Cardiovascular researchers funded by Societa Italiana di Cardiologia scholarships describe the funding and their research to Jennifer Taylor, BSc, MSc, MPhil.

The Societa Italiana di Cardiologia (SIC; see www.sicardiologia.it) provides scholarships for research on cardiovascular disease. Scientists are using them to investigate a number of different areas, including ischaemic heart disease, heart modelling, cardiac arrhythmias, and accelerated coronary atherosclerosis in the young, and in a variety of countries such as Belgium, Italy, the Netherlands, the United States, and Switzerland.

Cristina Balla, MD, PhD student, Department of Cardiology, Medical School, S. Andrea Hospital, Sapienza University, Rome, Italy

Dr Balla received a SIC scholarship in 2011 to conduct research abroad. The grant aims to promote international exposure of Italian PhD students and to build strong international collaborations beyond the year of support. As a result, Dr Balla was able to work as a research fellow in the lab of Federica del Monte, MD, PhD, at the Cardiovascular Institute, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA. The long-term development of this research experience was to establish a translational cardiology programme in collaboration with the Cardiology Department at Sapienza University in Rome, led by Professor Massimo Volpe, MD, (see http://circ.ahajournals.org/content/120/7/i37.full.pdf+html). In Boston, Dr Balla merged her clinical interest in arrhythmia with investigations into the molecular basis of electrical instability of the diseased myocardium, and acquired knowledge and new skills in basic research. Specifically, she increased her knowledge of the abnormalities in Ca2+ cycling associated with cardiac arrhythmias and heart failure and investigated the molecular alterations in human idiopathic dilated cardiomyopathy, focusing on protein misfolding and its role in Ca2+-dependent electrical instability. She studied the role of presenilin in Ca2+ homeostasis and myocardial function using a mouse model of loss of function of the cardiac isoform of presenilin.

In September 2011, Dr Balla presented her results, which showed that lack of presenilin-2 is associated with altered Ca2+ signalling, impaired cardiac contractility, an overall failing phenotype, and an increased arrhythmogenicity, as a J. N. Cohn Young Investigator award finalist of the Heart Failure Society of America. Within the same investigation, Dr Balla also studied the response of the failing heart to the accumulation of misfolded proteins using human tissue obtained at heart transplantation. Dr Balla plans to complete her training in cardiac electrophysiology and develop a career as an independent clinician scientist. She says, “I want to study the interplay between specific gene profiles and acquired cardiac disease in determining the unfavourable arrhythmogenic substrates that may lead to cardiac sudden death in heart failure patients.” This will include setting up a dedicated lab in her home institution in Rome and using her experience to build up an international collaborative research group to obtain European and international funding.

Reference

On other pages...
Lara Fornai, MV, PhD, researcher, Cardiovascular Pathology Unit, Department of Cardiovascular, Thoracic, and Vascular Science, University of Padua, Padua, Italy, and Foundation for Fundamental Research on Matter, Institute for Atomic and Molecular Physics, Amsterdam University, Amsterdam, the Netherlands

Dr Fornai is using an SIC scholarship to devise a novel method capable of generating a 3-dimensional molecular atlas of the rat heart. “Using imaging mass spectrometry, this can now be performed without the use of targeted chemical or biological labels,” she says. “As a result, 3-dimensional imaging mass spectrometry offers a unique new discovery tool where a plethora of molecular volumes can be generated directly from a collection of histological sections.”

New technologies, such as imaging mass spectrometry, are enabling molecular discovery in cardiovascular disease processes and its integration in diagnostic pathology. Secondary ion mass spectrometry is a new technology for local small molecule analysis directly on heart tissue surfaces. It provides high-resolution spatial images (500 nm pixel size) of molecules up to a molecular weight of 1500. Dr Fornai investigated the lipidomic profile of explanted human heart with heart failure. Mass spectral images clearly showed the different anatomical structures of the heart and their remodelling produced by diseases.

Dr Fornai hopes to identify novel and useful fragments of biomolecules in specific major areas of the explanted heart tissue: the pericardium, the myocardium, and the endocardium. This work would be innovative for research in heart failure by characterising molecules that map the spatial organisation in the heart’s structure.

The collaborative project between the Cardiovascular Pathology Unit, University of Padua, directed by Professor Gaetano Thiene, MD (see http://circ.ahajournals.org/content/118/19/f109.full.pdf+html) and the Institute for Atomic and Molecular Physics, directed by Professor Ron Heeren, PhD, is supervised by Professor Annalisa Angelini, MD, at the Cardiovascular Pathology Unit, University of Padua. The project has further expanded, setting up research collaboration with the Special Pathology Unit of Professor Marialuisa Valente, MD, at Padua University and the Mass Spectrometry Centre at the University of Florence, Florence, Italy with Professor Gloriano Moneti and Dr Giuseppe Pieraccini.

“The highly collaborative and integrated nature of this group of investigators allows us to keep focussed on clinically relevant problems and provide rapid paths to translational medicine,” says Dr Fornai.

Stefania Rizzo, MD, pathologist and PhD fellow, Cardiovascular Pathology Unit, Department of Cardiac, Thoracic, and Vascular Sciences, University of Padua Medical School, Padua, Italy

Dr Rizzo received a foreign fellowship grant from the SIC in 2011 for her project on accelerated coronary atherosclerosis in the young to allow her to spend the last 6 months of her PhD in the research group of Professor Giulio Gabbiani, MD, PhD, and Dr Marie-Luce Bochaton-Piallat, PhD, at the Department of Pathology and Immunology, Faculty of Medicine, University of Geneva, Geneva, Switzerland.

Dr Rizzo will investigate the molecular and cellular biology of accelerated coronary atherosclerosis in young people, in whom it exhibits distinctive features in terms of extent, site, and morphology of the plaques. It mostly consists of a single-vessel obstructive disease, usually affecting the proximal segment of the left anterior descending branch and characterised by fibrocellular plaques with exuberant proliferation of smooth muscle cells/myofibroblasts, and a variable amount of connective tissue, in the absence of a necrotic lipid core. Plaque instability leading to acute coronary syndrome may be due to endothelial erosion with lumen thrombosis or vasospasm. The vasospasm could be explained by both intimal hyperplasia, mostly composed of smooth muscle cells, and preserved tunica media.

Dr Rizzo’s project aims to identify the role of smooth muscle cell to myofibroblast differentiation in the formation of these atherosclerotic plaques in the young. She says, “Better knowledge of this phenomenon could allow a therapy to target plaque vulnerability and its consequences.”

The project will be supervised by Professors Gaetano Thiene, MD, and Cristina Basso, MD, PhD, expert investigators of the cardiovascular substrates of juvenile sudden death, and by Professor Gabbiani and Dr Bochaton-Piallat.

“The grant offers me the opportunity to learn new techniques to transfer to our lab in Padua,” says Dr Rizzo. “In Geneva, we will also exchange ideas and different approaches to researching cellular vascular biology to apply to cardiovascular pathology.”
Luigi Di Serafino, MD, PhD, clinical and research fellow in interventional cardiology, Cardiovascular Center Aalst, Onze-Lieve-Vrouw Clinic, Aalst, Belgium

Dr Di Serafino received an SIC scholarship in 2010 for the research project "Role of Endothelial Progenitor Cells on the Development of Coronary Collaterals in Patients With Coronary Artery Disease." "This has been the biggest opportunity for my career and for my scientific interests," he says. "I have had the chance to work in a reputed cath lab headed by Bernard De Bruyne, MD, PhD, where I could combine my experience in basic research with coronary pathophysiology."

Before receiving the funding, Dr Di Serafino worked as an interventional cardiologist at the Federico II University of Naples, Naples, Italy. He moved to the Cardiovascular Center Aalst for his SIC-funded research project because the centre is well known for its studies on coronary pathophysiology and collaborations. Dr Di Serafino is working on a number of projects investigating endothelial and platelet dysfunction as cardiovascular risk factors and cellular biomarkers of myocardial inducible ischaemia. His supervisors and mentors are Emanuele Barbato, MD, PhD, William Wijns, MD, PhD, Jozef Bartunek, MD, PhD, and Guy R. Heyndrickx, MD, PhD. The main purpose is to discover the pathophysiological mechanism triggered by myocardial ischaemia responsible for neovascularogenesis and collateral formation in patients with coronary artery disease. Understanding the pathophysiological mechanisms underlying the mutual communication among ischaemic tissues, atherosclerotic plaques, and progenitor cells could result in novel therapeutic strategies to treat ischaemic heart disease.

Working as a fellow at the Cardiovascular Center Aalst has made Dr Di Serafino understand the importance of tailoring percutaneous coronary interventions on the basis of fractional flow reserve to improve the clinical outcome for patients. He says, “The fractional flow reserve technique provides interventionalists with an ‘all-in-one approach’ to detect ischaemia and decide on the most appropriate treatment.’’

Demonstrating the safety and feasibility of the fractional flow reserve technique in complex anatomical cases, such as patients who have undergone coronary artery bypass graft surgery, is one of the projects Dr Di Serafino started with his fellowship in Aalst. The study showed that even in these complex anatomical cases, fractional flow reserve-guided percutaneous coronary intervention of intermediate stenosis in bypass grafts is safe and results in better clinical outcomes than angio-guided percutaneous coronary intervention.

**References**


Sonia Pennella, Biologist (BD), PhD student and research fellow, Advanced Research Laboratory of Cardiology and Angiology, University of Modena and Reggio Emilia, Modena, Italy, and University Sapienza, Rome, Italy

In Modena, Pennella is studying the proarrhythmic effects of intramyocardial administration of bone marrow stem cells and their effects on atrial fibrillation under the supervision of Professor Anna Vittoria Mattioli, MD, PhD, for a PhD in molecular and regenerative medicine. She has received an SIC scholarship to conduct a project on cellular molecular technologies in cardiovascular disease at the Sapienza University of Rome under the supervision of Professor Giacomo Frati, MD. Her investigations form part of a collaborative project between the universities of Modena and Rome on therapeutic strategies with stem cells in acute myocardial infarction. Both labs are members of the Istituto Nazionale per le Ricerche Cardiovascolari (National Institute of Cardiovascular Research), a university consortium of investigators from different scientific backgrounds with a common interest in basic and pathophysiological cardiovascular research. The Istituto Nazionale per le Ricerche Cardiovascolari has financed equipment for the project. Pennella aims to analyse and explore key aspects of cell therapy with a special emphasis on cardiac regenerative stem cells. She will investigate the proarrhythmic effects of intramyocardial injection of bone marrow stem cells in a preclinical model to establish whether it is possible to omit any steps in the process.

In the first arm of the project, Pennella will induce an acute myocardial infarction by ligation of the left anterior descending coronary artery, isolate bone marrow stem cells, and evaluate the presence of arrhythmic events after administering the cells. Proarrhythmic status and electrical remodelling will be calculated and analysed using specific electrocardiographic analysis software. In the second arm of the project, Pennella will compare the effects of intramyocardial injections of bone marrow stem cells and cardiospheres. Histological evaluation of cellular engraftment will be performed postmortem. Pennella says, “The histology, immunohistochemistry, and molecular biology will allow us to correlate functional and anatomical data with activation of the intracellular pathways. In the future we hope to establish further analytical techniques to better study the homing of cells.”

Serena Vitale, PhD, research fellow, Cardiology Research Laboratories of University of Perugia, Perugia, Italy, in collaboration with University of Modena and Reggio Emilia, Italy

Dr Vitale is using an SIC scholarship to carry out research in the Cardiology Research Labs directed by Professor Giuseppe Ambrosio, MD, PhD, at the University of Perugia. The Universities of Modena and Perugia are working on a collaborative project on the therapeutic project on the therapeutic strategies with stem cells in acute myocardial infarction. Dr Vitale’s project aims to analyse and explore key aspects of cardiac regenerative stem cell therapy, with a special emphasis on the pathophysiological mechanisms of stem cell recruitment in postischaemic tissues and on the events or interventions that may promote or inhibit this phenomenon.

The first arm of the project will evaluate in vivo recruitment of stem cells in postischaemic tissues using a model of intravital video microscopy of rat cremaster muscle, which allows direct visualisation and in vivo monitoring of the various phases of stem cell homing. This model, which has been widely used to study the effects of ischaemia reperfusion on the microcirculation and recruitment of neutrophils is not destructive, so it enables repeated measurements to be carried out over time. In the second arm of the project, Dr Vitale will use an in vivo model of rabbit myocardial infarction induced by ligation of the left coronary artery. The larger size of the animal will allow the use of imaging techniques (echocardiography, positron emission tomography) to assess myocardial response in terms of recovery of cardiac function and arrhythmic risk, thus obtaining supplementary and complementary information to that achieved by intravital video microscopy. In both settings, histology, immunohistochemistry, and molecular biology will allow the correlation of functional and anatomical data with activation of the intracellular pathways.

From 2003 to 2006, Dr Vitale studied the extracellular matrix of the ischaemic heart for her PhD under the supervision of Professor Stefania Montagnani, MD. She then studied the therapeutic use of mesenchymal and cardiac stem cells to repair cardiac damage in various experimental conditions, such as diabetes mellitus or senescence, at the Institute of Cardiovascular Research, New York Medical College, Valhalla, NY, under the direction of Professor Piero Anversa, MD.
Alberto R. De Caterina, MD, interventional cardiologist, Ospedale del Cuore G. Pasquinucci, Fondazione Toscana G. Monasterio, Massa and Istituto Scienze della Vita, Scuola Superiore Sant’Anna, Pisa, Italy

Dr De Caterina received funding from the SIC to conduct a prospective study he designed to test the pathophysiological and clinical utility of remote conditioning in ST-elevation myocardial infarction (STEMI). The study will test the hypothesis that the application of remote ischaemic preconditioning might be associated with an acute improvement of coronary microcirculatory dysfunction soon after vessel recanalisation. More importantly, it will test whether a combined conditioning protocol, including remote ischaemic preconditioning and postconditioning, is associated with an increase in myocardial salvage index and a decrease of final infarct size measured by magnetic resonance imaging.

In the study, 120 consecutive patients with STEMI undergoing primary percutaneous coronary intervention will be randomised by ambulance nursing staff to remote ischaemic preconditioning or placebo. Randomisation will take place directly during transport to the hospital, a hub centre that coordinates a STEMI network including 7 spoke centres and covering an area of 1300 km². Patients randomised to remote ischaemic preconditioning will receive 4 cycles of inflation and deflation of an arm cuff. Control patients will have a similar cuff placed around the upper arm that will not be inflated. At the end of primary percutaneous coronary intervention, the status of the coronary microcirculation will be invasively assessed by measuring coronary flow reserve and the index of microcirculatory resistance.

Patients initially allocated to remote ischaemic preconditioning will then receive remote ischaemic postconditioning soon after the end of primary percutaneous coronary intervention, at 6 hours and then daily from day 2 to day 4 after the index event. As well as routine angiographic, electrocardiographic, and echocardiographic evaluation, patients will undergo cardiac magnetic resonance imaging within 10 days after the index event to evaluate the presence and extent of microvascular obstruction and to measure the area of oedema (as a quantification of the area at risk) and at 4-month follow-up to quantify final infarct size.

Dr De Caterina says, “The funding I have received from the Italian Society of Cardiology will allow me to set up the initial complex phase of the organisation of the study, which involves the cooperation of a vast number of people, the coordination of 7 spoke centres, and the active involvement of ambulance staff.”

Angelo Quagliana, MD, researcher, Division of Cardiology, University Hospital Paolo Giaccone, University of Palermo, Palermo, Italy

Dr Quagliana received a young researcher award from the SIC in 2011. The lab group includes Salvatore Evola, MD, PhD, and is directed by Professor Salvatore Novo, MD, FESC, FACC. Their research focuses on the alteration of coronary microcirculation in a selected group of patients presenting with chest pain and unharmed coronary arteries. They have investigated the ability of essential hypertension to interfere with the regulation of blood flow in the coronary region as a potential cause of anginal syndrome in the absence of atherosclerosis. The pathophysiological mechanisms underlying endothelial dysfunction are not well understood, and the links between it and microvascular resistance to vasodilatory stimuli are even less clear.

Dr Quagliana says, “Our aim was to develop new diagnostic tools that could gauge the myocardial perfusion in angiographic sequences usually deemed to be limited in this regard.” Dr Quagliana and his colleagues tested some indices that have the potential to show evidence of altered regulation of flow resistance without added risk to the
patient or any increment in procedural cost. Using funding from the SIC, they compared the angiography results with perfusion imaging from myocardial single-photon emission computed tomography and tested the capacity of these indices to predict the results of myocardial perfusion imaging. The study of endothelial function in the same subjects is ongoing to clarify the links between the 2 processes that play a role in the onset of microvascular angina.

The group is also working on primary and secondary prevention of coronary artery disease, cardiovascular imaging, and interventional cardiology. They are conducting research on preclinical atherosclerosis and its capacity to overcome the current limits of cardiovascular risk charts, the role of systemic inflammation in the recovery of patients who have undergone a procedure to treat patent foramen ovale, the role of N-terminal prohormone of brain natriuretic peptide in the prognosis of patients with heart failure or acute coronary syndromes, and other topics considering cardiology patients holistically. Dr Quagliana says, “SIC funding has been indispensable for our projects, providing us with means that would otherwise be difficult to obtain.”

Reference
European Perspectives

Circulation. 2012;126:f79-f84
doi: 10.1161/CIR.0b013e318273f791
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/126/14/f79.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/