List of Researchers and Research Lines

1: Scientist/Supervisor: **Andrés, Vicente.** (vandres@cnic.es)
Research line: **Mechanisms of cardiovascular disease and aging**
Summary: We investigate cellular, molecular and genetic mechanisms involved in atherosclerosis and restenosis postangioplasty. We also investigate the role of A-type lamins in the regulation of pathophysiological processes, such as cell differentiation, T cell activation, cardiovascular disease and aging. We implement a multifaceted approach that combines in vitro, cellular, animal and human studies and a variety of technologies, including mouse genetic engineering, proteomics, transcriptomics, FRET, confocal microscopy, and yeast 2-hybrid screening.

2: Scientist/Supervisor: Dos Santos **Benedito, Rui Miguel** (rui.benedito@cnic.es)
Research Line: ***In vivo*** **analysis of angiogenesis in Notch and VEGF signalling mutants**
Summary: Several studies in the past have revealed the importance of cell-to-cell signaling for the differentiation and patterning of the vascular system. One of the most important and well-conserved mechanisms of cell-to-cell communication involves the Notch family of receptors and their transmembrane ligands Delta and Jagged. In recent years we have investigated the function of several components of the Notch signaling pathway and how they generate heterogeneity among endothelial cells during angiogenesis and arterial-venous differentiation. We found that differential expression and activity of the different Notch ligands and modulators is responsible for the diversity of cell behaviors necessary for normal and pathological vascular sprouting and growth. The group investigates different aspects of the 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 or in a quiescent vasculature. 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, disease or homeostasis of 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

3: Scientist/Supervisor: **de la Pompa, Jose Luís** (jlpompa@cnic.es)
Research Line: **Signaling in cardiac chamber development and cardiomyopathy**
Summary: Notch is a local cell signaling mechanism that regulates cardiomyocyte proliferation, differentiation and maturation during ventricular development. Notch signaling abrogation in humans leads to left ventricular non compaction cardiomyopathy. We want to study the underlying mechanism of Notch function during this developmental-disease process. We use cardio-specific genetically modified mouse models, combined with molecular, cell biological and image analysis of cardiac development and function.

4: Scientist/Supervisor: **de la Pompa, Jose Luís** (jlpompa@cnic.es)
Research Line: **Signaling in cardiac valve disease and cardiomyopathy.**
Summary: We are studying the role of Notch and interacting signals (BMP2, NFATc1) in the development and disease of the cardiac valves. These different pathways are required for cardiac valve development but very little is known about their role in the adult valve and about their potentials interaction. We will use cardio-specific genetically modified mouse models, combined with molecular, cell biological and image analysis of cardiac development and function.

5: Scientist/Supervisor: **de Pozo, Miguel Ángel** (madelpozo@cnic.es)
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

6: Scientist/Supervisor: **de Pozo, Miguel Ángel** (madelpozo@cnic.es)
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

7: Scientist/Supervisor: **Enríquez, Jose Antonio** (jaenriquez@cnic.es)
Research line: **Mitochondrial implication in cardiovascular diseases**
Summary: Cardiovascular diseases remain the major cause of death in the developed word. Mitochondrial physiology and biogenesis are deeply involved in the initiation and progression of the disease, through reactive oxygen species (ROS) production, energy deficiency and decrease in mitochondrial respirasome formation, as initial steps in the formation of the plaques. This project aims better understand the involvement of mitochondria in cardiomyopathies using different models of mitochondrial diseases that curses with increase ROS production.

8: Scientist/Supervisor: **Flores, Ignacio** (iflores@cnic.es)
Research line: **Role of telomerase in heart rejuvenation**
Summary: After a myocardial infarction, embryonic and foetal genes are re-expressed in adult zebrafish and mice hearts, indicative of an attempt 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.

9: Scientist/Supervisor: **G. Gálvez, Beatriz** (bgonzalez@cnic.es)
Research line: **Characterization of migration structures in cardiac stem cells**
Summary: Our group is interested in improving the migration and differentiation properties of cardiac stem cells in order to be used in future cell-based therapies. The main objective of this project is the characterization of membrane cell structures implicated in the migration of cardiac stem cells. We will use in vitro and ex vivo assays, cell culture of stem cells populations and state-of-the-art confocal microscopy and imaging analysis.

10: Scientist/Supervisor: **González, Susana** (sgonzalez@cnic.es)
Research line; **Epigenetic regulation of adult 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.

11: Scientist/Supervisor: **Hidalgo, Andrés** (ahidalgo@cnic.es)
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.

12: Scientist/Supervisor: **Ibañez, Borja** (bibanez@cnic.es)
Research line: **beta-adrenergic modulation during ischemia/reperfusion: from cells to relevant animal models**
Summary: During the last years our group has made some discoveries on the role of beta blockade in reducing infarct size. Ina preclinical model of myocardial infarction, we have demonstrated that the pre-reperfusion beta1 selective blockade is able to reduce infarct size as evaluated by non-invasive imaging. As a consequence we are embarked in a clinical trial testing this hypothesis. At this stage we have decided to come back to the bench to further study the mechanism of action by which the beta adrenergic modulation is cardio-protective during an evolving myocardial infarction. We have a multidisciplinary project in which we are covering from the in vitro molecular pathways involved in this cardio-protection, to the development of small (mouse) and large (pig) animal models of myocardial infarction. State-of-the-art non-invasive imaging (magnetic resonance imaging) is used to evaluate the effect of therapies in the different models. By joining our group, the cicerone student will be exposed to the basic research techniques as well as to different models of cardiovascular disease, ranging from mice ischemia/reperfusion to pig catheter based myocardial infarction

13: Scientist/Supervisor: **Laclaustra, Martin** (mlaclaustra@cnic.es)
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.

14: Scientist/Supervisor: **Lara, Enrique** (elara@cnic.es)
Research line**; Molecular regulation of heart failure and recovery**
Summary: Myocardial infarction leads to a massive loss of cardiomyocytes and contractile function. To test the therapeutic potential of CnAbeta1, a unique isoform of the phosphatase calcineurin, we have generated inducible transgenic mice in which CnAbeta1 is induced after infarction specifically in cardiomyocytes. The Cicerone researcher will help characterize the molecular mechanisms underlying cardiac regeneration and recovery in these mice

15: Scientist/Supervisor: **Manzanares, Miguel** (mmanzanares@cnic.es)
Research line: **Regulatory genomics of heart development & disease**
Summary: In the lab we aim to understand how gene expression is regulated in a spatially and temporally controlled manner during development of the heart, and how this relates to the occurrence of cardiovascular disease (CVD). In this Cicerone project, the student will study the regulatory potential of genomic regions that have been associated with an increased risk of CVD and are located near to developmental regulators.

16: Scientist/Supervisor: **Manzanares, Miguel** (mmanzanares@cnic.es)
Research line: **Deciphering cardiovascular regulatory codes by integrated data management**
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 building an in-house browser that will combine available gene expression, epigenetic and data form functional assays in a genome-wide manner in order to construct a predictive score to find regulatory regions in the genome associated to cardiac genes, and also to disease. For this Cicerone project, it is necessary that the student has some prior knowledge and a keen interest in bioinformatics.

17: Scientist/Supervisor**: Martín, Pilar (pmartinf@cnic.es)**
Research line**: Control of inflammation in cardiomyopathy and heart transplant rejection**
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 molecules involved in the control of these diseases.

18: Scientist/Supervisor**: Méndez-Ferrer, Simón (smendez@cnic.es)**
Research line**: Novel neuroendocrine regulation of stem cells as a therapeutic target**
Summary**:** We are currently uncovering new neuroendocrine pathways that regulate bone marrow stem cells. Importantly, a disruption of these regulatory pathways critically contributes to diseases that cannot be cured with current treatments. Therefore, these studies offer new promising therapeutic targets. The student will use cutting-edge research models, technologies and equipment to dissect this novel regulation of stem cells and translate it into clinical trials.

19: Scientist/Supervisor**: Méndez-Ferrer, Simón (smendez@cnic.es)**
Research line**: Stem cell niche deconstruction for optimized cell therapy**
Summary**:** One of the great challenges in cell therapy is the difficulty to culture adult stem cells. The main reason for that is our limited knowledge of the stem cell niche. Our current studies are dissecting the origin and regulation of niche cells. We have also devised a novel assay to expand stem cells, which will be soon tested in a multicenter clinical trial. The student will combine cutting-edge imaging with in vivo functional studies to deconstruct stem cell-niche interactions.

20: Scientist/Supervisor: **Mercader, Nadia** (nmercader@cnic.es)
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.

21: Scientist/Supervisor: **Mercader, Nadia** (nmercader@cnic.es)
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.

22: Scientist/Supervisor: **Ramiro, Almudena R.** (a.rodriguez@cnic.es)
Research line: **B cells in cancer and autoimmune disease**
Summary: B cells play a fundamental role in the immune response through the generation of protective and highly specific antibodies. However antibodies and the mechanisms that diversify them are also involved in autoimmune disease and cancer. Our lab studies these mechanisms using animal models and a combination of molecular analyses including next generation sequencing.

23: Scientist/Supervisor: **Redondo, Juan Miguel** (jmredondo@cnic.es)
Research line: **Vascular wall remodeling: Molecular and cellular mechanisms and *in 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

24: Scientist/Supervisor: **Redondo, Juan Miguel** (jmredondo@cnic.es)
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

25: Scientist/Supervisor: **Ricote, Mercedes** (mricote@cnic.es)
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.

26: Scientist/Supervisor: **Ricote, Mercedes** (mricote@cnic.es)
Research line**: Role of macrophage nuclear receptors in cardiac homeostasis and injury.**
Summary: Activation of the immune system is a good candidate for triggering tissue regeneration; however the molecular pathways that directly link the immune system to myocardial regeneration remain poorly understood. In this project, we will focus on the role of macrophage nuclear receptors (NRs) in cardiac homeostasis, and in the inflammatory response after myocardial infarction. We will use tissue-specific knockouts, transcriptomics, in vivo imaging, and the latest techniques in cell-fate mapping to unravel the role of macrophages in cardiovascular physiology.

27: Scientist/Supervisor: **Sabio, Guadalupe** (gsabio@cnic.es)
Research line: **Role of stress kinases in diabetes, obesity and hepatocellular carcinoma development**
Summary: Obesity is associated with increased risk for epithelial tumors such as hepatocellular carcinoma (HCC). Obesity is associated with a chronic inflammatory state, with the release of cytokines such as Interleukin 6 (IL-6) and tumor necrosis factor (TNF), both known HCC mediators. Mitogen-activated protein kinases (MAPK) are intracellular signaling molecules involved in cytokine synthesis. Of these kinases, p38MAPK is a key kinase involved in TNF and IL-6 production. We will determine whether p38MAPK signaling contributes to the chronic inflammation observed in obesity. We therefore plan to study whether modulation of p38 activity affects HCC development and/or obesity-mediated HCC development.

28: Scientist/Supervisor: **Ruiz-Cabello, Jesús** (jesusmaria.ruiz-cabello@cnic.es)
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.

29: Scientist/Supervisor: **Ruiz-Cabello, Jesús** (jesusmaria.ruiz-cabello@cnic.es)
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.

30: Scientist/Supervisor: **Sabio, Guadalupe** (gsabio@cnic.es)
Research line: **Role of stress kinases in cardiac hypertrophy**
Summary: The activation of stress activated protein kinases pathway has been associated with the development of cardiac hypertrophy in models of angiotensin II-induced cardiac hypertrophy. On the contrary, it has been also reported by other groups that inhibition of this pathway does not induce cardio protective effects. Using animals models with specific deletion of this pathway we are going to study the role of these kinases in hearth hypertrophy.

31: Scientist/Supervisor: **Sánchez Madrid, Francisco** (fsanchez.hlpr@salud.madrid.org)
Research line: **Mechanisms of MTOC guidance and Genetic Transfer at the Immune Synapse: novel modes of Immuno-modulation**
Summary: To assess the role of MTOC polarization as a signalling and structural platform for the control of secretion during Immunological Synapse (IS) formation; 2.-To define the mechanisms and functional consequences of intercellular transfer of miRNA via the IS.

32: Scientist/Supervisor: **Sancho, David** (dsancho@cnic.es)
Research line: **Immune myeloid receptors sensing tissue damage in inflammation and immunity.**
Summary: Recognition of tissue damage by immune myeloid cells may lie at the root of immune pathologies associated with an accumulation of dead cells, including many autoimmune and autoinflammatory diseases. Recently, it has been shown that sensing of radio or chemotherapy-killed tumor cells by the immune system is essential to mount an adaptive response that contributes to the success of the chemotherapy and the total elimination of the tumor. We have generated mice deficient in immune myeloid receptors sensing necrosis and we are characterizing them in models of viral infection, autoimmunity, atherosclerosis and tumor chemotherapy. These studies can open new avenues in the treatment of these diseases and the design of better vaccines.
http://www.cnic.es/es/inflamacion/inmunobiologia/index.php

33: Scientist/Supervisor: **Sancho, David** (dsancho@cnic.es)
Research line: **Dangerous-self, immune regulation and metabolism.**
Summary: Dangerous-self signals coming from damaged tissues may modulate immunity and inflammation through recently identified receptors that we are characterizing at the laboratory. Using animal models deficient in these receptors and many biochemical, cell biology and immunology techniques, we are addressing the role of sensing damage through these receptors in the regulation of metabolism. Preliminary results show that inflammation underlying obesity and metabolic syndrome may be related with sensing of damage through these receptors. These studies can reveal innovative ways of treatment of these diseases.
http://www.cnic.es/es/inflamacion/inmunobiologia/index.php

34: Scientist/Supervisor: **Torres, Miguel** (mtorres@cnic.es)
Research line: **Regulation of cardiovascular progenitors by hypoxia**
Summary: Heart formation requires the participation of several cardiovascular progenitors that contribute to the different cardiac structures. Embryonic cardiogenesis takes place in a low oxygen environment, and knock out mice for the canonical hypoxia pathway display cardiovascular abnormalities. Nevertheless the role of physiological hypoxia during early cardiac development remains unexplored. Using transgenic mice models of gain and loss of function of hypoxia canonical pathway in different cardiovascular progenitors, together with reporter Embryonic Stem Cell (ESC) lines that will serve as in vitro model, the Cicerone student will be involved in the characterization of cardiogenesis regulation by low oxygen tensions. The student will learn different techniques such as mouse embryo dissection and manipulation, histological analysis, immunohistochemistry, RT-PCR, Western blot and ESC culture among others.

35: Scientist/Supervisor: **Vázquez, Jesús** (jvazquez@cnic.es)
Research line: **The deep mitochondrial redox proteome in models of cardiovascular disease.**
Summary: Using front-end proteomics technologies, we plan to address the role of reactive oxygen species and to study oxidative damage on mitochondrial proteins in animal models of ischemia-reperfusion and preconditioning. We also plan to dissect the molecular mitochondrial determinants of aging and a model of maladaptive cardiac hypertophy, and determine the mitochondrial targets of oxidative damage produced in animal models of premature aging.