted to the study of psychiatric aspects of somatic diseases and psychosomatics. The present study is the expected result of the systematic study of depression in medical populations. The previous development was the study of depression in internal medicine, medical patients.

➤ POSSIBLE CONTRIBUTIONS

- Active and Healthy Ageing
- Dementia and Depression in the Elderly
- Neurodegenerative disorders and cardiovascular effects
- Scientific and clinical validation of experimental results
- Development and validation of new therapies
- Health Promotion and Prevention

➤ EXPERIENCE IN RESEARCH PROJECTS

The Psychosomatics and Liaison Psychiatry Unit has participated in several projects on a regional, national and international basis.

Line I: Some studies reported in the international literature, including trans-national studies completed in European consortiums funded by BIOMED and similar EU programmes are considered to be international reference. The principal investigator has been member of the Executive Committee of EURODEP (Depression in European countries) and EURODEM (Dementia across European countries).

Line II: We coordinated the REPEP Network, the “Red” (RETIC) of the National Research Institute Carlos III devoted to this field of enquiry. A multi-center, cooperative study in seven Spanish hospitals has been completed, documenting a high prevalence of depression; negative implications, including increased mortality in the follow-up period; and somatic associations (Lobo et al., 2007). The REPEP, which was the final development of many previous studies, has provided important experience and hypotheses to concentrate our efforts at present in the specific psychopathology associated with medical diseases, as diabetes mellitus or myocardial infarction.

In this field of research, we have been the coordinating group in Spain of large European studies, such as the E.C.L.W. Study (13 countries, 90 hospitals, 15.000 patients) about liaison psychiatry and psychosomatics in general hospitals (Huyse et al., 2001); or the development of the INTERMED system, an original method to screen for “complex” medical patients with psychiatric co-morbidity, and social problems (Lobo et al., 2007). The principal investigator has also been member of the Executive Committee of these European Consortiums, also supported by BIOMED or similar European funded research programmes.

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MEDICINE AND PSYCHIATRY

This is a research group “consolidated” according to the criteria of the *Instituto Aragonés de Ciencias de la Salud* (I+CS) and the Regional Government (Aragón) It is also member of the CIBER of Mental Health (CIBERSAM), the consortium of competitive research groups according to the criteria of the National Research Institute Carlos III. In CIBERSAM, the Zaragoza Group is the coordinator of the research areas congruent with the subject matter of this Project (Area IV). The Group has also considerable experience in the training of young researchers (50 Doctoral Thesis, etc.), has international connections with excellence centers abroad (Johns Hopkins or the Iowa University

in U.S.A.; the Institute of Psychiatry and the Institute of Neurological Diseases in the U.K.; the Universities of Amsterdam and Groningen in Europe; etc.). The Group has also develop and/or validated in Spain international questionnaires / interviews and other documentation instruments (n = 19).

EXPERIMENTAL RESOURCES

Projects will be implemented from the *Hospital Clinico Universitario* in Zaragoza. The Psychosomatics and Liaison Psychiatry Unit cares for close to 5% of all hospital admissions, the referral rate for medical units being several times higher than the European average. The psychiatric research group is directed by the P.I. coordinator and Chief of the Service (AL), University Professor. The team is completed with clinicians and professors in both disciplines, and in Social and Prevention Medicine; with appointed researchers in all these disciplines and some residents; and a statistician with a total of 12 researches. Specialized nurses and technicians are also available for any Project. Both, the Psychosomatics and Psychiatry Units are fully equipped and have specific research facilities. The laboratory of the Biochemistry and Immunology Services of the General Hospital are also available as well as the facilities of the *Instituto Aragonés de Ciencias de la Salud* (I+CS), the regional research Institute, and the research Units from the University of Zaragoza are also available.

The Psychiatric team is a Group member and Coordinator of the research area related to medical patients in CIBERSAM, the research consortium of the most competitive Groups in Spanish psychiatry, under the patronage of the national *Instituto de Salud Carlos III* (ISCIII). CIBERSAM has an important collaborating network and experimental resources and experts in all fields of translational research in the remaining Groups are available for consultation and collaboration. Data management may be handled with the “PsyGrid” system, an original system used by CIBERSAM in collaboration the Polytechnic University of Valencia and originally developed at Oxford University. This is a user-friendly interface system that may be used to manage research projects, registries (patients), scales and questionnaires, facilitating data entry and consultation.

Please refer to: www.cibersam.es/openccms/openccms/system/modules/es.oneclick.cibersam/elements/jsp/banners/psygrid.jsp and the mental health research network PsyGrid in the United Kingdom (www.psygrid.org).

Pharmacogenomic and Metabolomic Unit

Research line: Pharmacogenetics

Contact: M^a Luisa Bernal (mbernal@unizar.es)

TOPIC :	2012-2.1.1.-1: Clinical utility of -omics for better diagnosis and treatment of rare diseases
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➤ **PREVIOUS EXPERTISE**

The Group of Pharmacogenomic and Metabolomic of Universidad de Zaragoza research is focused on development and conduct of pharmacogenomic and metabolic studies for rare diseases knowledge, including diagnosis and treatment, as well as, development and improvement of (already existing and new) orphan drugs. Its overall goal is to provide new approaches for the study of biological mechanisms of these diseases which will provide improvements in the clinical protocols of treatment

One of the key activities consists in the definition of underlying metabolic mechanisms and profiles of the different variations and phases of the studied disease. Another step is the qualitative identification and evaluation of target metabolites as specific molecular and metabolic biomarkers which are associated with initiation and / or promotion of the processes that may be responsible of the different variations and / or phases of the studied disease.

Another technique is to study the pharmacogenetic polymorphisms in the patients in relation to the drug-response used in the disease to improve their therapeutic effect. And analysing the relation between pharmacogenomic/pharmacogenetic and metabolomic data in affected cells.

The team of Dr. Bernal uses an application of innovative research approaches methodologies to elucidate the metabolic pathways of specific molecular compounds, evaluating metabolic drug-response *in vitro* to characterize the drug metabolic pathways, in order to improve the pharmacological effectiveness.

All these research activities could be used in several rare diseases by means of collaboration with other research groups. Professor Bernal and her team collaborate with other groups that have direct contact with the patients (such as Zaradem workgroup of Psychiatry Department of the Clinical Hospital belongs to CIBERSAM network or research group of Clinical Genetics and Functional Genomics who works with Cornelia of Lange syndrome patients).

➤ **POSSIBLE CONTRIBUTIONS**

- Determination of Pharmacogenetic Polymorphisms
- Determination in vitro of drug metabolic pathways
- Identification and evaluation of metabolic biomarkers
- Analysis of metabolic pathways by mass spectrometry
- Pharmacogenomic analysis by polymerase chain reaction (PCR) and real time quantitative.

➤ **EXPERIENCE IN RESEARCH PROJECTS**

The Pharmacogenomic and metabolomic group has participated on a wide range of research projects related to Pharmacogenetic field. They collaborated with Karolinska Institute (Sweden) performing several projects related with the influence of the genetic polymorphisms on the antidepressant and anticancer drugs in order to individualize the treatment.

The group has experience in the determination of genetic polymorphisms. Studies of several enzymes of the Cytochrome P-450 (CYP2D6, CYP2A6, CYP3A5, CYP2C19, CYP2C9, etc) as well as the enzymes responsible of xenobiotic conjugation (GST, NAT2...) or transport enzymes (ABP family...) has been performed in the Pharmacology Lab. It also has experience in the single-cell molecular analysis of volatile compounds and in the analysis of living plant tissues or single cell from different human tissues by video mass-spectrometry.

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DEPARTMENT OF PHARMACOLOGY AND PHYSIOLOGY

The department of Pharmacology was founded in 1991 by joining the research areas of Pharmacology and Physiology. Its research activities dealt with health sciences, involving different areas.

Experimental Resources

Microscopy and Chromatography Laboratory	Image Stream, High resolution microscopy in flow. Amnis Inverted microscope with Differential Interference Contrast HPLC (High performance liquid chromatography) HPLC-Agilent y el 4000QTRAP
Molecular Biology Laboratory	DNA Extractor AutoGenFlex 3000 PCR thermal cyclers (Termociclador Veriti, Applied Biosystems, Termociclador Primus 96 advanced, PeqLab) Pirosequencer PSQ 96MA, Biotage Liquid Chromatography WAVE3500HT, Transgenomic Microarrays Automatic Hibrydator, Discovery, Microarrays lecture, Genepix4100A, Axon Instruments Espectrophotometer Nanodrop-1000 Electrophoresis - Electro-Fast System Standard and Electro-Fast System Wide
Spectroscopy Laboratory	Spectropolarimeter Fluorescence Spectrophotometer UV/visible Spectrophotometer 4800plus MALDI-TOF/TOF MSMS and Tempo LC-MALDI

Stress and health issues
Contact: Santiago Gascón (sgascon@unizar.es)

TOPIC :	SIS.2012.2.2.1-1: Supporting actions on Innovation in the classroom: teacher training on inquiry based teaching methods on a large scale in Europe
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➤ **KEYWORDS**

Stress, depression, anxiety, violence at work, aggressions at work, work-related stress, health spending, prevention

➤ **RESEARCH LINES**

The Stress and Health Issues group belongs to the Department of Psychology of the University of Zaragoza. One of its research lines is related to stress and health issues. Its research is oriented to study the effects of stress upon human health. They have focused its research in the analysis of the effect of stress in public sector, mainly in the work of high school teachers. The group has used this case as a model example to study professional behaviour under pressure in complicated or violent environments.

Its research considers that teaching may be a highly rewarding task but also could become an important source of stress and, therefore, the origin of a psychological pathology. Some reasons that could provoke this pathology could be dealing with unmotivated groups, mutual disrespect or tension relationships. In these cases, teachers begin to work mechanically, avoiding any kind of involvement. It could become the first symptom of burnout. Furthermore, a greater rate of physical and psychiatric symptoms has been found in professionals who have suffered episodes of violence from pupils or pupils' families. Burnout is an increasing concern of European society although is limited to some specific jobs. The Stress Group believes that is absolutely important to know about the current reasons of its origin and the best ways to diagnose and treat it.

The European Institutions have begun to recommend to member countries to oblige their organisations to evaluate these risks and to share their experiences regarding the methods of intervention applied. Nowadays, very few companies carry out a rigorous evaluation of these risks and european professionals do not have a clear methodology for the application of these preventive measures. To develop new procedures in this field is one of the main priorities to the Stress and Health Group

➤ **POSSIBLE CONTRIBUTIONS**

- Burnout´s diagnosis and treatment
- Stress in Public Service Workers (especially teachers)
- Study of the stress upon human health
- Design of European Policies related to stress and burnout
- Evaluation of work related risks
- Knowledge on European Regulations in work related risks
- Stress Prevention

➤ **EXPERIENCE IN RESEARCH PROJECTS**

The group led by Dr. Gascón has a wide experience in collaboration with partners of other countries. They have built a mighty consortium that formed by eight universities and business partners, all of them European. This already formed consortium has expertise in fields such as Psychology, Preventive Medicine, Occupational Medicine, Epidemiology, Psychiatry, Education, Economy, and Microelectronic Engineering. Therefore, they have a large multidisciplinary team of researchers willing to develop their objectives, and also the facilities and partners. Also, they count with the support of the governments of Spain, Portugal and Italy (Departments of Education and Departments of Science and Technology) which have supported previous efforts and project of the members of the consortium.

Also, the Stress and Health Issues group collaborates with several non-European groups like the Canadian Centre of Organizational Research and Development from Acadia University (coordinated by profesor Michael Leiter) or the american-based California University (with a group coordinated by professor Christina Maslach's).

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DEPARTMENT OF PSYCHOLOGY

The Department of Psychology and Sociology of the University of Zaragoza is formed by 150 teachers and researchers who are divided into 3 different cities and several colleges from Zaragoza, Huesca and Teruel. The headquarters of the department are placed in the Faculty of Psychology in Teruel.

Some of the research fields that are covered by the department are:

- Social Anthropology
- Behavioural Sciences
- Psychological Assessment and Treatment
- Basic Psychology
- Social Psychology
- Labour Psychology and social services
- Psycobiology

In the region of Aragon, the economy is dominated by the automotive industry and the logistics sector, together with a large number of medium-sized companies operating in sectors such as ICT, business services, railway and tram construction, renewable energy, etc. There are also larger companies based in Zaragoza, such as Opel (one of the biggest factories in Europe), Bosch-Siemens Hausgeräte (which has 2 factories), Inditex (a logistics center for the clothing brands of Zara, Stradivarius, Massimo Dutti, etc.), Saica (paper production), Adidas (headquarters for Spain) and Safa-Galénica (Boots Healthcare pharmaceutical company). Researchers from the Department of Psychology studies have a long-term research relationship with these companies and other institutions (Regional Government, banks and financial services, Chamber of Commerce, business associations, entrepreneurship initiatives, labour unions, etc.) providing an optimum environment for teaching, as well as for research activities and projects.

Primary Health Care Group
Research line: Telemedicine in Mental health
[Contact: jgarcamp@gmail.com](mailto:jgarcamp@gmail.com)

TOPIC :	
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➤ **PREVIOUS EXPERTISE**

The group coordinates the research on mental health in primary care in Spain in the frame of Primary Care Prevention and Health Promotion Research Network (redIAPP) and is formed by Psychiatrists, family doctors and psychologists and experts in neuroscience. The group is specialized on prevention, early detection and treatment of some psychiatric disorders such as depression, anxiety and burnout. They have experience on the use of new technologies for the early detection of psychiatric disorders using changes in biological parameters and on the use of new technologies on the treatment and management of psychiatric patients.

One of main concerns of this group is the development of psychotherapy programs by internet and the use of mobiles and daily electronic devices for the treatment of these patients. Currently, they are developing and testing neurofeedback programs (NFB) for cognitive rehabilitation in patients with fibromyalgia and Attention deficit hyperactivity disorder (ADHD) in adults. Pain and the psychological aspects related to it is another of the research lines of the group. It has established a long-term collaboration with associations of patients with fibromyalgia and somatoform disorders, having a wide experience on treatment of this kind of patients and on support to family and its environment. Moreover, they have studied the pathways that these patients use in the health system and mechanisms to improve communication and efficacy at the different levels of the health system

The Primary Health Care group has a huge experience on detection and treatment of mental disorders in immigrants and they have developed studies on the epidemiology of these disorders and on management from individual to family or social approaches. Important aspects of this particular field, such as training in cultural specific, social environment expertise or education issues are all taking into account. One of its current research lines consists in the development of a computer-assisted psychological treatment especially designed for immigrants with depression.

➤ **POSSIBLE CONTRIBUTIONS**

- New technologies in psychology/psychiatry
- New technologies for early detection of psychiatric disorders using changes in biological parameters
- Neurofeedback in mental health patients
- Development of Psychotherapy programs on line (including internet services, mobile phones and daily electronic devices)
- Prevention and treatment of mental health problems in immigrants.
- Experience and Know How in Fibromyalgia and Somatoform Disorders
- Qualitative studies and meta-analysis
- Real and diary contact with a huge number of patients and their specific situations

➤ **EXPERIENCE IN RESEARCH PROJECTS**

The group has participated in more than 50 research projects (both within national and international contexts) related to the most frequent mental health problems in primary care, such as depression, anxiety, somatoform disorders...

The last one of them was named "Efficacy and cost-effectiveness of computerised cognitive therapy for depression in primary care: a controlled, randomized and a qualitative study" and was funded by Carlos III Health Institute.

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At the moment, the University consists of twelve faculties that offers Master degrees (5 years) and PhD programmes on Sciences, Business, Law, Humanities and Languages, Medicine, Sports, Veterinary and Engineering. There are also eleven Technical Schools on Engineering, Education, Business, Tourism, Nursing and Physiotherapy and Social Studies that teach 3 years degrees. It is distributed in campuses located in Zaragoza, Huesca and Teruel.

UNIZAR takes part on European Projects since FP4 and is currently involved in more than 120 ongoing European research projects, including several European programmes (such as FP7, Interreg, Cost, DG Sanco, Cytel, etc). UNIZAR has a European Projects Office which helps and assists the researchers during the preparation and management of the proposal.

MENTAL HEALTH IN ARAGON GROUP

Psychiatrists, family doctors and psychologists and experts in neuroscience constitute the mental health research group in Aragon. The general aim is the research and systematic assessment of the efficacy, effectiveness and efficiency of preventive, diagnostic and therapeutic interventions in mental health in primary care. Among the specific objectives, research in the management of patients with somatisation disorders/fibromyalgia and patients that overuse the health care services, in the psychopathology of first and second generation immigrants and in the prevention of depressive disorders stand out and prevention/treatment of burnout syndrome in professionals.

The different research lines of the group are:

- High prevalence mental disorders in Primary Care/general population: depression, somatoform disorders, fibromyalgia and burnout.
- Epidemiology, diagnosis and management of affective, anxiety, somatoform disorders and burnout.
- High clinical impact of the group research projects in the REDIAPP due to the burden of this kind of mental disorders in primary care health services.
- Development of innovative interventions for the prevention and promotion of mental health
- Pharmacological treatments (clinical trials on catastrophization) and psychotherapeutic interventions (comparisons of specific treatments for patients with somatoform disorders in PC) to improve treatment of prevalent mental disorders in primary care.
- Validation and design of new psychological instruments to detect/monitorize different mental disorders in primary care.

Moreover, the Mental Health Group in Aragon counts with research structures such as:

- Data banks:
 - Depression patient data base
 - Somatoform disorder patients
- These databases collect variables such as socio-demographic and clinical characteristics, disease progression, medical and psychiatric history, concomitant diseases, use of medicines and health resources, etc. Follow up data of this cohort will be collected to improve our knowledge on the progression and consequences of this disease.
- Fibromyalgia syndrome patients. N=250 patients from primary care. We studied the main psychological constructs of pain (catastrophism, acceptance, coping, flexibility mindfulness and perceived injustice) in relation with mediating variables (anxiety and depression) and outcome variables (pain and global function). Also we have neuroimaging and genetics variables of some of this patients.
- Immigration: Data on N= 890 immigrant patients from primary care.

The group counts with the clinical and research equipments of the University of Zaragoza, Aragon Health Service and of the Instituto Aragonés de Ciencias de la Salud. It includes libraries, hardware and software, housing, transversal research units (genetics, etc).

Molecular Mechanisms of glycosyltransferases involved in human diseases

Contact: [Ramon Hurtado \(rhurtado@bifi.es\)](mailto:rhurtado@bifi.es)

TOPIC :	2012-2.3.0-1 Diagnostics for infectious diseases
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➤ PREVIOUS EXPERTISE

Ramon Hurtado is a molecular and structural biologist based on the Institute of Biocomputation and Physics of Complex Systems (BIFI). He works with glycosyltransferases, glycosylhydrolases or carbohydrate binding modules involved in human diseases.

His main technique is the use of X-ray crystallography to understand proteins at atomic level. Also, he also uses other biophysical techniques, such as fluorescence, calorimetry or SPR to complement his crystallographic studies.

Currently he is working on essential glycosyltransferases involved in regulation of Notch and cell wall remodelling of *Aspergillus fumigatus* and *Candida albicans*. Both type of glycosyltransferases are drug targets to treat several types of Leukemias, possibly neuroblastomas and Aspergillosis/Candidiasis.

In other words we want to get insights on the catalytic mechanism of essential proteins, which can be potential drug targets to search/develop compounds against them, in order to treat different human diseases.

➤ POSSIBLE CONTRIBUTIONS

- Biophysical characterisation of proteins/enzymes at atomic level complemented with solution studies
- Functional screening of chemical libraries
- Searching for chaperones and inhibitors of proteins involved in human diseases
- Drug development for Leukemia T-ALL, ATL, neuroblastoma, Aspergillosis or Candidiasis
- Biotechnological and therapeutic applications
- X-ray crystallography
- Fluorescence
- Calorimetry
- SPR

➤ EXPERIENCE IN RESEARCH PROJECTS

Ramon Hurtado has participated in several research projects related to medical applications on a regional, national and international basis.

He collaborated in Fungwall Project which was funded by EC within "FP6 Life sciences, genomics and biotechnology for health" priority. This project was focused on investigate mechanisms of fungal cell wall synthesis in order to identify new antifungal targets to control human fungal infections in Europe.

At a national level, he has worked on development of drugs against pathogenic Trypanosomatids such as *Trypanosoma cruzi* and *Leishmania major*.

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Cristallography Laboratory	Thermostatic chamber at 18°C with anaerobic system Cold room at 4°C
Cell culture Laboratory	Dedicated culture rooms to a variety of cell types and expression systems (both prokariotic and eukariotic)
Centrifugation Laboratory	Preparative centrifuges Ultracentrifuge
Screening Laboratory	Multi-mode microplate reader Multi-plate well centrifuge

Computing resources

Equipment	Description	Comments
Caesaraugusta	512 PPC, 24TB, 4,4TFLOPS	Node of the Spanish Supercomputing Network (RES).
Terminus	815 cores "em64t", OpenSUSE Linux, 12 TB Lustre, 8TFLOPS, CPD 140m2, SAI 120kVA, gigabit + infiniband	BIFI's distributed memory cluster.
Janus	256 FPGAs, 22TB	Dedicated supercomputer simulating Spin-Glasses.
Piregrid	248cores	BIFI's site controls and is connected to 3 sites: Pau, Toulouse and Zaragoza. Grid focused on private companies.
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Ibercivis	Total users: 24.000 citizens. Total number of cores: 125.000 cores. Active users: 3.200 citizens. Active number of cores: 14.000 cores (connected weekly)	Spanish and Portuguese volunteer computing network. This infrastructure is connected with the FP7 project EDGI infrastructure (grid and cloud). 10 scientific applications running in production.
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Visualisation laboratory	6 projectors+filters,50 3D glasses, 2 screens ,12 infrared optitrack cameras, Kinect, Wiimote	Immersive & augmented reality, didactical units deployed with our own graphical engine.

Stem cell physiology, apoptosis and mitochondria

Research line: Stem cells and apoptosis

Contact: **José Alberto Carrodegua** (carrode@unizar.es)

TOPIC :	2012-1.4-3 Innovative strategies for translation of stem cell based therapies in regenerative medicine
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➤ **PREVIOUS EXPERTISE**

The research lines lead by Dr. José A. Carrodegua deal with the involvement of mitochondria-mediated apoptosis in several pathologies, cell proliferation and differentiation. They have previous experience in the study of mitochondrial transcription and replication, Alzheimer´s disease, mitochondrial proteins involved in apoptosis, and stem cell self-renewal, differentiation and death. A current research line deals with high-throughput techniques for the identification of chemicals that induce stem cell differentiation or specific death with applications in regenerative medicine. A new collaborative research line focuses on the development of microfluidics-based chips for molecular and cell biology applications.

The group uses a broad combination of Molecular Biology, Biochemistry and Cell Biology techniques to carry out basic as well as applied research in the fields of cancer biology, degenerative diseases and regenerative medicine.

➤ **POSSIBLE CONTRIBUTIONS**

- Cancer research related to mitochondria
- Degenerative diseases
- Stem cell proliferation and differentiation
- Regenerative medicine
- Involvement of mitochondria in stem cell biology and degenerative diseases
- Identification of bioactive compounds by screening of chemical libraries
- Molecular biology, biochemistry and cell biology techniques
- Selection of specific cell types with bioactive chemicals
- Multidimensional live cell microscopy
- Protein and nucleic acids analysis and engineering
- Immunochemical techniques
- Electrophoretic techniques: nucleic acids, proteins, bidimensional and blue-native electrophoresis of proteins
- Development of novel devices for cell culture applications in the fields of biomedicine and biotechnology.

➤ **EXPERIENCE IN RESEARCH PROJECTS**

The group has participated in several regional, national and international projects and maintains collaborations at regional, national and international levels, has produced two patents related to applications of antibodies and protein domains derived from novel proapoptotic mitochondrial proteins (PSAP isoforms, antigenic determinants, method of preparation and application of antibodies. PSAP-derived polipeptides able to induce apoptosis and their applications) and is currently preparing a new patent application dealing with the identification by high-throughput screening of chemical compounds that induce specific death in stem cells, with applications in cell therapy and regenerative medicine.

The group has also established contacts with around 30 international research groups working in different disciplines for the assembly of consortia to participate in international projects and networks.

They have also established contacts with private companies, and are currently seeking more companies, to participate in collaborative projects and grant applications in the fields of biomedicine and biotechnology.

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Computing resources

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Molecular Biology Laboratory	PCR thermal cyclers DNA and protein electrophoresis systems Protein immunoblot system 2D electrophoresis and analysis system Electroporator Water purification and ultrapurification system Yeast manipulation cabinet Chemical safety cabinets
Cristallography Laboratory	Thermostatic chamber at 18°C with anaerobic system Cold room at 4°C
Cell culture Laboratories	Mammalian cell culture laboratory with laminar flow cabinets, CO ₂ incubators, inverted microscopes, centrifuge and criogenic containers. Bacteria and yeast cell culture laboratory with orbital shakers and incubators
Centrifugation Laboratory	Preparative centrifuges and ultracentrifuge
Screening Laboratory	Multi-mode microplate reader Fluorescence microplate reader Microplate centrifuge Microplate thermal incubator

Protein Targets Group

Research line: Protein stabilization for biotechnological and medical applications

Contact: [Javier Sancho \(jsancho@unizar.es\)](mailto:jsancho@unizar.es)

TOPIC :	IMI Topic 7
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➤ PREVIOUS EXPERTISE

The *Protein Targets* group at BIFI has gathered over the years a wide, integrative know-how in protein science with a deep, specific expertise in protein stability and stabilization in connection with both biotechnological applications and protein folding diseases.

Protein Targets combines Molecular Biology, Biochemistry, Biophysics and Computational skills to understand the basic principles of protein stability and protein stabilization.

One of the main fields of interest of the group is applying its knowledge in protein stabilization to protein targets with industrial (synthesis, formulation,) diagnostic or therapeutic applications.

➤ POSSIBLE CONTRIBUTIONS

- Protein Stability
- Thermostabilization
- Prediction of mutational effects on protein stability
- Screening and design of stabilizing protein ligands
- Protein Folding
- Misfolding Diseases
- Biotechnological and therapeutic applications

➤ EXPERIENCE IN RESEARCH PROJECTS

The group develops its own software of protein stability analysis to assist in practical protein stabilization projects and has research contracts with companies aiming at stabilising proteins used in industrial environments.

Protein Targets has participated in several projects related to medical applications of protein research on a regional, national and international basis. The group is member or a transnational network called "Protein aggregation in neurodegenerative diseases" from basis science to therapies studying aggregative diseases, such as Alzheimer and Type II diabetes

Protein Targets owns several patents directly related to its protein research. One of them is "Compositions for the treatment of hyperphenylalaninemia" with priority in Norway and extended to the whole European Union, USA, Canada and Japan. Its main use is to stabilize and rescue the activity of an unstable defective human enzyme (PAH) causing a rare disease called phenylketonuria.

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Protein Targets Group
Research line: Protein-based diseases and Experimental drug discovery
[Contact: Javier Sancho \(jsancho@bifi.es\)](mailto:jsancho@bifi.es)

TOPIC :	
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➤ **PREVIOUS EXPERTISE**

The *Protein Targets* group at BIFI has gathered over the years a wide, integrative know-how in protein science with a deep, specific expertise in protein/protein and protein/ligand interaction in connection with protein inhibition and protein stabilization.

Protein Targets combines Molecular Biology, Biochemistry, Biophysics and Computational skills to understand the molecular basis of conformational diseases (both gain of function and loss of function) and of infectious diseases, and uses basic principles of protein/ligand interaction to identify, by means of high throughput screening methods, novel bioactive compounds (antimicrobials, pharmacological chaperons, etc).

Diseases with clear protein targets are a main focus of interest, including *Helicobacter pylori* infection, hepatitis c, phenylketonuria, Alzheimer, type II diabetes, familial hypercholesterolemia or cancer.

➤ **POSSIBLE CONTRIBUTIONS**

- Functional screening of chemical libraries
- Infectious diseases (H. pylori, hepatitis,...)
- Misfolding diseases (Alzheimer, Type II diabetes, Phenylketonuria, Familiar Hypercholesterolemia,...)
- Prediction of mutational effects on protein stability
- Screening and design of protein ligands and inhibitors
- Animal diseases
- Drug Development

➤ **EXPERIENCE IN RESEARCH PROJECTS**

Protein Targets has participated in several projects related to medical applications of protein research on a regional, national and international basis.

The group lead a project funded by Genoma España called “Development of Inhibitors against *H. pylori* infection”, which was focused on designing and testing new antimicrobials against the human pathogen: *H. pylori*.

Also, Protein Targets owns several patents directly related to its protein research. One of them is “Compositions for the treatment of hyperphenylalaninemia” with priority in Norway and extended to the whole European Union, USA, Canada and Japan. Its main use is to rescue a defective human enzyme (PAH) causing a rare disease called phenylketonuria. Another patent is “Use of compounds as inhibitors of the flavodoxin of *Helicobacter*” which protects novel antimicrobials against *Helicobacter pylori* infection, which causes duodenal ulcer and is related to MALT lymphoma and gastric cancer.

The group is member or a transnational network called “Protein aggregation in neurodegenerative diseases: from basis science to therapies” studying aggregative diseases, such as Alzheimer and Type II diabetes.

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Zaragoza Logistics Center

2012-2.3.2-2: Prevention and treatment for HIV/AIDS, malaria and tuberculosis
2012-3.2.1: Improving the organization of health service delivery
2012-3.4-1: Research on Health systems and services research in low and middle income countries
2012-2.3.2-3: Low-cost interventions for disease control in resource poor settings

Contact: Jeanett Bolther, jbolther@zlc.edu.es

Zaragoza Logistics Center (ZLC) is a non-profit research institute established in 2004 by the Government of Aragon in Spain in partnership with **Massachusetts Institute of Technology (MIT)**. It has been created as in Zaragoza (Spain) as an international centre of excellence for **education and research in logistics and supply chain management**. The ZLC is directly linked to the development of PLAZA – the largest logistics park in Europe and it has partnered with the Center for Transportation and Logistics at MIT to form the MIT-Zaragoza International Logistics Program. Furthermore, ZLC is the headquarters of the National **Centre of Excellence in Logistics**, CNC-LOGISTICA (www.cnc-logistica.org), established by the Spanish Ministry of Science and Education, and coordinators of the **Spanish Technology Platform in Logistics, Intermodality and Mobility**, of Logistop (www.logistop.org).

➤ KEYWORDS

personal health systems, design and management of health care operations, the improvement of clinical decision making processes, Global Health Supply Chain, Humanitarian logistics **and** Information systems in the supply chain.

➤ RESEARCH LINES

ZLC has two top-class and international researchers who have expertise on **personal health systems**. Both of these professors' research expertise and interest is on the **design and management of health care operations** and **the improvement of clinical decision making processes** for neurological diseases and their major risk factors. In carrying out their research work, they bring together operations, engineering tool and methods and health informatics with epidemiological techniques. Other research areas of ZLC are the **Global Health Supply Chain, Humanitarian logistics** and **Information systems in the supply chain**.

Prof. Kucukyazici's research expertise and interest is on the design and management of health care systems in order to improve the equity and efficiency of these systems. In carrying out her research work, she brings together operations, engineering tool and methods and health informatics with epidemiological techniques.

Professor Kucukyazici's research expertise in this specific field involves identifying and evaluating policy and programme interventions in order to improve patient flows, and accordingly the equity and efficiency in health systems. In particular, in her recent research (collaborating with Prof. Verter), she proposes a methodological framework to provide a road map to clinicians and system planners in developing and evaluating policies and interventions. The framework models the multiple care-provider patterns of by utilizing operations research methods, and incorporates case-mix bias and care provider clustering. It also provides a comprehensive approach that captures multi-objectives of the policy makers (i.e. reduce inequities between different patient groups and improving overall health outcomes), by which the trade-off between efficiency and equity in the system can be analyzed in details. This framework is applied to the data of 4,000+ stroke patients discharged from an acute care hospital in Quebec in order to test various policies for developing chronic disease management strategies, and designing community-based care. These findings are likely to provide a basis for designing community-based post-stroke care initiatives in Quebec Stroke Network.

Prof. Kucukyazici can contribute on developing quantitative models to identify and evaluate policy and programme interventions.

Professor Verter's research expertise in this field involves improving accessibility to healthcare facilities that provide preventive care services. In particular, he worked on the design of facility networks for breast cancer screening.

Preventive healthcare programs can save lives and contribute to a better quality of life by reducing the need for radical treatments, such as surgery or chemotherapy. Flu shots, blood tests, mammograms, and anti-smoking advice are among the most well-known preventive services. The substantial savings in the costs of diagnosis and therapy as well as the lower capital investment associated with preventive healthcare programs have been recognized for three decades. In contrast with sick people who need urgent medical attention, the potential clientele of preventive healthcare often do not feel the necessity to receive these services and may not participate in preventive programs offered in their region. The achievement of desired participation level continues to be a challenge to many preventive healthcare programs. According to many empirical studies, the convenience of access to the facilities is a crucial factor to influence people's decision to participate.

Recognizing the significance of accessibility, Professor Verter developed a methodology for designing a network of preventive healthcare facilities so as to maximize participation to preventive programs. The number of facilities to be established, the location of each facility, and the capacity at each facility are the main determinants of the configuration of the healthcare facility network. The capacity at each facility is represented by the number of service teams and the total time needed to receive preventive services at a facility is used as a proxy for its accessibility. The total time comprises the time spent during transportation to the facility as well as the time spent at the facility while waiting and receiving services. Typically, the level of participation to a preventive program decreases with the expected total time to receive the services. In order to ensure service quality, however, the preventive healthcare facilities cannot be operated unless the size of their clientele fulfils a minimum workload requirement.

➤ EXPERIENCE IN RESEARCH PROJECTS

Current European Projects

- SECURESCM – Secure supply chain management. FP7-ICT-2007, Topic: 1.4 Secure, dependable and trusted infrastructures.
- Greensupplychain2009 – Effective green supply-chain management technologies in the competitive economic environment with pollution emission trade system. FP7 Marie Curie Action (FP7-PEOPLE-IIF-2009)
- CASSANDRA – Common assessment and analysis of risk in global supply chains. Security Theme project (FP7-SEC-2010-3).
- FLOUE – Facility Location Optimization under disruptions and in an Uncertain Environment. FP7 Marie Curie Action (FP7-PEOPLE-2010-IEF)

