List of Researchers and Research Lines

1: Scientist/Supervisor: **Alicia García Arroyo:**
Research line: **Cellular and molecular players in inflammation-induced angiogenesis** Summary: Angiogenesis, the formation of new vessels from pre-existing ones, is essential for organ development but also for promotion and resolution of inflammatory responses. This process requires fine-tuned orchestration of cell-cell interactions together with coordination of defined molecular pathways such as membrane-type matrix metalloproteinases (MT-MMPs) and their substrates. We will use ex vivo and in vivo assays in genetically modified mice, mathematical and proteomics approaches, and state-of-the-art confocal microscopy and imaging analysis to elucidate molecular and cellular partners relevant to inflammation-induced angiogenesis.

2: Scientist/Supervisor: **Andrés Hidalgo**
Research Line: **Immune regulation of a stem cell niche**
Summary: A niche is a functional unit composed of cells and molecules that preserves stem cells and regulates their function throughout life. In the bone marrow, hematopoietic stem cells are regulated by multiple cells characterized by the production of the chemokine CXCL12. Using CXCL12-GFP reporter mice and live imaging, we have observed that the physiology of these niches is controlled by immune cells: neutrophils and macrophages. We wish to understand how this modulation takes place and how these innate immune leukocytes impact the physiology of stem cells.

3: Scientist/Supervisor: **David Filgueiras**
Research Line: **Magnetic Resonance Imaging-based 3D Modeling of Ventricular Substrate for Accurate Characterization of In Vivo Scar-Related Monomorphic Ventricular Tachycardia: Translational Study From Pigs to Humans.**
Summary: Radiofrequency catheter ablation has become the first line treatment for a number of cardiac arrhythmias including ventricular reentrant tachycardia (VT). Precise information about the arrhythmogenic substrate and its functional behavior during the ablation procedure may improve the success of ablation of ischemic scar-related VTs. The objective of this proposal is to generate realistic and interactive, Magnetic Resonance Imaging (MRI)-based 3D electro-anatomical models of the ventricles, which will be used to predict successful ablation strategies aimed at terminating VT.

4: Scientist/Supervisor: **David Filgueiras**
Research Line: **Biological and Computational Characterization of Mechanisms Underlying Paroxysmal and Persistent Atrial Fibrillation in a Pig Model that Resembles Clinical Progression of the Arrhythmia.**Summary: Atrial Fibrillation (AF) is the most common sustained cardiac arrhythmia. Some patients suffer paroxysmal AF indefinitely, but a large proportion progress to persistent or permanent AF. However, the precise mechanisms have not been established. The objective of this proposal is to test the hypothesis that sustained atrial fibrillation triggers an inflammatory response that activates signaling pathways which are common to the electrical and structural remodeling leading to sustained reentry with increased complexity and AF perpetuation.

5: Scientist/Supervisor: **David Sancho**
Research Line: **Immune myeloid receptors sensing tissue damage in inflammation and immunity.**
Summary: Tissue damage sensing modulates inflammation and immunity. We are analyzing the role of specific myeloid receptors sensing tissue damage in models of infection, autoimmunity, inflammation and cancer. We use a combination of approaches at the cellular, biochemical and in vivo level, including analysis of animals deficient on the receptors at the physiological level, transcriptomic analysis, and in vivo imaging.The student will learn many techniques working in vitro (cell culture, molecular biology, biochemistry, flow cytometry and Immunology techniques) and will learn about the in vivo models that we are developing in the lab. The student will also be intellectually involved in the discussions and implications of this work for the treatment of these diseases and the design of better vaccines. http://www.cnic.es/es/inflamacion/inmunobiologia/index.php

6: Scientist/Supervisor: **David Sancho**
Research Line: **Sensing infection and tissue damage affects myeloid cell metabolic plasticity.**
Summary: The student will help to explore how sensing infection and cell death affects the metabolic status and mitochondrial metabolic plasticity on myeloid cells. Our preliminary data show that pathogen sensing affects the metabolism of the myeloid cell with possible implications on myeloid cell function as the basis for innate and adaptive immune responses. We hypothesize that the sensing of cargo´s nature upon phagocytosis dictates a metabolic switch in myeloid cells. The student will learn many techniques working in vitro (cell culture, biochemistry, flow cytometry, cell metabolic assays, and Immunology techniques) and will learn about the in vivo models that we are developing in the lab to address this problem. The student will also be intellectually involved in the discussions and implications of this work for opening new avenues in the modulation of inflammation, immunity and tolerance. http://www.cnic.es/es/inflamacion/inmunobiologia/index.php

7: Scientist/Supervisor: **Enrique Lara-Pezzi**
Research line: **Gene therapy of myocardial infarction and heart failure**
Summary: Myocardial infarction leads to a massive loss of cardiomyocytes and a decline in contractile function. We have recently shown that overexpression of the calcineurin variant CnAbeta1 following myocardial infarction improves cardiac function and reduces remodelling. We have now generated a viral vector capable of overexpressing CnAbeta1 in cardiomyocytes. The Cicerone researcher will help investigate the potential benefit of this gene therapy approach to treat myocardial infarction in mice.

8: Scientist/Supervisor: : **Enrique Lara-Pezzi**
Research line: **Bioinformatic analysis of alternative splicing in the infarcted heart**
Summary: Although mortality associated to myocardial infarction (MI) has diminished, heart failure (HF) prevalence has not declined in the past 30 years and represents a heavy health and economic burden. Our knowledge of the molecular mechanisms that lead to ischemic HF is still very limited. We largely ignore the variety of isoforms that are generated for each gene by alternative splicing (AS) in the infarcted heart, how AS is regulated and how AS trans-regulatory factors impact the response to MI, remodelling and the development of HF. In this project we will investigate the changes in alternative splicing that take place after myocardial infarction. The student will need some prior knowledge of Perl and/or Python programming.

9: Scientist/Supervisor: **Francisco Sánchez-Madrid**
Research line: **Novel Mechanisms of cell-cell communication in the immune response".**Summary: The immune system plays a key role in sensing and eliminating cells undergoing viral infection and tumorogenesis. Recently, specific microRNAs derived from T cells, both T regulatory (Treg) and T helper cells (Th17), have been shown to play and important role in the regulation of immune responses. Also, previous research in the laboratory has demonstrated the unidirectional transfer of microRNA-loaded exosomes (Extracellular Vesicles, EVs) from T cells to antigen-presenting cells (APCs). These fields have attracted interest among scientists as a better understanding of the mechanisms of transfer and functional consequences of exosomal microRNA may open new perspectives for cancer inmunotherapy. Our working hypothesis is that the transfer of microRNA-bearing exosomes may play a key role in the intercellular communication both during the immune synapse and the regulation of antitumoral immune responses, and therefore in the establishment of the early stages of the immune response that will determine tumor fate. To address these issues, we propose to analyze the composition of (i) Treg/Th17-derived EVs during immune responses and (ii) EVs transferred from the T cell to the APC during IS as a means to identify putative targets for therapy; and iii) We will also analyze the functional consequences of the EV-mediated microRNA transfer to recipient cells in both contexts, assessing antitumoral responses and angiogenesis; microRNAs with potencial antitumoral effects will be included in the functional studies.

10: Scientist/Supervisor: **Guadalupe Sabio**
Research line: **Role of p38MAPK in obesity induced liver cancer**Summary: Obesity is associated with increased risk for epithelial tumours such as hepatocellular carcinoma (HCC). This is related with the fact that obesity is associated with a chronic inflammatory state, with the release of cytokines such as interleukin 6 (IL-6) and tumour necrosis factorα (TNFα, both known HCC mediators. Regarding the molecular mechanisms involved, mitogen-activated protein kinases (MAPK) are intracellular signalling molecules involved in cytokine synthesis. Among these kinases, p38MAPK is a key kinase involved in TNFα and IL-6 production. We will determine whether p38MAPK signalling contributes to the chronic inflammation observed in obesity. Our preliminary results indicate that the p38MAPK pathway could be involved in insulin resistance. We therefore plan to study whether modulation of p38 activity affects HCC development and/or obesity-mediated HCC development.

11: Scientist/Supervisor: **Guadalupe Sabio**
Research line: **Role of p38MAPK in heart development**
Summary: The p38 MAPK pathway transduces a variety of extracellular signals regulating cellular responses to stress, being implicated in cell proliferation, differentiation and apoptosis. Its implication in the development of human diseases it is being deeply studied. Four p38 MAPK family members have been identified: p38α, β, γ and δ.
Preliminary data from our laboratory show that these kinases may control cytokine production during acute and chronic inflammatory processes. Moreover, studies with genetically modified mice made in our laboratory confirm that p38MAPKs have a role in the development of the heart.
Therefore, our main objective is to determine if the regulation of the p38MAPK signaling pathway could have beneficial effects in the development of cardiovascular

diseases. The main objective of this project is to deeply study the physiological role of the p38MAPKs from different points of view. Firstly, through the description of new components which belong to this signaling pathway. As well as studying its implication in the development of inflammatory and cardiovascular diseases. We deeply believe that this project will lead to the identification of new therapeutic targets for several diseases such as cardiac hypertrophy or hypertension.

12: Scientist/Supervisor: **Ignacio Flores**
Research line: **Role of telomerase in heart rejuvenation.**
Summary: After a myocardial infarction, embryonic and fetal genes are re-expressed in adult zebrafish and mice hearts, indicative of an attemp of cardiomyocytes to restore a young state from an elderly state. Telomerase, the enzyme that elongates telomeres, has been associated with the rejuvenation process. In this project, the Cicerone student will analyze the role of telomerase activity in the heart rejuvenation process using telomerase loss- and gain-of function models.

13: Scientist/Supervisor: **Jesús Ruiz-Cabello**
Research line**; Imaging of perfusion in pulmonary hypertension using molecular imaging approaches**
Summary: We are currently studying the role of imaging in the characterization of pulmonary hypertension. The main objective of our project will be to characterize and quantify pulmonary perfusion as an early indicator of the disease. We will use different animal models and imaging approaches, mainly using MRI and PET imaging with 18FDG uptake, and specific peptide-based radiotracers. The student will be integrated in a chemistry-based laboratory with different strategies for functionalization and will work in a multidisciplinary and multimodality imaging environtment.

14: Scientist/Supervisor: **Jesús Ruiz-Cabello**
Research line**; Advanced imaging analysis**
Summary: This project aims to training the student in imaging analysis of functional cardiovascular data (e.g., cine, tagging, flow imaging). The student will become familiar with fucntional cardiovascular imaging processing, and will learn the software Osirix for image processing and will learn to implement plugins/tools for advanced imaging analysis in this platform. Basic knowledge of programming will be required.

15: Scientist/Supervisor: **Jesús Vázquez**
Research line: **The deep mitochondrial redox proteome in models of cardiovascular disease.** Summary: Using front-end proteomics technologies, including gel separation of supercomplexes and a novel data-independent mass spectrometry scanning technique (DiS) that improves performance of conventional shotgun approaches, we plan to study different models of cardiac pathologies that increase oxidation of Cys sites of mitochondrial proteins. These models include ischemia-reperfusion, aging and maladaptative cardiac hypertrophy (EndoG KO model), where we have found that oxidation increases mainly in OxPhos complexes and Krebs cycle proteins. Different computational methods will be applied to perform an extremely detailed structural map of components of mitochondrial oxidative phosphorylation supercomplexes, including molecular determinants of assembly. These results will help to better understand the mechanisms underlying mitochondrial oxidative damage and their implications in mitochondrial functionality.

16: Scientist/Supervisor: **Jorge Alegre-Cebollada**
Research line: **Single-molecule dissection of the mechanobiochemistry of cardiac proteins** Summary: The human heart is a formidable mechanical machine that pumps thousands of liters of blood every day. We are far from understanding how the heart works at the molecular level. A key component of heart tissue is the giant protein titin, which sets the passive elasticity of cardiac muscle. Following an interdisciplinary approach that includes proteomics and single-molecule manipulation techniques, we will uncover posttranslational modifications regulating the elasticity of titin, both in health and disease.

17: Scientist/Supervisor**: Jose Antonio Enríquez**
Research line**: Evaluation of mitochondrial physiology in cardiac performance**
Summary**:** Cardiovascular diseases remain the major cause of death in the developed word. Mitochondrial physiology biogenesis and OXPHOS system performance are deeply involved in the initiation progression of the disease, through reactive oxygen species (ROS) production, energy deficiency decrease in mitochondrial respirasome formation, as initial steps in the formation of the plaques. Genoxphos group aims better understand the involvement of mitochondria in cardiomyopathies using different models of mitochondrial diseases that curses with increase ROS production.

18: Scientist/Supervisor**: Jose Luis de la Pompa**
Research line**: Notch signaling in cardiac chamber development and disease**
Summary**:** The Notch pathwya is essential for cardiac chamber development (Grego-Bessa et al., 2007; de la Pompa & Epstein, 2012) and Notch signaling alterations cause human cardiomyopathy (Luxán et al., 2013). The project will study the underlying molecular mechanism using genetically modified mouse models and zebrafish, cell biology, biochemistry, NGS, imaging analysis and validation in human tissue samples.

19: Scientist/Supervisor**: Jose Luis de la Pompa**
Research line**: Intercellular signaling in cardiac valve development and disease**
Summary**:** Notch cooperates with various signals (ie: Bmp2) to promote cardiac valve formation (Luna-Zurita et al., 2010; de la Pompa & Epstein, 2012) and its alterations cause human cardiac valve disease. The project will study the underlying molecular mechanism using genetically modified mouse models and zebrafish, cell biology, biochemistry, NGS, imaging analysis and validation in human tissue samples.

20: Scientist/Supervisor: **Juan Miguel Redondo**
Research line: **Vascular wall remodeling: Molecular and cellular mechanisms and i n vivo animal models**
Summary: Extensive artery wall remodeling is a major feature of vascular diseases such as atherosclerosis, aneurysm and restenosis. We have set up in the lab animal modes of these three pathologies, and generated mice deficient in target molecules of the Angiotensin II signaling pathway that are resistant to these diseases. We plan to elucidate the molecular and cellular mechanisms that account for such protection.
http://www.cnic.es/es/inflamacion/endotelio/index.php

21: Scientist/Supervisor: **Juan Miguel Redondo**
Research line: **Role of calcineurin (CN) in cardiac remodeling**
Summary: Many biologically central processes including the regulation and development of the immune and cardiovascular systems are regulated by the Calcineurin. We plan to use mouse models of cardiac hypertrophy (CH) induced by infusion of Ang-II or transversal aortic constriction (TAC). In these models, we will define the time profile of cardiac remodeling processes during disease progression and will assess the impact of CN deletion on disease progression using r inducible CRE-mice conditionally KO for CN in cardiomyocytes. We also plan to identify genes relevant to the development of CH by comparative whole genome analysis of the gene expression profiles induced by TAC and by infusion of Ang II. Genes induced in both models of CH, as well as other relevant genes identified, will be analyzed in human heart biopsies from patients undergoing aortic stenosis surgery.

Additional info: http://www.cnic.es/es/inflamacion/endotelio/index.php

22: Scientist/Supervisor: **Martín Laclaustra**
Research line: **Epidemiology of cardiovascular disease biomarkers and metabolic risk factors.**
Summary: Through the use of state-of-the-art statistical methods, the student will analyze data from several Spanish cohort studies and from US surveys to find relationships between metabolic and biochemical measurements and cardiovascular disease. Currently ongoing proyects include the study of oxidative damage and mitochondrial biogenesis from an epidemiological perspective. Likewise, the student will become familiar with the different stages of clinical research.

23: Scientist/Supervisor: **Mercedes Ricote**
Research line: **Contribution of nuclear receptors to cardiovascular physiology: from stem cells to tissue regeneration.** Summary: Emerging evidence suggests that nuclear receptors (NRs) play a role in the homeostasis of adult stem cells. This project will focus on the role of NRs in differentiation, mobilization, proliferation and self-renewal of hematopoietic stem cells and its possible application for cardiac repair. A combination of biochemical, cellular and in vivo model systems will be used, incorporating tissue-specific knockouts, transcriptomic analysis, in vivo imaging and bioinformatics approaches.

24: Scientist/Supervisor: **Miguel Ángel del Pozo**
Research line: **Interplay between Rab8 and Caveolin-1 in Membrane Trafficking and Mechanosensing**

Summary: Caveolae are submicroscopic plasma membrane (PM) invaginations involved in viral entry, lipid metabolism, signaling and cell detection & response to mechanical force. Caveolins (Cav1 to -3) are the main proteins responsible for this unique PM domain, working cooperatively with cholesterol and cavins (1-4) in caveolar formation, function and dynamics. Their importance as membrane organizers and sensors is highlighted by links between caveolae dysfunction and human disease, including cardiovascular disorders, lipo- & muscular dystrophies and cancer. Increased surface tension triggers Cav1 delivery to the PM, but the underlying mechanisms are poorly known. Our preliminary evidence suggests that several GTPases of the Rab family (master regulators of polarized vesicle trafficking) - in particular Rab8- are involved in Cav1 recycling/exocytic delivery to the PM. In fact, a functional

interaction between Cav1 and Rab8 has been recently suggested (Verma et al, MBC 2010). The Cicerone student will be involved in a project to study the interplay between Cav1 and Rab8 in membrane trafficking and mechanosensing. Using loss & gain of function approaches, s/he will learn molecular, cell biology and biochemistry tools, state-of-the-art microscopic imaging (in particular Total internal reflection fluorescence for high spatio-temporal resolution particle tracking of Cav1 and Rab8-fluorescently labeled vesicles) image analysis SW and bioinformatics tools.

Some recent publications of the group: Parton & del Pozo, Nature Reviews Mol Cell Biol 2013, Echarri J Cell Sci 2012, Echarri & del Pozo, Curr Biol 2012, Navarro EMBO J 2012, Goetz Cell 2011, Muriel J Cell Sci 2011, Strippoli J Cell Sci 2010, Cerezo Mol Cell Biol. 2009, Grande J. Cell Biol. 2007, Bravo-Cordero, EMBO J 2007 (CNIC Rab8 collaborator), del Pozo Nature Cell Biol 2005 & Science 2004. More information on the group: http://www.cnic.es/es/inflamacion/integrinas/index.php The scientific report of the group (2008-2011) can be downloaded from http://www.cnic.es/es/cnic/scientific_report.php

25: Scientist/Supervisor: **Miguel Ángel del Pozo**
Research line**: Integrins, Rho GTPases and Caveolae in Membrane Trafficking, Mechanotransduction and Cell Migration** Summary: Our interest is in the mechanisms through which integrins, Rho/Rac GTPases and caveolae components (caveolins, cavins, curvature proteins, etc) cooperate to regulate gene expression, cell cycle progression, migration, polarization, vesicle trafficking, cytoskeletal rearrangements and mechanotransduction, key processes in the pathogenesis of cancer and inflammatory and cardiovascular diseases. The Cicerone student will be involved in a project to study vesicle trafficking and cytoskeletal reorganization in response to mechanical cues, including Rac1 nucleocytoplasmic shuttling and determining the importance of this GTPase in the structure and functionality of the nucleus. S/he will learn molecular, cell biology and biochemistry tools, state-of-the-art microscopic imaging (in particular Total internal reflection fluorescence), image analysis SW and bioinformatics tools.
Some recent publications of the group: Parton & del Pozo, Nature Reviews Mol Cell Biol 2013, Echarri J Cell Sci 2012, Echarri & del Pozo, Curr Biol 2012, Navarro EMBO J 2012, Goetz Cell 2011, Muriel J Cell Sci 2011, Strippoli J Cell Sci 2010, Cerezo Mol Cell Biol. 2009, Grande J. Cell Biol. 2007, del Pozo Nature Cell Biol 2005 & Science 2004. More information on the group: http://www.cnic.es/es/inflamacion/integrinas/index.php The scientific report of the group (2008-2012) can be downloaded from http://www.cnic.es/es/cnic/scientific_report.php

26: Scientist/Supervisor: **Miguel Manzanares**
Research line**: Embryonic pluripotency and early lineage specification in the mouse blastocyst**
Summary: In the lab we aim to understand how the stem cell state that occurs in the early embryo is maintained, as well as which are the mechanisms that allow cells to escape pluripotency and engage in specific lineages. In this Cicerone project, the student will use different genetic models in mouse where the expression of key pluripotent regulators and epigenetic factors can be modulated and analyze the effect on the establishment of early lineages in the preimplantation embryo.

27: Scientist/Supervisor: **Miguel Manzanares**
Research line: **Bioinformatic analysis of the regulatory basis of cardiovascular disease.**Summary: The genome encompasses not only the instruction to build proteins, but also the instructions that determine when, where and how much each gene is expressed. Proximal and distal regulatory elements are present in the non-coding portion of the genome, but are difficult to find based on sequence alone. We are combining available gene expression, epigenetic and functional data in a genome-wide manner in order to construct a predictive score to find regulatory regions in the genome associated to cardiac disease. For this Cicerone project, it is necessary that the student has some prior knowledge and a keen interest in bioinformatics.

28: Scientist/Supervisor: **Nadia Mercader**
Research line: **Fibrosis regression during cardiac regeneration in the Zebrafish**
Summary: Unlike mammals, the zebrafish is able to remove massive fibrotic heart lesions and to regenerate the lost tissue. Thus, endogenous mechanisms exist in this species allowing the degradation of fibrotic tissue and its replacement by newly formed cells. The aim of this project is to elucidate the molecular mechanisms of fibrotic tissue degradation in the zebrafish. We will analyse the expression of genes differentially expressed during different stages of regeneration. We will also study the function of some proteins during regeneration by administration of chemical inhibitor. Some of the techniques that will be used during this study are histological stainings, immunohistoquemistry, mRNA in situ hybridization.

29: Scientist/Supervisor: **Nadia Mercader**
Research line: **Epicardium development in the zebrafish**Summary: The epicardium is the outer layer enveloping the myocardium. Epicardial derived cells contribute to cardiac development by promoting myocardial maturation and giving rise to progenitor cells for the coronary vasculature and fibroblasts among others. The zebrafish offers the unique opportunity to monitor embryonic development in vivo. We take advantage of its external fertilization to study the formation of the epicardium in real-time. This project will address the role of biomechanical forces controling epicardium morphogenesis and dissect the regulatory gene network involved in epicardial precursor cell differentiation. Some of the techniques that will be used during this study are advanced confocal and multifoton microscopy, mRNA in situ hybridization, immunohistoquemistry, manipulation of embryos and RNA microinjection.

30: Scientist/Supervisor: **Pilar Martín**
Research line: **Study of experimental cellular therapies against graft versus host disease and heart transplant rejection**
Summary: Summary: Given the recently described importance of the C-type lectin CD69 in the control of Th17/Treg balance, in heart and lung inflammatory diseases, by the host laboratory, the aim of the proposed project is to dissect the role of these populations in the pathogenesis of these diseases in conjunction with CD69 proficiency or deficiency.

31: Scientist/Supervisor: **Pilar Martín**
Research line: **Control of inflammation in cardiomyopathy and heart failure**
Summary: Inflammation and autoimmune abnormalities play an important role in the progression of heart failure among other diseases. Understanding peripheral mechanisms

operating in autoimmune and chronic inflammatory diseases is critical for the design and development of novel therapies. Our group seeks to identify new regulatory cells and miRNAs involved in the control of these diseases.

32: Scientist/Supervisor: **Rui Benedito**
Research line: **In vivo analysis of angiogenesis in mice**
Summary: The group investigates different aspects of vascular biology using advanced mouse models and imaging technologies. We are generating several new mouse lines that will allow us to induce precise genetic modifications during angiogenesis. The Cicerone student will be involved in a project to identify the best transgenic animals and do a pre-evaluation of the function of specific genes during development and disease in the cardiovascular system. The work will involve handling of mice and dissection, state-of-the-art imaging techniques, as well as molecular and cell biology techniques.
Some recent publications: Benedito R. et al., Nature 2012; Benedito R. et al., Cell 2009; Benedito R. et al., Science 2009. More information on the group: http://www.cnic.es/en/desarrollo/angiogenesis/index.php

33: Scientist/Supervisor: **Simón Méndez**
Research line: **Neural regulation of stem cells as a therapeutic target**
Summary: We investigate new pathways that allow stem cells to function in an integrated manner with the organism's demands. One of these pathways is the sympathetic nervous system, which regulates the traffic of blood stem cells (Nature 2008) mainly through its action on mesenchymal stem cells (Nature 2010) that can support them (Cell Rep 2013). The student will join a highly motivated young research group to study the emerging implications of this regulation in diseases, using the mouse as a research model and cutting-edge technologies.

34: Scientist/Supervisor: **Simón Méndez**
Research line: **Novel endocrine regulation of stem cells**
Summary: We have recently uncovered a new regulatory pathway of adult stem cell self-renewal, survival and proliferation by steroidal hormones. This regulation can be exploited for therapeutic purposes. Interestingly, activation of this pathway has disparate effects on progenitor cells depending on their differentiation stage. The student will use in vitro and in vivo pharmacological experiments, sophisticated metabolic and imaging techniques to dissect this regulatory pathway.

35: Scientist/Supervisor: **Susana González**
Research line: **Impact of epigenetic mechanisms on age-associated cardiovascular pathophysiology.**
Summary: We hypothesize that inadequate orchestration of epigenetic mechanisms play vital roles in age-related adult cardiomyopathies. Aided by conditional knockout models and parabiotic assays, this study has uncovered crucial role for epigenetic Polycomb regulator in the adult heart.

36: Scientist/Supervisor: **Susana González**
Research line: **Epigenetic regulation of adult hematopoietic stem cells**
Summary: We are studying the role of the epigenetic Polycomb-mediated silencing mechanism in stemness maintenance, with particular emphasis on the self-renewal capacity and the microenvironment of haematopoietic stem cells (HSCs), a key adult stem cell population with diverse regenerative capacity.

37: Scientist/Supervisor: **Vicente Andrés**
Research line: **Mechanisms of aging and associated cardiovascular disease**
Summary: Aging is the main risk factor for cardiovascular disease (CVD), which is responsible for 1/3 of deaths in developed countries. By 2020, CVD is expected to become the main health problem worldwide, in part due to the progressive aging that the world is experiencing. CVD and aging are greatly accelerated in Hutchinson-Gilford progeria syndrome (HGPS), a rare genetic disorder characterized by premature aging and death (average lifespan: 13yr) that is caused by the abnormal expression of progerin (see www.progeriaresearch.org). This mutant form of lamin A is also expressed in aged tissues of non-HGPS individuals, suggesting a role in normal aging. By analyzing cultured cells and genetically-modified mice using a variety of molecular and cellular biology techniques, the student will learn about mechanisms underlying CVD and aging.