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SUBPROGRAMA RAMON Y CAJAL

CONVOCATORIA 2011

Nombre: **ORTEGA PORCEL, FRANCISCO B** **Referencia:** RYC-2011-09011

Area: Medicina Clínica y Epidemiología

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Titulo:

PHYSICAL ACTIVITY AS A HEALTH PROMOTION STRATEGY IN GENERAL AND TARGETED POPULATIONS

Resumen de la Memoria:

Obesity, diabetes and cardiovascular diseases are major public health concerns in most of western countries, including Spain. There is growing evidence indicating that increasing physical activity and physical fitness levels might benefit most of common chronic pathological conditions. Physical activity refers to any body movement that increase the resting energy expenditure, while fitness is a set of attributes related to a person's ability to perform physical activities that require aerobic fitness, endurance, strength or flexibility.During the last 10 years, the applicant has worked on different national and international project (AVENA, EYHS, HELENA, ALPHA studies) in order to increase the current knowledge about the benefits of physical activity and physical fitness enhancement on obesity and cardiovascular disease risk factors. This work has been focused mainly on children and adolescents, based on the belief that health promotion should start as early as possible, before the clinical signs of disease appear, usually in adulthood. Most recently, the applicant has had the opportunity to collaborate with world leading scientists from USA, and developed different research topic related to physical activity, fitness and health outcomes in adult population (ACLS study, a follow-up study conducted on more than 40,000 adults). In addition, the applicant has recently applied his epidemiological knowledge and skills to further investigate the role that physical activity and fitness have on a relatively new (yet frequent) disease with rather unknown aetiology, fibromyalgia.With some exceptions, the work carried out by the applicant so far has been mainly focused on cross-sectional data. The goal of the applicant for the upcoming years is to move forward in the research evidence scale, by focusing his work on longitudinal studies and randomized controlled trials. In this context, the future research lines that the applicant will develop are: 1) using data from a 3, 6 and 10 years follow-up study in Spanish, Swedish and Estonian young people, respectively, to identify lifestyle factors that predict the development of obesity and related diseases from childhood to young adulthood (recently funded I+D+I project (UP 2) based on a previous pilot study coordinated by the applicant (EDUFIT study), to design, get funding, and carry out a school-based multicenter randomized controlled trial to determine the effect of increasing physical education on obesity and other risk factors; 3) to examine the relationship of physical activity and fitness with cardiovascular disease events and mortality (ACLS study); 4) to determine the potential benefits of physical activity on fibromyalgia symptomatology (recently funded I+D+I project (2011-13).All these research lines have a common and central line, the study of potential benefits of physical activity on health in different populations: children/adolescents, healthy adults and fibromyalgia patients. This large amount of work will be successfully carried out thanks to the active national and international networks developed in the last years, during the implementation of the multicenter projects mentioned above. The knowledge derived from this research will contribute to design and implement more successful health promotion strategies.

Resumen del Curriculum Vitae:

The applicant graduated in Sport Sciences and Physical Activity in 2002, at the University of Granada. During the last 2 years of his degree, the applicant volunteered to participate in the data collection of a National observational study (funded by the FIS), named the AVENA study. After this project, the applicant has actively participated in a number of major international projects: HELENA, EYHS, ALPHA, ACLS, among others. The applicant has gone through the different steps proposed by the Spanish Ministry of Education (MEC) to became part of the Scientific and University system in Spain. In the last year of his degree (2001/2), the applicant got a starting-up research grant (Beca de Colaboración, MEC) at the School of Medicine, Granada. Immediately after his graduation in Sport Sciences, the applicant started his PhD Thesis in the program of Exercise Physiology at the School of Medicine. The beginning of his PhD studies were supported by the Government with 2 consecutive grants from the National Sport Council (Consejo Superior de Deportes, CSD) and in 2005 the applicant got the National training grant for PhD students (Beca FPU, MEC). The applicant did 2 research stays at Karolinska Institutet as a PhD student (4-5 months each), where he officially started a separate PhD Thesis. In 2008, the applicant completed his PhD Thesis in Exercise Physiology at the University of Granada (composed of 9 published papers from the AVENA and the HELENA studies, 8 as first author), and also his PhD Thesis in Medical Sciences at the Karolinska Institutet (composed of 5 published papers as first author from the EYHS). In 2009, the applicant got the National post-doc grant (beca post-doctoral del MEC) to stay at Karolinska Institutet for 2 years. From 2008 to date, the applicant did 3 research stays at the University of South Carolina (4 months + 2 visits of 1 month each), to work on the ACLS study, a world-famous follow-up study in epidemiology.The applicant has coordinated his own projects (see CV) and supervised a number students (4 PhD students, 2 finished and 2 in process). The applicant has accumulated experience and developed skills in: 1) leadership to conduct collaborating projects at both national and international level; 2) scientific independency and capacity to develop an own group; 3) networking; 4) data management and statistical analysis; 5) drafting and publishing scientific papers in high impact journals; 6) presenting scientific findings in meetings/congresses over the world. The applicant has published 115 papers in journals indexed in JCR-ISI, being 60% of papers published in the 1st quartile of their field and nearly 90% in either the 1st or 2nd quartile. The applicant is first, second or last author in more than half of these papers. The applicant has published, as a first author, in high impact journals (e.g. JACI, IF=9.17) and has highly cited papers (e.g. a paper published in 2008 has already got 79 citations; h-index=16). The accumulated impact factor is 336 and the median impact factor is 2.5, which is above the median impact factor of all the areas related. He has also got 3 scientific awards (see CV). By the current submission, the applicant aims to come back to the Spanish University and to implement and share with his future workmates and students all the experiences, knowledge and skills accumulated during these years.

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SUBPROGRAMA RAMON Y CAJAL

CONVOCATORIA 2011

Nombre: **DE CID IBEAS, RAFAEL** **Referencia:** RYC-2011-07822

Area: Medicina Clínica y Epidemiología

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Titulo:

Personalized medicine:Genetic and genomic characterization of a healthy population by sequencing analysis

Resumen de la Memoria:

The rapid advances in understanding the genetic basis of complex human diseases, as well the advances in genomics research make it imperative the development and application of new strategies to apply to the field of public health. In continuation with my previous research work, this line of research proposes the study of the genetic and genomic variability in the Spanish human population, having as final objective the delineation of the strategy for its use and application into the field of tailored medicine. Large-scale array-and sequence-based studies are now possible, allowing the genomic characterization of whole genome for large populations. However, the set up of a sample collection and its rigorous linkage to comprehensive and long-term clinical follow-up data from repository public health lacks in most studies, and has become essential for undergoing this research. For this goal, I firstly aim the creation of a dynamic database that combines both clinical and genomic information in a small representative population of the Spanish Population, trough the integration of electronic medical records and genomic information. This longitudinal study shall consist of individuals recruited from Spanish healthy general population, submitted to periodic health follow-up surveys. Furthermore, other groups of patients who have been diagnosed for complex disorders (cancer and other frequent pathologies in Spanish population) and for which a periodic follow-up will is available will be analyzed. The research will focus on the definition of the genetic and genomic variability, mainly by the depth examination of the variability of all the coding regions. Even if coding represents a small fraction of the Human genome, it represents the source of most of the human mutations detected and thus the priority of research in the first phase of the study. Next Generation Sequencing (NGS) techniques and specifically Human Exome Analysis will be used to analyze genomic variability. This project will require the development of new tools of genomic annotation that allows the systematic and accurate identification of inter individual variability present, expected to be at low frequency in human populations, allowing the identification of specific molecular alterations. We will analyze this genomic variability to predict genetic signatures, related to the disease and differential specific response to drug treatments, leading to the optimization of individual treatment or implementing better therapies.

Resumen del Curriculum Vitae:

I obtained a degree in Biology and PhD in Biology by the University of Barcelona (2003). Since 1997 my researches focus on genetic and genomic analysis of complex human diseases. My research works aims to understand the mechanisms underlying human chronic diseases. I have done my PhD studies at Centre of Molecular and Medical Genetics-IRO (Barcelona, Spain), then I have had a seven year PhD researcher experience at (1) Centre of Genomic Regulation (2003-2007, Barcelona, Spain), (2) Centre national de Genotypage (2007-2009, Paris, France) and (3) Genethon (2009-actual, Paris, France). I developed my thesis project on the study of complex diseases (asthma and psoriasis) under the direction of C. Lazaro and X. Estivill (1998-2003), for which I create a biobank of psoriasis DNA samples. As result of the thesis, ten papers were generated (six issued directly from the thesis works, three out them as the first author, and two international collaborations papers). During my PhD I started a new research line on genomic-wide studies of immune diseases by CGH microarrays and a paper as first-author in Nature Genetics in January 2009 (IF: 34.284) summarizes the main findings. I supervised and directed a thesis project (Gene x Environment interaction and asthma; 2004-2009), and I have been the principal investigator of a 3-year FISS funded research project (2004-2007), both projects aiming the understanding the role of the genes on the environmental effects in genetic human complex conditions (ten papers were generated, for three I am the last author). I start collaborations with the Centre for Research in Environmental Epidemiology (Barcelona, Spain) leading national and international epidemiological projects (ECHRS, INMA, SAPALDIA) having huge data on environmental exposures and standardized outcomes. As part of my interest in complex conditions I studied the role of common genetic variation related to several common disorders, some of the significant discoveries are the identification of pharmacogenomic biomarkers for drug-replacement treatments, and the identified of common variants of a classical mendelian gene involved in monogenic disease, as risk factors for common chronic disorders. I also collaborate dynamically in the set up of a high-throughput genotyping facility for the study of complex disorders and for pharmacogenomic research (National Genotyping Centre; www.cegen.org). I was involved in the planning of laboratory installations, staff selection I execute several tasks as programme manager; giving support in design and interpretation of the genotyping project. Then, at CNG, I have use linkage regions signals found in a GW study for Psoriasis to characterize structural variants. An international metanalysis study was launch from these works. Nowadays, at Genethon, I¿m the coordinator of a specific work package in an international scientific project funded by the European Union (NMDCHIP project), leading the research for gene discovery in Neuromuscular disorders. I developed and use high-throughput DNA technology for genomic analysis (aCGH and NGS techniques), to uncover complex inheritance patterns of patients attaints of Neuromuscular disorders, for which at least 30% lack of genetic signature. As the result of my research activity I have published 47 papers (accumulated impact factor of 319.86, being first author from 6 (four Q1, accumulated IF of 52.49) and last author of 3 (two Q1, accumulated IF of 14.29).

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CONVOCATORIA 2011

Nombre: **PEREZ DE DIEGO, REBECA** **Referencia:** RYC-2011-07597

Area: Medicina Clínica y Epidemiología

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Titulo:

Progenitores de linfocitos B-1 en sangre de adultos

Resumen de la Memoria:

Mouse hematopoietic stem cells (SC) create antibody (Ig)-producing B-lymphocytes through three development pathways, originating distinct B-1a, B-1b and B-2-restricted progenitors. However, prior research in humans only detected common lymphoid progenitors (CLP), the B-2 pathway homolog. Such proposed evolutionary variation would make medical translation of B-1 lineages role impossible. The latter is relevant because B-1 cells have distinct non-redundant functions: they are responsible for the production of most natural antibodies, and are implicated in defence against lethal microorganisms and homeostatic clearance of damaged body components that fail in prevalent degenerative diseases in the elder, such as atherosclerosis, regulate autoimmunity and cause prevalent cancers.Notably, the recent discovery of human B-1 progenitors in neonates revisited the above paradigm. Their Pax-5+CD34+CD19+CD10- phenotype, genotype, and precursor-product relationships, which are all distinct from B-2/CLP specified progenitors, were defined. It makes now possible to characterize adult human B-1a and B-1b progenitors, putative prenatal/neonatal counterpart differences, and B-1 lineages implication in disease. The aims are relevant because fetal and adult-type B-1 cells, and putative SC loss of potential to create them with age, are different in mice. None of those issues has been investigated in human.I first propose the phenotypic, genotypic and functional precursor-product characterization in adult B-1a and B-1b lineage progenitors. Next, the proposed research will address the potential differences between neonatal and adult SC in their capacity to generate non-convectional (B-1a and B-1b) B-lineages, in a unique biological model to study human SC aging in peripheral blood, which is a current source of SC in transplants and gene therapy. Finally, we will focus on translational research. On the one hand, limited numbers of donor SC severely limit the success of regenerative medicine protocols, and laboratory research. We will investigate combinations of protocols to improve self-renewal of SC and expand them ex vivo. On the other hand, the improved knowledge in B-1 cells, and expansion of SC/progenitors will be applied to study common variable immunodeficiency disorders (CVID), primary immunodeficiencies with abnormalities in immune B cell maturation that result in hypogammaglobulinemia and decreased ability to produce specific antibodies, in which B-1 lineage role has not been addressed in humans but is admittedly key in mouse.

Resumen del Curriculum Vitae:

Previous to finish my Bachelor¿s degree, I started to work at the Department of Biochemistry and Molecular Biology, Alcalá University (Madrid, Spain). I was financed by the Ministry of Education to study immune system deregulation by the effect of environmental contaminants. The results of this work were reported in two congresses. I finished Bachelor¿s degree with the qualification of extraordinary prize of Degree in Chemistry at Alcalá University.I developed my PhD at the Immunology Unit, Hospital ¿la Paz¿, Autónoma University of Madrid (Madrid, Spain), working in a project supported by Fondo de Investigacion Sanitaria directed by M. C. Garcia Rodriguez, MD, PhD. It was focused on the identification of the molecular gene defect in congenital agammaglobulinemias and study of its functional and clinical consequences. The results were published in three papers in journals within the 25% higher impact factor in immunology. During these years I moved to collaborate in several internationally recognized centres as the Laboratory of Immunogenetics, NIAID-National Institutes of Health (NIH) (Rockville, MD, USA) and Spanish National Cancer Research Center (CNIO) (Madrid, Spain). The results of these collaborations were reported in two papers. Moreover I presented my work in seven congresses, and I finished my PhD with the qualification of extraordinary prize of Doctorate in Biochemistry by Autónoma University.Continuing with the collaboration started at CNIO during my PhD, I decided to move there as postdoctoral researcher at the Signal Transduction Group, directed by J. Bravo, PhD. I worked during two years in an European project supported by Sixth EU framework Programme for Research and Technological Development. The results of this work were published in one paper and one congress. This postdoctoral in basic research gave me a broad vision about research and a background in proteins that it has been extremely useful to continue my career in immunology. I moved to do my second postdoctoral at the Laboratory of Human Genetics of Infectious Diseases, Paris René Descartes University (Paris, France). The work was focused to study the susceptibility to herpes simplex virus encephalitis and it was supported by several projects directed by Prof. J. L. Casanova. During this postdoctoral, I developed an independent project in collaboration with Prof. J.Godovac-Zimmermann. In order to realize this new project I moved to the Molecular Cell Dynamics, University College of London (London, UK) to learn and use new proteomics techniques. The results of this postdoctoral have been published in two journals within the 25% higher impact factor in immunology and biochemical research methods, and they have been presented in two national congresses, four international congresses and four seminars. At present, I have obtained a public and competitive fellowship, which is specifically oriented to integrate researches under Ramón y Cajal contracts. The work is focused on the study of adult human B cell progenitors under the supervision of A. de la Hera, MD, PhD at the Department of Medicine, Alcalá University. The scientific production during three years as PhD student and five years as postdoctoral researcher has been twenty-one communications in congresses and seminars and eight papers (seven of them as first author and four of them as corresponding author).

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SUBPROGRAMA RAMON Y CAJAL

CONVOCATORIA 2011

Nombre: **HERNANDEZ SAEZ, CARLOS** **Referencia:** RYC-2011-09571

Area: Medicina Clínica y Epidemiología

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Titulo:

IDENTIFICATION OF NEW TARGETS INVOLVED IN THE HAART-ASSOCIATED METABOLIC SYNDROME IN THE LIVER

Resumen de la Memoria:

Introduction of antiretroviral therapy has improved the survival of patients infected with HIV-1. Treatment usually consists of a combination of at least 3 different drugs, which is known as ¿Highly-Active Anti-Retroviral Therapy¿ (HAART). However, chronic HAART treatment leads to the development of metabolic disorders, such as lipodistrophy, dislipidemia, insulin resistance and diabetes, called ¿HAART-associated metabolic syndrome¿ (HAMS). The aim of this project will be to study the effect of antiretroviral drugs in hepatic lipid metabolism and the mechanisms leading to the development of HAMS in the liver. I propose the following specific aims: (1) To set up in vivo animal models to analyze several metabolic parameters in the liver and in the plasma after treatment with single or a combination of antiretroviral drugs. Other tissues will be also considered (brown adipose tissue, muscle). (2) To identify candidate genes involved in the development of metabolic disorders in the liver taking advantage of animal models from aim 1. I will perform general screenings (DNA microarrays) and investigate the activation of specific pathways as well as transcription factors related with hepatic lipid metabolism. (3) To study the role of candidate hits from the aim 2 in HAMS. In these experiments I will use cellular models of gain-of-function or loss-of-function to establish their importance. To study their regulation by antiretroviral therapy could be also relevant. When possible I will use mouse models to unravel the role of candidate hits in the development of HAMS. (4) To correlate the results obtained from these studies with clinical data from patients with metabolic disorders and/or patients under antiretroviral treatment. The impact of AIDS in the society and the severity of the epidemic promoted the use of antiretroviral drugs very quickly after development. Nowadays we need to deal with several side effects for the population of these chronically treated patients. This project would help us to discover new pathways causing HAMS and to define new and better therapeutical approaches.

Resumen del Curriculum Vitae:

Licenciado en Ciencias Químicas por la Universidad de Valencia (1997) y Diplomado en Estudios Avanzados en Farmacología (1999-2001). Comencé a realizar la Tesis Doctoral en 1999 en el Departamento de Farmacología de la Facultad de Medicina de Valencia bajo la dirección de la Dra. M. Dolores Barrachina, donde estudiamos la expresión de las óxido nítrico sintasas en el tracto gastrointestinal. Sin embargo, fruto de una colaboración, posteriormente me incorporé al Centro Nacional de Investigaciones Cardiovasculares bajo la dirección del Dr. Jesús Mateo, donde desarrollé la investigación que dio lugar a mi Tesis Doctoral (Noviembre 2005), sobre la regulación por el óxido nítrico del factor de transcripción inducible por hipoxia (HIF-1). Una vez doctorado continué trabajando junto a la Dra. Barrachina en Valencia, donde comenzamos a investigar el papel de HIF-1 en la recuperación del daño gástrico producido por la aspirina. En noviembre de 2006 me incorporé al laboratorio del Dr. Jiandie Lin en el Life Sciences Institute de la Universidad de Michigan (USA) en calidad de investigador post-doctoral, donde he estado trabajando hasta enero de 2011. Durante esta estancia he estudiado el papel de la familia de coactivadores PGC-1, y especialmente PGC-1β, en el metabolismo lipídico hepático. En febrero de 2011 me he incorporado a la Fundación de Investigación del Hospital Dr. Peset de Valencia con un contrato de Investigador Doctor. A lo largo de estos años he participado en varios proyectos de investigación en distintos centros, que han dado lugar por el momento a 14 artículos de investigación, así como numerosas presentaciones a congresos tanto nacionales como internacionales. Además, recientemente escribí junto al Dr. Lin un comentario sobre otro artículo en la revista Cell Metabolism y en mi etapa post-doctoral en Valencia codirigí el trabajo de investigación necesario para la obtención del Diploma de Estudios Avanzados de dos doctorandas del laboratorio. Durante mi carrera científica he ido adquiriendo una gran experiencia en el estudio de la regulación transcripcional y su impacto en procesos fisiológicos que se ha visto acrecentada en los últimos años con mi estancia postdoctoral en la Universidad de Michigan.

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SUBPROGRAMA RAMON Y CAJAL

CONVOCATORIA 2011

Nombre: **TOMAS MESTRES, MARTA** **Referencia:** RYC-2011-07814

Area: Medicina Clínica y Epidemiología

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Titulo:

Epigenomics and cardiovascular disease: identification and analysis of the predictive value of these new biomarkers (EpigenCVD)

Resumen de la Memoria:

Coronary heart disease (CHD) is still the primary cause of death in Western countries. Genome-wide association studies (GWAS) have contributed to the knowledge of CHD architecture but a substantial part of the heritability of this trait remains still to be determined. Other potential factors, closer to phenotype than genotype, may explain CHD risk susceptibility determining gene expression regulation and their translation into transcriptome and finally proteome. Among these factors epigenetic changes may play a relevant role in CHD. These phenomena may not only improve understanding of CHD etiopathogeny, but also provide new biomarkers for clinical use. Since numerous regions that are variably methylated across individuals appear to be stable over time within individuals, ¿personalized¿ epigenetic signatures may provide individual disease risk information. However, very little is known on epigenomic phenomena. In consequence, the International Human Epigenome Consortium aims to map human epigenomes, mainly from healthy tissues, for further comparison with diseased tissues. I will take advantage of these new findings and data for my future in silico analyses. Epigenetic changes may play a role in CHD. In human and animal studies, global or repetitive DNA element methylation was lower in individuals with atherosclerotic disease, both in atherosclerotic lesions and in blood, or with high CHD risk. Methylation changes also occur at the promoter of atherosclerosis-related genes.Nevertheless, many questions remain unanswered, such as the epigenetics role in CHD event incidence. I hypothesize that epigenetic or related protein biomarkers in peripheral blood are associated with CHD risk and can be used as diagnostic markers for CHD. My main goal is to study whether human epigenetic modifications in a collection of genes, involved in CHD-associated metabolic pathways or related to CHD by GWAS, differs between healthy subjects and those who will present CHD, and concurs with differences in gene expression and the corresponding protein concentration in plasma or serum. My long-term aim is to evaluate whether adding this information into cardiovascular risk functions improves predictive capacity and warrants its use as a biomarker in the population. This approach takes advantage of my extensive experience with metrics that assess risk functions performance. I plan to determine epigenetic modifications in large epidemiology studies, with samples from easily available tissues, such as blood. Therefore, I have explored in silico the DNA methylation pattern of blood samples from healthy donors with public available data.Besides DNA methylation, I plan future studies of other epigenetic marks such as telomere length and nucleosome positioning and comparison of variations over time in the CHD pattern of epigenetic markers. This research line will open new horizons to study epigenome roles in classical risk factors (e.g., lipid profile, hypertension, smoking) and protective factors (e.g., physical activity, Mediterranean diet, treatment), and may identify new CHD risk factors.

Resumen del Curriculum Vitae:

My research career in Spain, Italy and USA has focused mainly on identifying genetic factors associated with coronary heart disease (CHD), related phenotypes, or arrhythmogenic diseases such as long QT syndrome (LQTS) by various approaches: 1stSNP genotyping, 2nd gene sequencing, 3rd genome-wide association studies (GWAS) and high-throughput technologies.I received my Biochemistry Degree at the University of Barcelona (Spain). I began my PhD in IMIM within the Pompeu Fabra University (Barcelona, Spain) doctoral programme, working on genetic and environmental risk factors and their cardiovascular impact, and intermediate phenotypes. I received my PhD in 2003 with 15 publications (three of them as a first author) in journals such as Arterioscler Thromb Vasc Biol, J Clin Endocr Metab, Atherosclerosis. As part of my PhD training, I visited Tufts University, USA (Prof. Ordovas) as a visiting scholar.During the first postdoctoral period in Barcelona, I worked with the Heracles network (www.redheracles.net) studying the role of ion channel gene variants on hypertension and cardiovascular risk, producing 6 publications (two of them as first author) in journals such as J Clin Invest, Circ Res, and Clin Chem. As a co-inventor, I participated in a HERACLES patent application to protect the BK channel finding, which were reported in the national media; other researchers support our findings. During that period I collaborated in several parallel association studies of candidate genes and cardiovascular risk (RECAVA network), with another 6 publications as a coauthor.In my second postdoctoral period in Italy, I had access to the world¿s largest collection of LQTS patients. I provided the first evidence of the role of NOS1AP variants, already related to cardiac repolarization in the general population by GWAS, in increasing risk of cardiac event in LQTS, and generated a new risk chart for these patients that better supports treatment decisions, with a publication in J Am Coll Cardiol as first author. Back in Spain, I collaborated in 2 international studies on GWAS gene variant role in different pathologies (stroke, steaosis) and with 2 papers in Ann Neurol and PLoS Genetics. My main research goal in the last 2 years has been to assess whether genetic markers recently associated with CHD in GWAS improve the prediction power of classical CHD risk functions (one paper published, another submitted as first author). GWAS have contributed to the knowledge of CHD architecture but a substantial part of the heritability of this trait remains still to be determined. Other potential factors explaining CHD risk broadly expanded my research interest into gene expression regulation, such as epigenetics modifications and their translation into transcriptomics and finally proteomics. These phenomena may not only improve the knowledge on the CHD etiopathogeny, but also provide new biomarkers of clinical value. This research on epigenomics, transcriptomics and proteomics related to CHD builds upon my experience with large sample volumes, team management skills, familiarity with multidisciplinary teamwork, and demonstrated ability to establish productive collaborations, attract funding and design new strategies. I have participated in international consortia and symposia, in technology transfer, and as PI of the two GWAS cohorts follow-up.