Awards: Finnish Foundation for Cardiovascular Research Grand Prize and Soisalo Award

Recipients of Finnish Foundation for Cardiovascular Research awards talk about their funding and research to Jennifer Taylor, BSc, MSc, MPhil.

Grand Prize 2011
Marja-Riitta Taskinen, MD, PhD, professor of medicine, Helsinki University Hospital, Biomedicum Helsinki, Helsinki, Finland

Professor Taskinen received the Grand Prize of €20,000 in 2011. She has contributed to ≈500 peer-reviewed articles and provided novel, cutting-edge discoveries concerning diabetic dyslipidaemia, insulin resistance, and nonalcoholic fatty liver disease. Her group recently showed that dual metabolic defects are required to produce hypertriglyceridemia in centrally obese subjects.1 Professor Taskinen comments, “This landmark article elucidates the role of liver fat content as the driving force for the overproduction of large, very low-density lipoprotein particles and the role of apolipoprotein CIII as the regulator of the removal capacity of triglyceride-rich lipoproteins.”

Professor Taskinen has been instrumental in organising the Fenofibrate Intervention and Event Lowering study that has provided novel data with respect to lipoproteins as cardiovascular disease risk factors. The group also reported that a replacement of traditional lipid measures by apolipoprotein B or apolipoprotein A-I provided no extra benefits in predicting cardiovascular disease risk in type 2 diabetes mellitus. Recently, Professor Taskinen’s team reported that incretin-based therapies improve postprandial lipaemia in people with diabetes mellitus.2 She says, “This discovery opens a new position for incretin-based therapies in diabetes care.” A series of articles by the group has elucidated the predictive values of lipid abnormalities as predictors of kidney disease and cardiovascular disease in type 1 diabetes mellitus. In addition, Professor Taskinen has contributed to understanding the metabolic and genetic defects in familial combined hyperlipidaemia and low high-density lipoprotein. The upstream transcription factor 1 gene on 1q21 was discovered to be a potential familial combined hyperlipidaemia gene regulating both glucose and lipid metabolism. Extensive phenotyping and genotyping of Finnish low high-density lipoprotein family members has helped to identify sequence variants for genotype effects. The metabolic studies identified major compositional differences in high-density lipoprotein subtypes and function in members of low high-density lipoprotein families. The lipidomics of high-density lipoprotein subclasses demonstrated extensive and significant compositional changes that also have functional consequences.

References
Grand Prize 2009
Markku Laakso, MD, PhD, academy professor, Institute of Clinical Medicine, Internal Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland

Professor Laakso was awarded the Grand Prize in 2009 for his work on cardiovascular disease complications, risk factors, type 2 diabetes mellitus, and insulin resistance, and their genetics. He was among the first to show that hyperglycaemia predicts cardiovascular disease complications in type 1 and type 2 diabetes mellitus. He also demonstrated that patients with type 2 diabetes mellitus are at the same risk for cardiovascular disease as nondiabetic subjects with a history of myocardial infarction, suggesting that type 2 diabetes mellitus is a “coronary heart disease equivalent.” He says, “This study was instrumental in changing the treatment guidelines for dyslipidaemia in the United States and other countries, and the article has been cited 2700 times so far.”

Professor Laakso was the first to show that asymptomatic atherosclerosis is associated with insulin resistance. In a series of articles on the association of insulin sensitivity with dyslipidaemias, he showed that low high-density lipoprotein cholesterol and familial combined hyperlipidaemia are associated with insulin resistance, whereas familial hypercholesterolemia is not. He also demonstrated that hyperinsulinaemic microalbuminuria is a new risk indicator for coronary heart disease, and that metabolic syndrome predicts coronary heart events.

Over the past 10 years, Professor Laakso has published several articles on the genetics of cardiovascular disease and its risk factors. With his collaborators, he identified new loci for early-onset coronary heart disease and the upstream stimulatory factor 1 gene (USF1) as a new risk gene for familial combined hyperlipidaemia. He has also been involved in studies identifying new gene variants for cardiovascular risk factors: type 2 diabetes mellitus, dyslipidaemia, blood pressure, and obesity. Professor Laakso has carried out all his research at the University of Eastern Finland, and his main international collaborators include Professor Francis Collins, MD, PhD, National Institutes of Health, Bethesda, MD; Professor Michael Boehnke, PhD, Ann Arbor, MI; Professor Päivi Pajukanta, MD, PhD, and Professor Jake Lusis, PhD, University of California Los Angeles, Los Angeles, CA; and Professor Karen Mohlke, PhD, North Carolina, NC.

References

Grand Prize 2007
Professor Yrjo Antero Kesaniemi, MD, PhD, FAHA, professor of medicine and chief of medicine, Oulu University Hospital and University of Oulu, Oulu, Finland

Professor Kesaniemi was awarded the Grand Prize in 2007 for his work on lipid metabolism, particularly cholesterol metabolism and its relation to atherosclerotic cardiovascular diseases, gene–environment interactions, the role of nutrition in lipid metabolism, metabolic syndrome, and the treatment of high cholesterol levels in the prevention of cardiovascular diseases. He received €20000 and a diploma, and he gave a presentation to the committee of the Finnish Foundation of Cardiovascular Research and the media.
“We conducted the landmark Scandinavian Simvastatin Survival Study (4S),” says Professor Kesaniemi. This randomised trial of cholesterol lowering in 4444 patients with coronary heart disease showed that simvastatin lowered total and low-density lipoprotein cholesterol, increased low high-density lipoprotein cholesterol, and improved survival.1

Professor Kesaniemi’s research has been conducted at the University of California, San Diego, with Professor Scott M. Grundy, MD, PhD, University of Helsinki, with Professor Tatu A. Miettinen, MD, PhD, and during the past 25 years in Oulu with his own research group.

Reference
example, that T-wave alternans, measured during routine exercise test, gives additional prognostic value over standard risk predictors,” he says. “Based on our work, I was invited by the International Society for Holter and Noninvasive Electrocardiology to participate in the preparation of the international guideline for T-wave alternans published in 2011.” The Finnish Cardiovascular Study, which recruited >4000 patients undergoing a routine clinical exercise test at the Tampere University Hospital, Tampere, Finland, is Dr Nieminen’s main source of data, but he also analysed the nationally representative Health 2000 Survey with >8000 participants.

From 2009 to 2010, Dr Nieminen worked as a visiting assistant professor at Harvard University and Beth Israel Deaconess Medical Center, Boston, MA, in the lab of Richard Verrier, PhD. He says, “During that period, in addition to the work on risk stratification and T-wave alternans, we performed large animal studies focusing on the effects of ranolazine.”

2010: Markus Juonala, MD, PhD, specialist in internal medicine and endocrinology, Turku University Central Hospital, Turku, Finland

Dr Juonala was awarded the Pauli Soisalo Memorial prize in 2010. His research is based on the Cardiovascular Risk in Young Finns Study, a multicentre follow-up study of 3596 Finns with a baseline age of 3 to 18 years to investigate the effect of childhood risk factors on the pathophysiology of atherosclerosis. Dr Juonala’s PhD thesis focused on the associations between childhood cardiovascular risk factors and early markers of atherosclerosis. As a postdoctoral researcher, he has been leading a group of PhD students. The primary focus of the group is to study the effects of metabolic risk factors in childhood and early adulthood on later cardiovascular health. Dr Juonala says, “This work has revealed that metabolic syndrome diagnosed in either childhood or adulthood is predictive of carotid atherosclerosis and its progression in adulthood, but that favourable changes in lifestyle associated with weight maintenance or reduction improve cardiovascular health.1

Dr Juonala has since continued his work at the University of Turku within the Young Finns Study group coordinated by Professor Olli Raitakari, MD, PhD, and Professor Jorma Viikari, MD, PhD. In addition, he has been an active member of the International Childhood Cohort (i3C) Consortium, a collaborative effort among several longitudinal cohort studies around the world (www.i3cconsortium.org). A recent article based on data from 4 cohorts (1 in Finland, 2 in the United States, and 1 in Australia) has given novel insights on the effects of childhood obesity. Dr Juonala says, “The study provided long-term follow-up data suggesting that cardiovascular risk factor status in adulthood is normalised if childhood overweight or obesity does not lead to adult obesity.”

References


2008: Tuomas Rissanen, MD, PhD, cardiologist, North Karelia Central Hospital, Joensuu, Finland

Dr Rissanen currently supervises 2 PhD students in the Department of Biotechnology and Molecular Medicine, A. I. Virtanen Institute, University of Eastern Finland, Kuopio, Finland. He received the Soisalo Prize in 2008 and comments, “It was an important kickoff for further studies in cardiovascular gene therapy, and it provided me with the opportunity to conduct research alongside clinical work.”

Dr Rissanen’s group has studied the possibility of promoting therapeutic vascular growth including capillary vessels (angiogenesis) and collateral arteries in ischaemic myocardium and skeletal muscle using gene therapy.

The programme of gene therapy for therapeutic angiogenesis was launched in 1998 by Professor Seppo Ylä-Herttuala, MD, PhD, FESC. Dr Rissanen has worked in this programme from the beginning, and 3 students have accomplished their PhD degree under his supervision so far. “We have developed both a novel chronic lower limb ischaemia model in the rabbit and a novel chronic percutaneous myocardial ischaemia model in the pig using a stent shaped in a bottle neck form to restrict coronary blood flow,” he says. “We have used both adenoviruses and adeno-associated viruses to induce gene transfer in ischaemic skeletal muscle and myocardium.”

In contrast to adenoviruses, adeno-associated viruses generate a long-lasting therapeutic effect up to 1 year, holding significant promise. The group has used vascular endothelial growth factors and hypoxia-inducible factors among others as therapeutic vascular growth factors. “We have shown that blood flow can be temporarily increased by 20- to 30-fold in skeletal muscle by adenoviral vascular endothelial growth factor gene transfer,” says Dr Rissanen. “The main histological finding in skeletal muscle and myocardium is dramatic capillary vessel enlargement together with sprouting angiogenesis.”

In myocardium, gene transfer is performed by a sophisticated percutaneous 3-dimensional mapping system. Some vascular endothelial growth factors mainly induce the growth of lymphatic vessels and can be used to alleviate tissue oedema. Therapeutic angiogenesis using intramyocardial gene transfer of vascular endothelial growth factor-D is currently being tested in a phase II clinical trial for “no-option” patients with severe angina.

Dr Rissanen says, “I have worked with enthusiastic skilled researchers without whom my work would not be possible. The contributions of Johanna Lähteenvuo, MD, PhD, Petra Korpisalo, MD, PhD, Juha Rutanen, MD, Henna Niemi, MD, Ismo Vajanto, MD, Antti Kivelä, MD, Tommi Heikura, MSc, Jussi Nurro, Paavo Halonen, and Professor Juha Hartikainen, MD, PhD, have been especially crucial.”

Jennifer Taylor is a freelance medical journalist.
Each year the Swiss Society of Cardiology awards the Cardiovascular Biology prize for original work in cardiovascular disease carried out by a scientist <40 years of age who is a Swiss citizen or working in Switzerland. The prize of CHF 30,000 must be used to continue his or her research.

“The Prize Encouraged Me to Study the Biology of Inflammatory Progenitors and the Mechanism of Myocardial Fibrogenesis in Inflammatory Dilated Cardiomyopathy More Extensively”

Gabriela Kania, PhD, independent research associate, Cardioimmunology Group, Department of Cardiovascular Research, Institute of Physiology, University of Zürich, Zürich, Switzerland, won the Cardiovascular Biology prize in 2010 for her 2009 article “Heart-Infiltrating Prominin-1+/CD133+ Progenitor Cells Represent the Cellular Source of Transforming Growth Factor Beta-Mediated Cardiac Fibrosis in Experimental Autoimmune Myocarditis.” She says, “In this article, we identified inflammatory progenitor cells as the key compartment of pathological remodelling in inflammatory heart disease and pointed to the critical role of epigenetic factors in this process.”

An appropriate inflammatory response to stress and injury, whether viral, autoimmune, ischaemic, or mechanical, attenuates injury, enhances survival, accelerates repair, and preserves organ function. In contrast, an inappropriate response amplifies injury, promotes cell death, enhances fibrosis, and accelerates organ failure. Heart-specific inflammation (myocarditis) is a common cause of pathological tissue remodelling and heart failure, with the phenotype of inflammatory dilated cardiomyopathy. “In my research, I take advantage of the experimental autoimmune myocarditis model to study mechanistic and physiopathological aspects of the progression of acute cardiac inflammation into end-stage heart failure,” says Dr. Kania.

The end-stage heart failure in experimental autoimmune myocarditis is identical to the phenotype observed after infection with cardiotropic viruses and mirrors important aspects of human inflammatory dilated cardiomyopathy. Recently, Dr. Kania studied how single cytokines modulate postinflammatory fibrogenesis and heart failure progression by affecting progenitor cell fate and function. She says, “I believe that therapeutic strategies modulating the in vivo fate of inflammatory progenitors might prevent cardiac fibrosis and pathological remodelling.”

The ultimate goal of Dr. Kania’s research is to translate basic research principles into clinical studies. In basic research, she plans to continue her studies on the cardiovascular physiopathology cross-talking between stem cell research and heart pathology, mainly in inflammatory dilated cardiomyopathy, but she aims to broaden her research interests into other cardiovascular disorders as well. “Synergistically, I plan to transfer the experimental knowledge about the physiopathology of the inflamed heart into the clinical setup and confront this understanding with the cardiovascular outcomes,” says Dr. Kania.

“Generally, my research touches the processes mediating inflammation resolution, pathological remodelling of the affected heart and the key role of inflammatory progenitors...”

Two recipients of the Swiss Society of Cardiology Cardiovascular Biology Prize, Gabriela Kania, PhD, independent research associate, Cardioimmunology Group, Department of Cardiovascular Research, Institute of Physiology, University of Zürich, Zürich, Switzerland, and Elena Osto, MD, PhD, postdoctoral fellow, Department of Cardiovascular Research, Division of Cardiology, Institute of Physiology, University of Zürich, describe their research to Jennifer Taylor BSc, MSc, MPhil.

Funding: Swiss Society of Cardiology Cardiovascular Biology Prize 2009 and 2010

Dr Kania with some of her colleagues in the Cardioimmunology Group. From left to right, Przemysław Błyszczyk, PhD, Dr Kania, Marta Bachmann, and Professor Urs Eriksson, MD, who heads the group. Photograph courtesy of Dr Kania.
in the transition from inflammation into the inflammatory dilated cardiomyopathy phenotype. I am convinced that I will fulfil my research goals in the near future, and I hope to lift my academic position to the professorial level.”

She adds, “The prize encouraged me to study the biology of inflammatory progenitors and the mechanism of myocardial fibrogenesis in inflammatory dilated cardiomyopathy more extensively. Furthermore, this funding allowed me to continue and finish several projects and opened new avenues in my scientific career. It facilitated my receipt of research grants and invitations to the editorial boards of the European Heart Journal and Stem Cell Studies and as a lead guest editor of the special issue ‘Stem Cells in Heart Failure’ in Stem Cells International.”

“During This Period, I Had the Opportunity to Connect and Network with Other Scientists in Zürich”

Elena Osto, MD, PhD, research associate, Department of Cardiovascular Research, Division of Cardiology, Institute of Physiology, University of Zürich, won the Cardiovascular Biology prize in 2009. She obtained a medical degree in 2002 and carried out specialist medical training in cardiology at the School of Medicine, Padua University, Padua, Italy. Since 2005, she has been a research fellow in the Department of Cardiovascular Research at the University of Zürich, directed by Professor Thomas F. Lüscher, MD, and has collaborated with Professor Francesco Cosentino, MD, PhD, to investigate molecular mechanisms of endothelial dysfunction. She was awarded the prize for her original research project on the pathophysiology of atherosclerosis focusing on endothelial dysfunction and foam cell formation in the setting of hypercholesterolaemia, which resulted in 2 articles in Circulation titled “Inhibition of Protein Kinase C Beta Prevents Foam Cell Formation by Reducing Scavenger Receptor A Expression in Human Macrophages” and “c-Jun N-Terminal Kinase 2 Deficiency Protects Against Hypercholesterolemia-Induced Endothelial Dysfunction and Oxidative Stress.” The prize was presented to Dr Osto in June 2009 during the Swiss Society of Cardiology annual congress in Lausanne, Switzerland. It allowed Dr Osto to work as a PhD student on new projects focusing on the molecular mechanisms underlying endothelial dysfunction and vascular inflammation driven by oxidative stress using in vitro and in vivo models. She says, “During this period, I had the opportunity to connect and network with other scientists in Zürich.”

Dr Osto completed her PhD at the University of Padua and moved back to Zürich in January 2011 for a 5-year fellowship supported by the Fondation Leducq Transatlantic Networks of Excellence in Cardiovascular Research Program. The network is an international collaborative research consortium with members in Europe and the United States and aims to elucidate novel aspects of high-density lipoprotein dysfunction in the development of cardiovascular disease and as a therapeutic target.

Under the guidance of Professor Lüscher and Professor Ulf Landmesser, MD (see http://circ.ahajournals.org/content/123/15/f85), Dr Osto’s current work in Zürich aims to unravel novel concepts on how and why high-density lipoprotein’s vascular protective effects (e.g., promotion of cholesterol outflow from macrophages and immune cells that accumulate in atherosclerotic plaques, inhibition of inflammation and clotting, and stimulation of vascular repair) are lost in patients with atherosclerosis and whether the beneficial properties of high-density lipoprotein might be restored by new pharmacological approaches.

References


Jennifer Taylor is a freelance medical journalist.
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