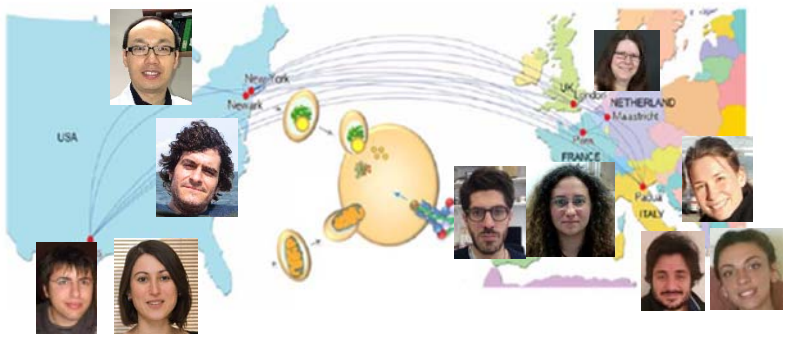
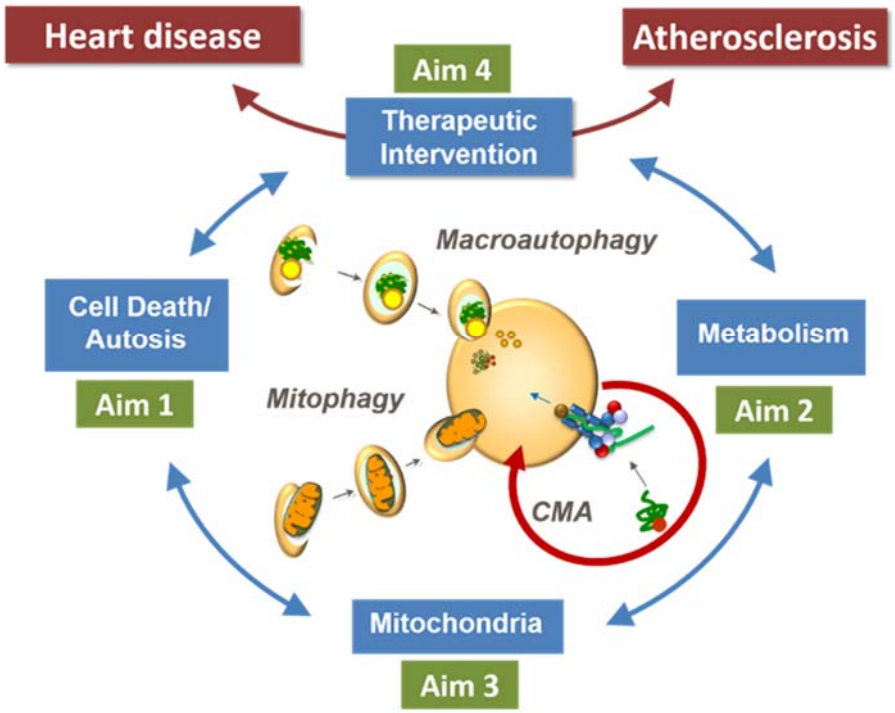
**“Modulating autophagy to treat cardiovascular disease”**

**ECI´s biosketch**



***Yun Chen – Richard Kitsis´ group***

Mitochondria play essential and diverse roles in the physiology of cells. Mitochondrial dynamic remodeling, programed 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 - Guido Kroemer's group***

Maria Chiara Maiuri obtained her PhD in pharmacology at the University of Napoli Federico II, Italy (2003). Then, she joined Guido Kroemer's team as a post-doctoral fellow. Since 2008, she is a permanent researcher in the team at the Centre de Recherche des Cordeliers, Paris, France. Chiara's research focuses on cell survival and cell death in physiopathological conditions. Currently, she is working on the molecular mechanisms controlling apoptosis and autophagy in human cancers. Other related projects aim at understanding the impact of autophagy in cystic fibrosis as well as in metabolism and obesity-related pathologies.

**Federico Pietrocola, Guido Kroemer's lab.**

**Federico Pietrocola** is a postdoctoral fellow at Cordeliers Research Center in Paris, France. After one-year Unipharma Fellowship at Curie Institut in France, Federico has joined Kroemer's lab in 2011 and obtained his PhD in Oncology in 2015. During his PhD, Federico has focused his attention on the crosstalk between the perturbations of metabolic homeostasis and the activation of autophagy. In particular, he found a correlation between Acetyl CoA levels and the activation of the autophagic process. This work has led to the identification and to a new molecular definition of Caloric Restriction Mimetics, molecules that are able to provoke (de) acetylation of proteins, culminating in the activation of autophagy. Federico is now investigating the pre-clinical (autophagy-dependent) potential of these agents in different pathological settings including, but not limited to, cancer, type 2 diabetes and obesity. Federico's main research interest is the relationship between variations of the metabolic status and autophagy, both in cell autonomous and non-autonomous manner. In the context of Leducq project, he will explore the pro-healthy effects of Caloric Restriction strategies in the prevention and treatment of cardiovascular diseases.

**Keywords** Acetylation; Caloric Restriction; Metabolic Syndrome; 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 Pattingre, 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 impared mitophagy, aminoacid metabolism and oxidative phosphorylation to study how one process affects the others in the heart.

***Biosketch Emilie Schrepfer – Scorrano´s group***

Dr Emilie Schrepfer is a postdoctoral fellow in Pr Luca Scorrano's lab at the Venetian institute of molecular medicine in Padua (Italy). She carried out her PhD in 2012 in Molecular and Cellular Biology at the Cancer Research Institute of Montpellier (France) in the team of Dr Laurent Le Cam. During her PhD, she characterized a novel level of regulation of the p53 pathway implicating the Mdm2 oncoprotein in the formation of an unpreviously described multiprotein complex associated with chromatin, independently of p53, and only in very specific experimental conditions, including some oxidative stresses.

In March 2013, Dr Schrepfer joined Luca Scorrano's team where she is interested in the interconnections existing between mitochondria and metabolism. In particular one of her project is to characterize the nature of the proteins associated with Mitofusin 2 in the formation and regulation of mitochondria-endoplasmic reticulum tethering. But she is also interested in a matrix mitochondrial protein phosphatase, called PPM1K, which appear to be at the crossroad between amino-acids catabolism and autophagy, to maintain the cell homeostasis in the context of fluctuating nutrient demand and supply.

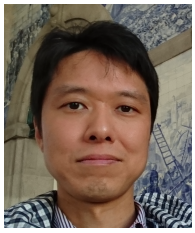
**Bianca Sander – Judith C. Sluimer's group**

**Bianca Sander** is a new PhD student of the Vascular Pathology group at the Maastricht University Medical Center. She has recently finished the master program "Molecular Cell Biology and Neurobiology" at the University of Technology in Kaiserslautern, Germany. During her master thesis, she supported fundamental research on Alzheimer's disease by analyzing the ubiquitination and endocytosis of the Amyloid Precursor Protein (APP) gene family.

During her PhD she will investigate the influence of different forms of autophagy as well as the therapeutical potential of autophagy regulation on advanced atherosclerosis. A main focus will be the reciprocal effects of autophagy on the (oxygen-) metabolism and the cell death of macrophages in atherosclerosis. The first project will be in cooperation with Ana Maria Cuervo and Julio Madrigal-Matute. It will assess the effect of chaperone-mediated autophagy (CMA) on atherogenesis as well as if PHD oxygen sensor degradation is the underlying mechanism by which CMA modulates cholesterol metabolism.

**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