MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **PLANAVILA PORTA, ANA**
Referencia: RYC-2014-16572
Área Científica: Biomedicina
Correo Electrónico: annaplanavila@hotmail.com

Título:

Identification and characterization of new cardiomyokines: a new approach for the treatment and prognosis of cardiac diesease

Resumen de la Memoria:

Cardiac hypertrophy and subsequent progression to heart failure represents a major cause of morbidity and mortality in western countries and remains a critical health problem. Therefore, the identification of novel protective agents is of crucial importance for improving preventive and therapeutic strategies. The term cardiomyokine has recently emerged to describe proteins secreted from the heart that have autocrine, paracrine and/or endocrine functions crucial for the maintenance of cardiac function. Because of their extracellular localization, secreted cardiomyokines, show promise as therapeutic targets or agents and could have important prognostic implications as potential biomarkers for cardiac disorders. Recently, we have identified for the first time the endocrine factor fibroblast growth factor-21 (FGF21) as a new cardiomyokine, expressed and secreted by the heart with protective autocrine functions. Moreover, the circulating levels of FGF21 have been associated to cardiac disease in humans pointing out this factor as a new biomarker for cardiac disorders. FGF21 is under the transcriptional control of Sirtuin-1 (Sirt1) and PPARalpha, both largely involved in the prevention of cardiac diseases. Accordingly, the main research line of this proposal is to identify new cardiomyokines and to elucidate their effects in cardiac disease models in order to identify new therapeutic agents and/or new clinical biomarkers for cardiac disorders.
To obtain proof of principle we will divide the study in three different stages:
In the first stage we will identify new potential cardiomyokines differently expressed in response to cardiac hypertrophy in wild-type and Sirt1-null mice by bioinformatics analysis. From the selected new cardiomyokines, in the second stage, we will study their effects in vitro, primary culture of neonatal cardiomyocytes, through gain [adenovirus overexpression/activators] and loss of function approaches [inhibitors], and in vivo through the study of mice with intravenous injection of adenoviral vectors overexpressing the selected cardiomyokines (AAV-9-CMV-heart specifics). Furthermore, we will perform the same kind of experiments inducing cardiac hypertrophy in vitro (phenylephrine) or in vivo (isoproterenol injection). Both approaches will be undertaken essentially in parallel, and information coming from both will establish a reciprocal cross-talk informative for the progression of experiments. Finally in the last stage, we will study the plasma levels of the selected cardiomyokines in patients suffering from cardiovascular disease in order to determine the viability of the cardiomyokine as a potential biomarker for cardiac damage. These studies will provide insight into prognostic and preventive mechanisms in cardiac disease.

Resumen del Currículum Vitae:

My research career has been mainly focused on the study of the molecular mechanism involved in cardiac disease, especially during cardiac hypertrophy development. My research career started in 2001 with the realization of the Master Degree in Pharmaceutical Sciences (Faculty of Pharmacy, University of Barcelona) under supervision of Manuel Vázquez-Carrera. Mark: Excellent with distinction. Directly related to this study, I published 1 paper. After finishing my Master Degree I performed my Ph.D. Degree (2002-2005) in Pharmaceutical Sciences (Faculty of Pharmacy, University of Barcelona) entitle: "New mechanisms involved in the development of insulin resistance and cardiac hypertrophy". Supervisor: Manuel Vázquez-Carrera, Ph.D. April, 2005. Mark: Excellent Cum Laude. Extraordinary PhD Award 2006. Directly related with my PhD I published 9 papers in which I was the first author. Eight of them were published in journals within the 25% higher impact factor in its knowledge area. I was awarded with a Post-Doctoral MEC/Fullbright fellowship (Ministerio de Educación y Ciencia de España) to perform my Post-Doctoral stay from 01/10/2005-30/11/2007 at Maastricht University. Cardiovascular Research Institute Maastricht (CARIM). Maastricht. The Netherlands. Title of the project: Role of Perosixome Proliferator-Activated Receptors (PPARs) during cardiac damage. Supervisor: Marc van Bilsen. From this project we published two papers and a chapter of a book. After my post-dococtal stay abroad I obtained a competitive Post-Doctoral contract Sara Borrell (2008-2010), Instituto de Salud Carlos III. I started a completely new research line at Francesc Villarroya's lab (Faculty of Biology, Universitat de Barcelona) focused on the study of the molecular mechanisms involved in the development of cardiac disease. This line, fully developed under my initiative and leadership, has provided results of extraordinary importance and highest international relief. Also I have developed successful partnerships with national (Hospital Clínic, IDIBAPs, CBATEG) and international groups (group of Dr. Vinciguerra, London) reflected by numerous international publications of high impact such as Nature Communications, Cardiovascular Research, JBC,"(5 original articles in which I am the corresponding author of 8 published articles, 2 invited reviews and a chapter of a book). Moreover, I have participated in many international congresses and I have been invited to give several talks related to my research line. Furthermore, I have been the supervisor of 2 Master Degree and since August 2010, I am supervisor of the Ph.D. Thesis of Ibon Redondo Angulo entitled "Role of Sirtuins in the transcriptional control of metabolism". Since 2012 I am participating actively (Research contract) in the European Project (Cooperation

Health. 7th Research Framework Programme (FP7). Ref: HEALTH-F2-2011-277713) entitled "Development of novel treatment strategies based on knowledge of cellular dysfunction in diabetes (BetaBat)". At present, I am an Associate Professor from the Biochemistry Department (University of Barcelona). Since 2008, I have been also performing official teaching at the Faculty of Biology (Universitat de Barcelona) in subjects of Bachelor's and Master's degree.

MINISTERIO
DE ECONOMÍA
Y COMPETITIVIDAD

SECRETARÍA DE ESTADO
DE INVESTIGACIÓN
DESARROLLO E INNOVACIÓN

SECRETARÍA GENERAL
DE CIENCIA, TECNOLOGÍA
E INNOVACIÓN

DIRECCIÓN GENERAL
DE INVESTIGACIÓN
CIENTÍFICA Y TÉCNICA

SUBDIRECCIÓN GENERAL
DE RECURSOS HUMANOS
PARA LA INVESTIGACIÓN

AYUDAS RAMÓN Y CAJAL
CONVOCATORIA 2014

Turno de acceso general

Nombre: **GONZALEZ GARCIA, INMACULADA**
Referencia: RYC-2014-16507
Área Científica: Biología Fundamental y de Sistemas
Correo Electrónico: inma.gonzalez@igh.cnrs.fr

Título:

Dissecting the different roles of PcG proteins

Resumen de la Memoria:

Since the beginning of my scientific career I was particularly interested in epigenetic mechanisms regulating gene expression and driving cell fate decisions during developmental. The subject of my thesis was the study of the function of the dRYBP gene in Drosophila melanogaster. My thesis project focused on understanding the function of dRYBP during development and its role in the epigenetic regulation mediated by the Polycomb and trithorax genes. Moreover, I studied the roles of dRYBP in apoptosis and the relation between the apoptosis induced by dRYBP and PcG/trxG proteins. Finally, I analyzed the role of the PcG protein Polyhomeotic (PH) in cancer development. During my Post Doc in the laboratory of Dr. Giacomo Cavalli (IGH, CNRS UPR1142, Montpellier), I used a genome wide RNAi screen to identify and characterize the function of the SUMOylation pathway in PcG nuclear organization and function. Currently, I am working in the laboratory of Dr. de Luco (IGH, CNRS UPR1142, Montpellier) trying to extend our knowledge on how chromatin and long non-coding RNAs regulate alternative splicing. I identified a lncRNAs involved in the establishment of the chromatin signatures that regulates cell-specific splicing patterns .

Resumen del Currículum Vitae:

Since the beginning of my scientific career I was particularly interested in epigenetic mechanisms regulating genome function. Epigenetic maintenance of gene expression states implies that the heritable state of gene activity does not require the continuous presence of the initiating signal nor does it involve changes in the DNA sequence. This epigenetic information is stored either as chemical modifications to cytosine bases of the DNA or as modifications to histone proteins that package and condense eukaryotic genomes. The importance of epigenetic processes, especially those resulting in the silencing of key regulatory genes have been reinforced after discovering their roles in dysregulation of normal growth and cancer development.

My career advancements or choices were largely driven by the will to get a better understanding in epigenetic processes, in particular in the function of Polycomb group (PcG) proteins in epigenetic gene regulation. PcG proteins have been identified as part of an epigenetic cellular memory system that maintains cell identity during development. Towards the end of my university studies, I decided to do my PhD in the laboratory of Dr. Ana Busturia (Centro de Biología Molecular in Madrid, Spain), who had a long standing experience in the mechanisms of transcriptional silencing mediated by PcG-proteins. I studied the function of dRYBP and showed that it can function as a Polycomb-dependent transcriptional repressor in the model system Drosophila melanogaster. This work allowed me to gain expertise in Drosophila genetics, and the study of epigenetic mechanisms regulating developmental processes.

After my PhD work, an EMBO short term fellowship allowed me to visit the laboratory of Dr. Giacomo Cavalli, a leading scientist in the field of nuclear organization and PcG function. I got introduced into genome wide mapping techniques, and I reinforced my interest into PcG protein function and genome organization. Therefore, I decided to do my Post Doc in the laboratory of Dr. Giacomo Cavalli (IGH, CNRS UPR1142, Montpellier), where I used a genome wide RNAi screen to identify and characterize the function of the SUMOylation pathway in PcG nuclear organization and function. During this work I obtained expertise in genome wide techniques like ChIP-seq or HiC and gained also expertise in biochemistry, microscopy imaging technologies and cell culture methods.

In July 2013 I moved to the laboratory of Dr. de Luco (IGH, CNRS UPR1142, Montpellier), who recently demonstrated an unexpected function of epigenetics in alternative splicing regulation. In my current work I try to extend our knowledge on how chromatin/epigenetics, PcG proteins and non-coding RNAs (lncRNA) regulate alternative splicing. During the last year in my current laboratory I acquired a lot experience in working with processing and purification of mRNA and with tools to characterize lncRNA like CHIRP (Chromatin Isolation by RNA Purification) to identify the genomic localization of a lncRNA.

The multitude of expertise and working skills in chromatin and developmental biology, epigenetics and genome organization acquired during my scientific career allows me now to submit this application.