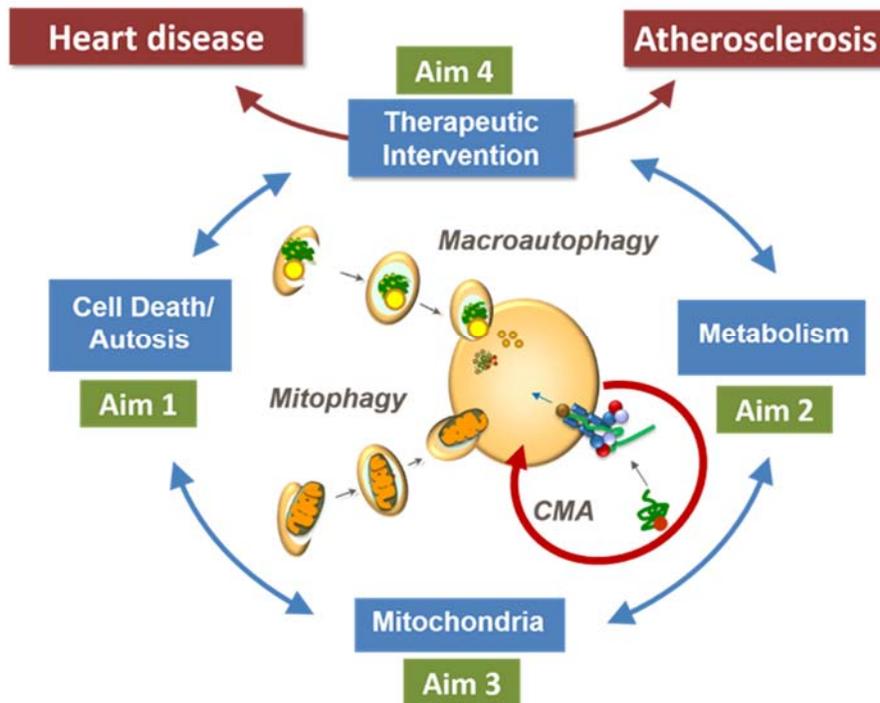
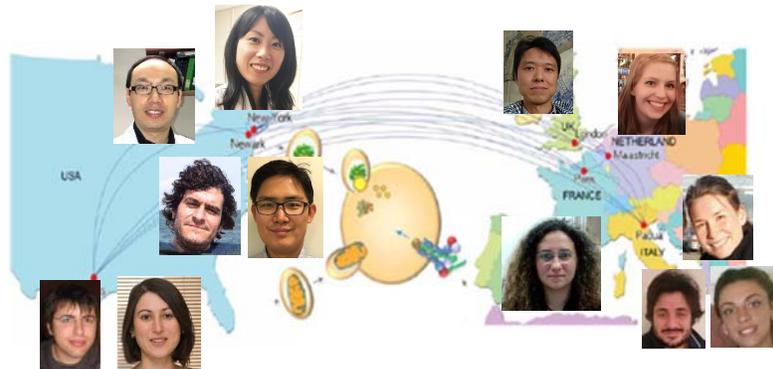


“Modulating autophagy to treat cardiovascular disease”

ECI’s biosketch





Yun Chen – Richard Kitsis' group



Mitochondria play essential and diverse roles in the physiology of cells. Mitochondrial dynamic remodeling, programmed regeneration and elimination, as well as energy metabolism are critical in embryonic development and cell homeostasis maintenance. Perturbations of mitochondrial fission-fusion dynamics, impairments of mitochondrial functions, and disturbances in mitochondrial mediated cell elimination, have been implicated in a wide variety of human pathologies, among which cancer, age-related diseases, and heart failure.

My research seeks to understand the mechanism of programmed apoptotic and necrotic cell death, mitochondrial dynamics and quality control, as well as chaperon-mediated autophagy in cell survival. After I completed my PhD in molecular biology and reproductive immunology at the Institute of Zoology, Chinese Academy of Sciences in Beijing, and postdoctoral training at UMDNJ-Robert Wood Johnson Medical School, I started my early-career research as a senior scientist at Washington University School of Medicine mentored by Dr. Gerald Dorn. My research has focused on molecular mechanisms of mitochondrial apoptosis, necrosis and mitophagy in heart disease. Our work has revealed that the death-promoting protein Nix stimulates both apoptosis and necrosis death pathways, determined by its subcellular localization in the mitochondria versus ER (Proc Natl Acad Sci USA, 2010). To study the biological roles of the mitochondrial outer membrane fusion proteins Mfn1 and Mfn2 in the heart, I generated cardiac specific conditional knockout mouse models. The results show that both Mfn1 and Mfn2 are essential in modulating mitochondrial fusion-fission remodeling, while only Mfn2, but not Mfn1, is critical for mitochondrial-ER Ca²⁺ flux, mitochondrial genomic integrity, and mitochondrial quality control. Phosphorylated Mfn2 is required for PINK1-Parkin mediated mitochondrial elimination (Science, 2013; Circulation Research, 2012;



Circulation Research, 2011). To explore the network of programmed cell death and survival, currently my research is focusing on studying the interaction between cell death (apoptosis, necrosis, and mitosis), and mitochondrial related macro-autophagy and Chaperon-mediated autophagy (CMA) in heart.

The long-term goal of my research is to understand the molecular and cellular mechanisms responsible for mitochondrial dysfunction/ function alteration and the effects of on cardiovascular diseases, and age-related diseases, and to apply this information to novel small molecular or genetic therapeutics.



Nina Kaludercic



Nina Kaludercic is a Research Scientist at the Neuroscience Institute, National Research Council of Italy, in Padova, Italy. Nina's main research interests include mitochondrial sources of oxidative stress and modulation of mitochondrial function in relation to cardiac disease. She obtained her PhD in Biochemistry and Biotechnologies at the University of Padova in 2008. During her PhD, she visited Dr. Nazareno Paolocci's laboratory at Johns Hopkins University in Baltimore to pursue a project focusing on the role of monoamine oxidases in maladaptive hypertrophy and heart failure. Nina continued her postdoctoral training in Dr. Paolocci's lab between 2008 and 2010, supported through the postdoctoral fellowship from the American Heart Association. This research led to the discovery of monoamine oxidase as a major mitochondrial source of oxidative stress and a key mediator of cardiac damage in the failing heart, and gained Nina the Postdoctoral Scientist award at the Experimental Biology meeting in 2010. In 2012, she obtained an independent position in Padova where she is now building her own research group. Currently, among other things, she is investigating the role of monoamine oxidases and mitochondrial oxidative stress in diabetic cardiomyopathy, and the underlying mechanisms that lead to mitochondrial dysfunction.



Julio Madrigal-Matute– Ana Maria Cuervo's group



Julio Madrigal-Matute is a postdoctoral fellow at the Albert Einstein College of Medicine in the Bronx (NY), USA. Julio obtained his PhD in Biochemistry, Biomedicine and Molecular Biology at the University Autónoma of Madrid in 2012. During his PhD, he studied the role of chaperones in atherothrombosis pathogenesis. After a one year in Dr. Fernandez-Hernando's lab at NYU, where he studied the interplay between miRNAs and other epigenetic modulators in lipid metabolism, he joined Ana Maria Cuervo's lab. Julio's main research interest is in the role of Chaperone-mediated autophagy (CMA) in metabolism. As part of the Leducq project he will be analyzing the role of CMA in atherothrombosis.

Keywords: atherothrombosis; chaperone-mediated autophagy; chaperones; diabetes; lipid metabolism; obesity.



Maria Chiara Maiuri received her PhD in Pharmacology in 2003 at the University of Napoli Federico II (Italy). Actually she is working as a senior researcher at the INSERM UMRS 1138, at the Centre de Recherche des Cordeliers (CRC; Paris, France). She is also the scientific director of the CRC Core Facilities. Chiara's research focuses on the molecular mechanisms controlling cell survival and cell death in physiopathological conditions. Currently, she is working on the impact of autophagy in metabolism and obesity-related pathologies.

Keywords: autophagy, apoptosis, cancer, metabolism, obesity



Sebastiano Sciarretta



Sebastiano Sciarretta is currently Adjunct Assistant Professor at the Department of Cell Biology and Molecular Medicine, Rutgers New Jersey Medical School, Newark, US. He is also Assistant Professor at the Department of Medical and Surgical Biotechnologies, Sapienza University of Rome, Italy. Sebastiano took his MD at Sapienza University of Rome in 2005. Then, he completed his Cardiology Fellowship in 2009 at Sant'Andrea Hospital, Sapienza University of Rome. During his clinical fellowship, Sebastiano focused on both clinical and basic research. He studied the impact of metabolic derangements on cardiac structure and function in patients with essential hypertension. He also studied the role of atrial natriuretic peptide in the regulation of vascular function. In 2009 Sebastiano moved to the laboratory of Jun Sadoshima as a post-doctoral fellow. In Dr. Sadoshima's laboratory Sebastiano studied the role of autophagy during cardiac stress. In particular, he elucidated the molecular mechanisms through which autophagy is regulated in response to myocardial ischemia. As part of the Leducq Network, Sebastiano will test the effects of pharmacological activation of autophagy during myocardial ischemia and remodeling.

Keywords: autophagy; ischemia; myocardial infarction; cardiac remodeling; metabolic syndrome; mTOR



Salwa Sebti – Beth Levine's group



Salwa Sebti is a postdoctoral fellow in Beth Levine's lab at UT Southwestern Medical Center in Dallas (Texas) USA. Salwa obtained her PhD in Cell Biology at the University of Montpellier (France) in 2013. Her graduate work with Sophie Patingre, her PhD mentor, uncovered the role of a nucleocytoplasmic shuttling protein on autophagy via the acetylation of key modulators. As a post-doc, Salwa is interested in further investigating the molecular regulation of mitophagy and the roles of mitophagy in disease prevention. She has demonstrated a specific role for mitochondrial-localized Beclin 1 in mitophagy and tumor suppressor function.

Keywords : Beclin 1, mitophagy.



Álvaro Fernández Fernández — Beth Levine's group



Álvaro Fernández Fernández is a postdoctoral fellow in Beth Levine's group at University of Texas Southwestern Medical Center in Dallas (USA). He got his PhD in Cell and Molecular Biology in 2015 at the University of Oviedo (Spain), studying the functional and pathological roles of the mammalian orthologues of autophagy protease Atg4 (called autophagins). Álvaro previously visited Beth Levine's laboratory during his PhD, where he participated in the analysis of molecular mechanisms involved in selective autophagy. As part of the Leducq Network he will study the regulation of autosis, a new form of cell death triggered by autophagy that can be blocked by cardiac glycosides, and its role in the development of cardiovascular diseases.

Keywords: autophagy, autosis, cell death, cardiac glycosides.



Lorenza Tsansizi – Scorrano's group



Lorenza Iolanda Tsansizi is a PhD student in Luca Scorrano's lab at the Venetian Institute of Molecular Medicine in Padova (Italy). Lorenza obtained her MSc in Molecular Medicine in the Department of Medicine of Athens. There she worked in Professor Yassemi Capetanaki's lab on the process of transdifferentiation of fibroblasts into cardiomyocytes. Her PhD project is dedicated to the Leducq's mission of health improvement by studying the regulation of mitophagy by mitochondrial metabolism in cardiac disease. More specifically she will use mouse genetic models of impaired mitophagy, aminoacid metabolism and oxidative phosphorylation to study how one process affects the others in the heart.



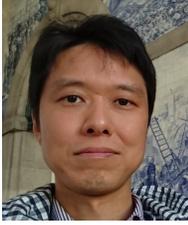
Martina Semenzato obtained her PhD in Biochemistry and Biotechnologies under the supervision of Prof. Fabio Di Lisa at the University of Study of Padova, Italy (2010). Afterward, she moved to the Venetian Institute of Molecular Medicine to join Luca Scorrano's laboratory as a postdoctoral fellow. Her main interest is the role of mitochondrial dynamics in cardiovascular diseases. In particular her project is focused on the impact of reactive oxygen species produce during cardiac ischemia reperfusion injury in mitochondrial dynamics. Another related project aim at characterizing the effect of downregulation of OPA1 protein in the heart.

Keywords: mitochondrial dynamics, OPA1, oxidative stress



Gihoon Nah is a postdoctoral fellow at the Rutgers University in the Newark (NJ), USA. Gihoon obtained his PhD in Dr. Yong-Keun Jung's laboratory in school of biological science, Seoul National University, Korea in 2013. During his PhD, he had studied on the regulation of Beclin-1 in response to amyloid beta 42 or oxidative stress. From 2016, he joined Dr. Junichi Sadoshima's lab. Now, he has been focusing on the beneficial or detrimental role of autophagy or mitophagy in the cardiomyocytes during several heart diseases. As part of the Leducq project, he will be investigating role of autophagic cell death in ischemia/reperfusion injury in the heart.

Keywords: Ischemia/reperfusion, autophagy, autophagic cell death, Beclin-1



Tomokazu Murakawa is a research fellow at the King's College London, UK. Tomokazu obtained his MD in 2003 and worked as a clinical cardiologist for six years. He received PhD in 2015 at Osaka University Graduate School of Medicine, Japan. During his PhD, he had been identifying a novel mitophagic receptor protein and found that Bcl-2 like protein 13 (Bcl2-L-13) is a mammalian homologue of Atg32 which is an essential protein for mitophagy in yeast. Tomokazu's main research interest is the role of mitophagy in the pathogenesis of heart failure.

As part of the Leducq project, he is studying detail mechanisms of Bcl2-L-13 mediated mitophagy and in vivo role of the molecule.

Keywords: heart failure; selective autophagy; mitophagy; mitochondrial dynamics



Risa Mukai is a postdoctoral fellow at Rutgers New Jersey Medical School (NJ), USA. Risa obtained her PhD in Molecular Biology and Virology at Tokushima Bunri University (Japan) in 2015. During her PhD training, she developed a broad background in molecular virology, with an emphasis on the biology of Human T-cell Leukemia type I. For her second round of postdoctoral training, she moved into the field of cardiovascular biology to study the regulation of autophagy *in vivo*, under Dr. Junichi Sadoshima. As part of the Leducq project, she will be elucidating the role of methylation in regulating autophagy in ischemic cardiomyopathy.

Keywords: energy-stress-induced autophagy; ischemic cardiomyopathy; methylation



Jenny de Bruijn started in September 2017 as a PhD-student in the Sluimer lab, Maastricht University Medical Centre. She obtained her medical degree at the University of Maastricht. During her Master's degree she expressed an interest in cardiovascular research and pathology, and completed an internship at the Sluimer lab. The role of chaperone-mediated autophagy in the atherosclerotic plaque is the focus of her current work.