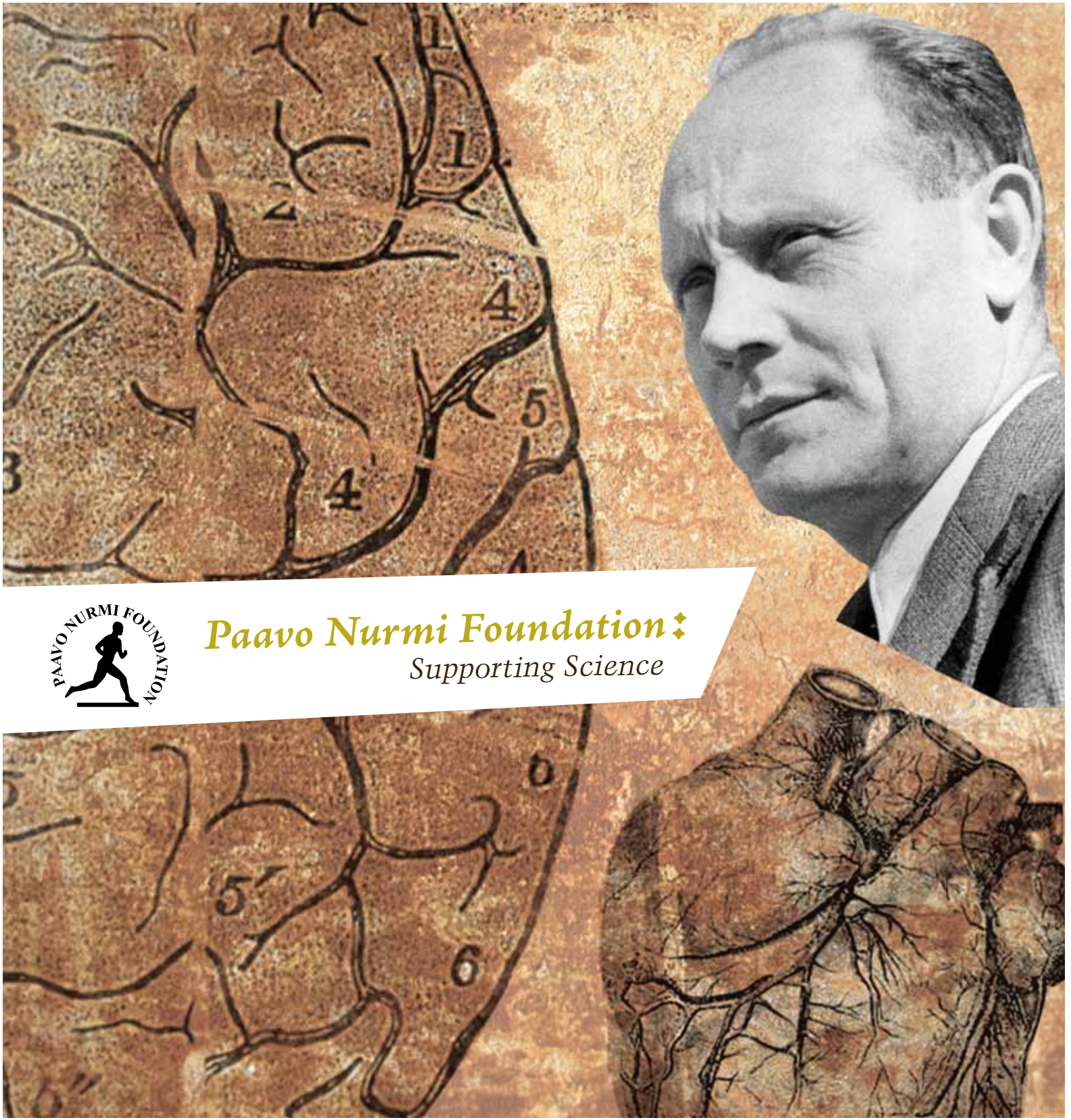
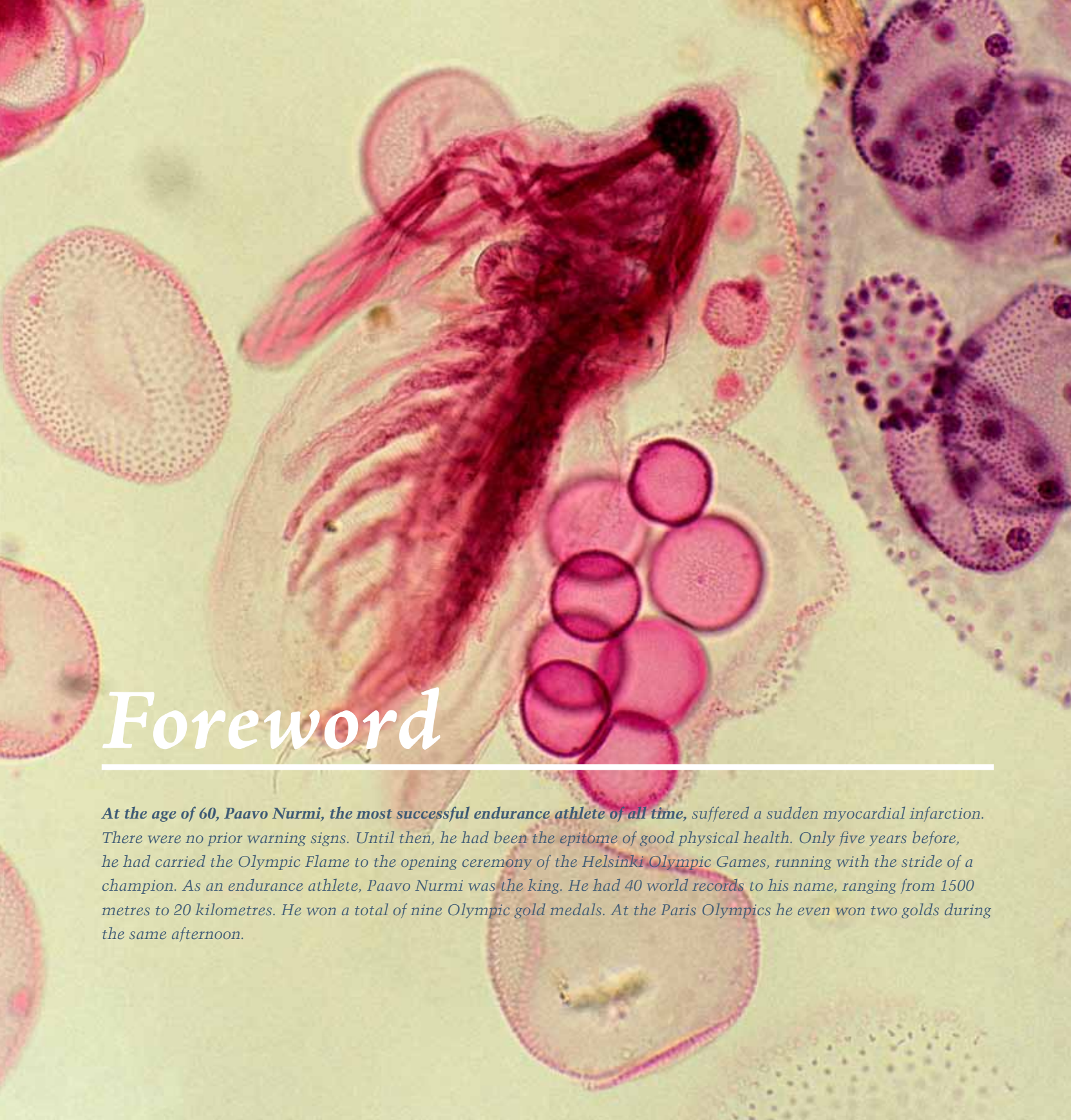


Paavo Nurmi Foundation

Supporting Science

Supporting Science



Foreword

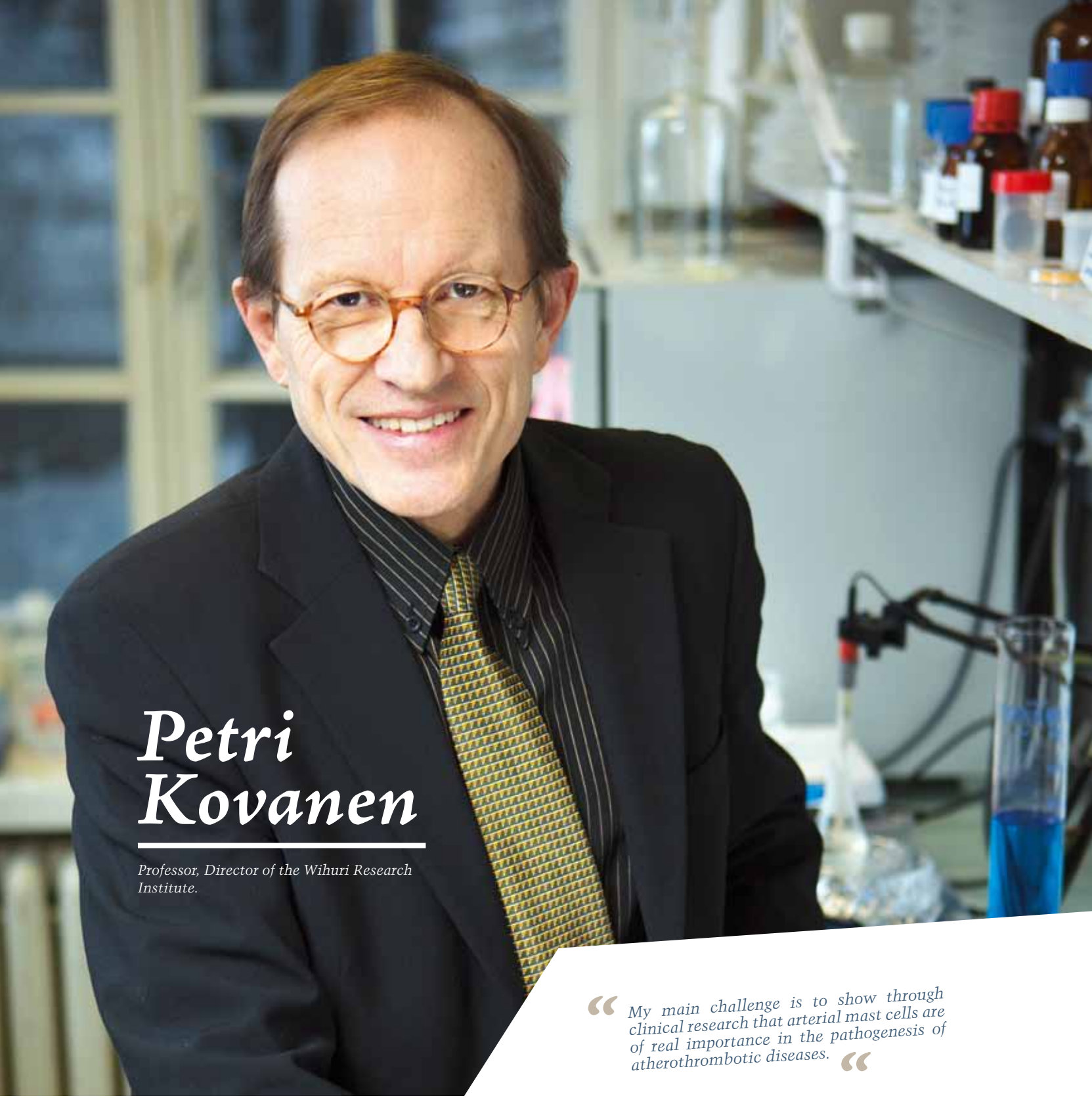
At the age of 60, Paavo Nurmi, the most successful endurance athlete of all time, *suffered a sudden myocardial infarction. There were no prior warning signs. Until then, he had been the epitome of good physical health. Only five years before, he had carried the Olympic Flame to the opening ceremony of the Helsinki Olympic Games, running with the stride of a champion. As an endurance athlete, Paavo Nurmi was the king. He had 40 world records to his name, ranging from 1500 metres to 20 kilometres. He won a total of nine Olympic gold medals. At the Paris Olympics he even won two golds during the same afternoon.*

During training, Paavo Nurmi was the very image of perseverance, willpower, self-discipline and talent. After his career as an athlete, he became a successful businessman. As such his principles were unchanged: only success and winning mattered. His reputation as a building contractor and investor also became legendary. While his success in the business world brought great wealth to the man who had been the poor son of a carpenter, it did not bring a long, healthy life. Paavo Nurmi had none of the risk factors for heart disease known at the time. He discussed the possible reasons for his illness at such an early age with leading heart experts, arriving at the conclusion that the illness was not fully understood. ***In 1968, being a practical person, Paavo Nurmi decided to establish a foundation carrying his name to solve the puzzle of heart disease.***

The Paavo Nurmi Foundation operates along two main lines: it arranges international conferences for top scientists and offers grants for individual researchers. *The themes of the conferences, which are held every few years, are selected with a view to the future. For each theme the aim is to clarify the current situation: what is not yet known and what should be done. Conference themes have included blood coagulation (1968) and myocardial infarction (1979), long before thrombolytic therapy was introduced in the treatment of vascular diseases. Another ground-breaking conference dealt with the role of infections in the pathogenesis of cardiovascular diseases. So far, there have been 16 conferences. Worldwide, these conferences have been considered crucial in keeping remote Finland in touch with the world's leading researchers, who are also respected by the Nobel Committee.*

By providing grants for individual researchers, the Paavo Nurmi Foundation became the first body in Finland to offer promising and already distinguished scientists the opportunity to engage in research work without the need for other paid employment. *Projects supported by the Foundation include the start of dialysis treatment and doctor ambulance services in Finland. Several young scientists have gone on to high academic achievements. Some of them are presented on the following pages. Of course, funding from the Paavo Nurmi Foundation has only been a small factor in their work. The Foundation is delighted to help promote the success of promising researchers.*

VESA MANNINEN
D.Med.Sc., professor
Paavo Nurmi Foundation
Vice-chairman



Petri Kovanen

Professor, Director of the Wihuri Research Institute.

“My main challenge is to show through clinical research that arterial mast cells are of real importance in the pathogenesis of atherothrombotic diseases.”

Petri Kovanen:

I graduated as a Specialist in Internal Medicine from the University of Helsinki in 1984. That same year, I was invited to be the "lipid expert" of the Wihuri Research Institute located in Kaivopuisto, Helsinki. The activities of the Institute's Salus hospital had been discontinued, but a decision had been made to continue basic research into heart diseases at the Salus laboratory. I am still on that road: first as Scientific Director, and since 1997, as Director of the Institute.

I have always been interested in natural sciences and their mysteries. My first particular interest was astronomy, followed by inorganic chemistry and biology. A small telescope, microscope and a home laboratory brought a touch of reality to my dreams. Antero Vipunen-style tricks also helped me. Several periods of illness prompted an interest in medicine: I wanted to breathe the hospital air, not as a patient but as a research physician, able to view even laboratory test tubes from a completely different angle. I studied medicine in Basel, Switzerland, where I also did my doctoral research in the Department of Physiological Chemistry. The subject of my research was fatty acids in skeletal muscle, and my thesis was completed in 1970. In Finland I completed a second doctoral thesis in 1975, in the scientific laboratory of Professor Esko Nikkilä. The purpose of this research was to shed light on cholesterol metabolism in fatty tissue. My third research location was in Dallas, where I worked from 1976 to 1980 in the laboratory of Michael Brown and Joseph Goldstein, who were later awarded the Nobel Prize. The work involved studying the metabolism of LDL particles. It is easy to remember the landmark moment of my Dallas years: I was overjoyed to see that statin medicines increased the number of LDL receptors in the liver. At the same time we learned how statins reduce the LDL cholesterol concentration in serum.

In 1984, the newly elected director of the Wihuri Research Institute, Docent Vesa Manninen, asked for my assistance in a research project initiated by Professor Pentti Halonen before his retirement. The project had an interesting non-mainstream research question that was typical of Prof. Halonen: how histamine release from mast cells might affect the blood lipid metabolism of a rabbit that had been fed cholesterol. That was the beginning of intensive research work with my colleague Jorma Kokkonen, research that I have continued to do until this day with different teams. I quickly altered the original research strategy: I was not interested in LDL cholesterol metabolism in the blood, but rather at the cellular level in the arterial wall. Thus began the still ongoing series of research projects to determine the effects of mast cells in the arterial wall on the pathogenesis of atherosclerosis. What happens to LDL and HDL lipoprotein particles in the arterial wall in the early stage of the disease, and how can mast cells affect the structure of the atherosclerotic plaque formed on the arterial wall in the late stage? I had the opportunity to discuss these research results with leading international researchers in 1989 during the symposium "Lipoproteins and Pathobiology of the Arterial Intima" supported by the Paavo Nurmi Foundation and held at Haikko Manor, Finland.

We have observed mast cells in the walls of atherosclerotic arteries. The more advanced the stage of the disease, the more mast cells there are in the arteries. The mast cells in atherosclerotic plaque are activated to secrete proteases, enzymes that break down proteins, into their environment. These enzymes may accelerate the accumulation of cholesterol in the plaque, and may subsequently weaken the structure of the plaques, making them more likely to rupture and cause atherothrombotic complications. Thus, mast cells in an atherosclerotic coronary artery may play a part in the pathogenesis of myocardial infarction, while the mast cells in an atherosclerotic carotid artery may make a person vulnerable to cerebrovascular disorders and trigger a stroke. Mast cells in a distended atherosclerotic aorta may weaken the structure of the aorta and increase the risk of aortic rupture.

My main challenge is to show through clinical research that arterial mast cells are of real importance in the pathogenesis of atherothrombotic diseases. Since the inhibition of mast cell function has no known adverse effects, and as medicines that inhibit their function are already being used, the potential for conducting such clinical experiments exists. The International Paavo Nurmi Foundation Award that I received in 1997 for research on cardiovascular diseases has spurred me on along my chosen research career.

Markku S. Nieminen

Director, Department of Medicine,
Helsinki University Central Hospital

“I am grateful to the Paavo Nurmi Foundation for the support they gave me in the 1980s and for their support to several researchers at my department, which has had a considerable impact on the development of cardiological research in Finland.”

Markku S. Nieminen:

I am Professor of Cardiology at Helsinki University Central Hospital Division of Cardiology, and since 2009, Director of the Department of Medicine.

Since 1972 the focal point of my career has been research into heart diseases. I became interested in heart diseases while attending clinical courses at the Faculty of Medicine. To ask about potential research topics, I contacted Professor Pentti J. Halonen, who was then at the I Division of Internal Medicine and who was also one of the founding members of the Foundation. My doctoral thesis concerned the application of echocardiography to determine the scale and normalisation of myocardial infarction, an internationally ground-breaking study at that time. The thesis was completed in 1977. I later graduated as a specialist in Internal Medicine, and during the first phase of my career I went to Harvard Medical School on a Fulbright scholarship, where I worked under the renowned Professor Eugene Braunwald in Peter B. Brigham's research laboratory for experimental cardiology. On returning to Finland in 1981, I specialised in cardiology and, partly thanks to my academic success, obtained a post as a cardiologist at the Cardiac Evaluation Unit at the HUCS I Division of Internal Medicine. Since then I have held the positions of Assistant Professor of Internal Medicine and Deputy Chief Physician of the outpatient clinic for Cardiology. Since 1997 I have been Professor of Cardiology and Chief Physician at the Division of Cardiology.

I have worked extensively with the Paavo Nurmi Foundation. In the 1980s, my research concerned myocardial infarction, medication for cardiac insufficiency and certain congenital heart problems. One of the key issues in myocardial infarction is the development of cardiac insufficiency. As a result, I treated patients with very severe insufficiency. I was also in a central position in developing a heart transplantation programme, in which I was the lead cardiologist from 1985 to the beginning of my duties as Chief Physician. Additionally, I was involved in introducing cardiac arrhythmia studies and angioplasty in Finland and also participated in developing cardiology education.

In addition to these numerous duties, I have led my own research group and engaged in research, particularly the study of coronary heart disease (CHD) and cardiac insufficiency. We have focused on the effect of lipid-lowering therapies such as fibrates on the development of CHD and seen that effective lipid-lowering treatment may halt the progress of coronary heart disease and reduce patient morbidity. Over the past few years, we have continued our research into coronary heart disease and myocardial infarction by launching an extensive study of over 5,000 patients to assess the molecular genetic mechanisms that affect the development of CHD and its serious consequences, including the mechanisms behind arrhythmia. We expect interesting results regarding certain regulatory genes that influence these mechanisms.

I have been very much involved in developing new pharmacotherapies for the treatment of cardiac insufficiency. For example, we have demonstrated the efficacy of levosimendan for this purpose, and shown that this product also improves the prognosis of the patients. Naturally, we have also noticed problems in the course of the project. We have also conducted an extensive series of studies on patients with acute insufficiency, and shown that certain important biomarkers indicating renal and cardiac insufficiency also correlate with the prognosis. While serving on the boards of the European Society of Cardiology and its insufficiency section, I led an extensive European exploratory study into cardiac insufficiency. We looked at the differences between patients with acute insufficiency and those with chronic insufficiency with regard to the mechanisms of cardiac disease and co-morbidity. The findings of the study have had international significance in the long-term planning of treatment for cardiac insufficiency.

Ilkka Pörsti

Professor of Internal Medicine, Specialist in Internal Medicine and Nephrology, Docent in Pharmacology, University of Tampere and Tampere University Hospital.

"When I was studying medicine, my father, who was a specialist in internal medicine, prompted me to seek research work as a way of succeeding in the world of medicine."

Ilkka Pörsti:

I am 50 years old, and a Professor of Internal Medicine, Specialist in Internal Medicine and Nephrology, and Docent in Pharmacology at the University of Tampere and Tampere University Hospital.

My working week is divided into three main areas: basic-level and specialist-level teaching for physicians, clinical patient work and research work. My duties also include administrative work both at the university and at the university hospital. In addition, I am in charge of a research group comprising five physicians working as doctoral researchers, five medical students, a Master of Science in Technology graduating soon, a Master of Biotechnology, a statistician and two study nurses.

When I was studying medicine, my father, who was a specialist in internal medicine, prompted me to seek research work as a way of succeeding in the world of medicine. I followed his advice and embarked on research work. However, my progress was slow, particularly at the early stage. My thesis was completed several years behind schedule, and it certainly did not deal with the first topic I examined. This slow progress was partly due to the guidance I received – or more to the point, did not receive, as was the case with many others. After I had acquired expertise in vascular research, I tested my abilities as research supervisor. Over the years, this has led to 11 completed doctoral degrees.

My research concerns the effects of hypertension and kidney disease on the cardiovascular system, particularly on the blood vessels. With regard to kidney disease, my particular interest lies in the hormonal regulation of calcium and phosphorus metabolism. Over the last four years, we have developed an extensive, non-invasive protocol for assessing the structure and function of the human cardiovascular system. We believe that this protocol will provide a lot of new information on the cardiovascular system.

The first vascular mechanism that hypertension disturbs is the dilation of blood vessels, i.e. their relaxation into a less constricted state. This is why the mechanisms that normally dilate the vessels do not function as well in hypertension, which over time makes the situation worse and increases blood pressure even more. In renal insufficiency, many adverse changes occur in the blood vessels, exposing the patient to worsening of vascular lesions and to harmful cardiovascular events. With the help of the cardiovascular system protocol, we have observed that there can be very different mechanisms behind a similar elevation in blood pressure. This has opened new possibilities in both the research and the treatment of hypertension.

Marja-Riitta Taskinen

Professor Emerita, researcher at the Division of Cardiology and member of a working group at Biomedicum.

“The real challenge today is to foster an interest in clinical research among young medical students and physicians and encourage them to continue in research even after completing their Ph.D. Clinical researchers seem to be an endangered species.”

Marja-Riitta Taskinen:

I am a Professor Emerita, and I work at the Division of Cardiology as a researcher, while my research group works at Biomedicum.

I was Professor of Internal Medicine at the University of Helsinki from 1991 to 2008, working in the III Division of Internal Medicine and, after the divisions merged, in the endocrinology and cardiology units. I have also been a visiting research professor at the University of Cincinnati, Ohio, from 1978 to 1979, and in the diabetes research unit of NIH (National Institute of Health) in Phoenix, Arizona, from 1983 to 1984. From 2000 to 2004, I was "Nordic Professor", a joint professorship between the Universities of Helsinki and Gothenburg. This was the beginning of close collaboration with the lipid researchers at the Wallenberg Institute, work that is still ongoing today.

When I was just "a young amanuensis", during Christmas leave, the haematologist Pekka Vuopio encouraged me to ask for a summer job in 1963 from Professor Esko Nikkilä, the Chief Physician of III Division of Internal Medicine, and that was where it all started. My first job was in the Department of Medicinal Chemistry, where Prof. Nikkilä's research laboratory was located. My first project was to develop a method for plasma insulin measurement to help study the connection between insulin and myocardial infarction. An article about my work was published in The Lancet in 1965. Today, high insulin concentrations and insulin resistance are known risk factors in coronary heart disease. The subject of my thesis, "Effects of free fatty acids and triglycerides on insulin secretion", was a great idea from Prof. Nikkilä. The subject is still topical, because over the last few years it has been shown that extra fat is also accumulated in the pancreas and cells, disrupting their functions. The Paavo Nurmi Foundation supported my research from 1985 to 1990. This enabled me to work as a researcher at a critical time when, among other issues, I was applying for the position of professor. Over the years, the Paavo Nurmi Foundation has also supported the younger members of my research group. This funding has been extremely important for our research.

We have had several lines of research. Our central aim has been to clarify the nature of lipid metabolism disorders, the underlying disorders of lipoprotein metabolism and the related genetics. My interest in HDL cholesterol and the disorders of its metabolism arose early in the 1980s, and I have continued this line of research after Prof. Nikkilä's passing. Low HDL and high triglyceride concentrations are associated with metabolic syndrome and type 2 diabetes, which are common risk factors in arteriopathy today. Over the last 10 years, we have used stable isotopes to trace the production and metabolism of triglycerides and apoproteins in the liver. Our studies have shown that hepatic steatosis increases the production of triglyceride-rich particles and their release into the bloodstream. This disorder is associated with the presence of small, dense LDL particles and a low HDL concentration. This dangerous triad is a typical disorder in patients with type 2 diabetes. I have also been involved in several extensive international studies into the effects of various medicines on blood lipid metabolism disorders. The most important of these has been the FIELD study, which involved a total of some 9,500 patients with type 2 diabetes from three countries (Australia, New Zealand and Finland). There were 1,500 Finnish participants from two centres, and I acted as the principal investigator in Finland. The study was published in The Lancet in 2005. The FIELD research group still produces important results: I was just recently in Sydney finishing a publication which shows that the traditional cholesterol ratios (total cholesterol / HDL cholesterol) are just as suitable for cardiovascular disease risk assessment as the apo B / apo A-I ratio. The fruits of my research work include about 350 original publications in international scientific journals, and over 100 literature reviews.

I find research work enjoyable, not only with regard to lab and patient work but also to the important tasks of supervising young researchers and acting as the voice of science both in Finland and internationally. I believe that information acquired from research should be transferred to the treatment of patients as quickly as possible.

Ville Valtonen

Professor, Chief Physician,
Division of Infectious Diseases,
Helsinki University Central Hospital.

“One of the most important events of my career as a researcher was the opportunity I got in 1992 to arrange with the support of the Paavo Nurmi Foundation an international conference in Hanasaari, Helsinki.”

Ville Valtonen:

I am glad to have had the opportunity to collaborate with many important researchers and to supervise young researchers.

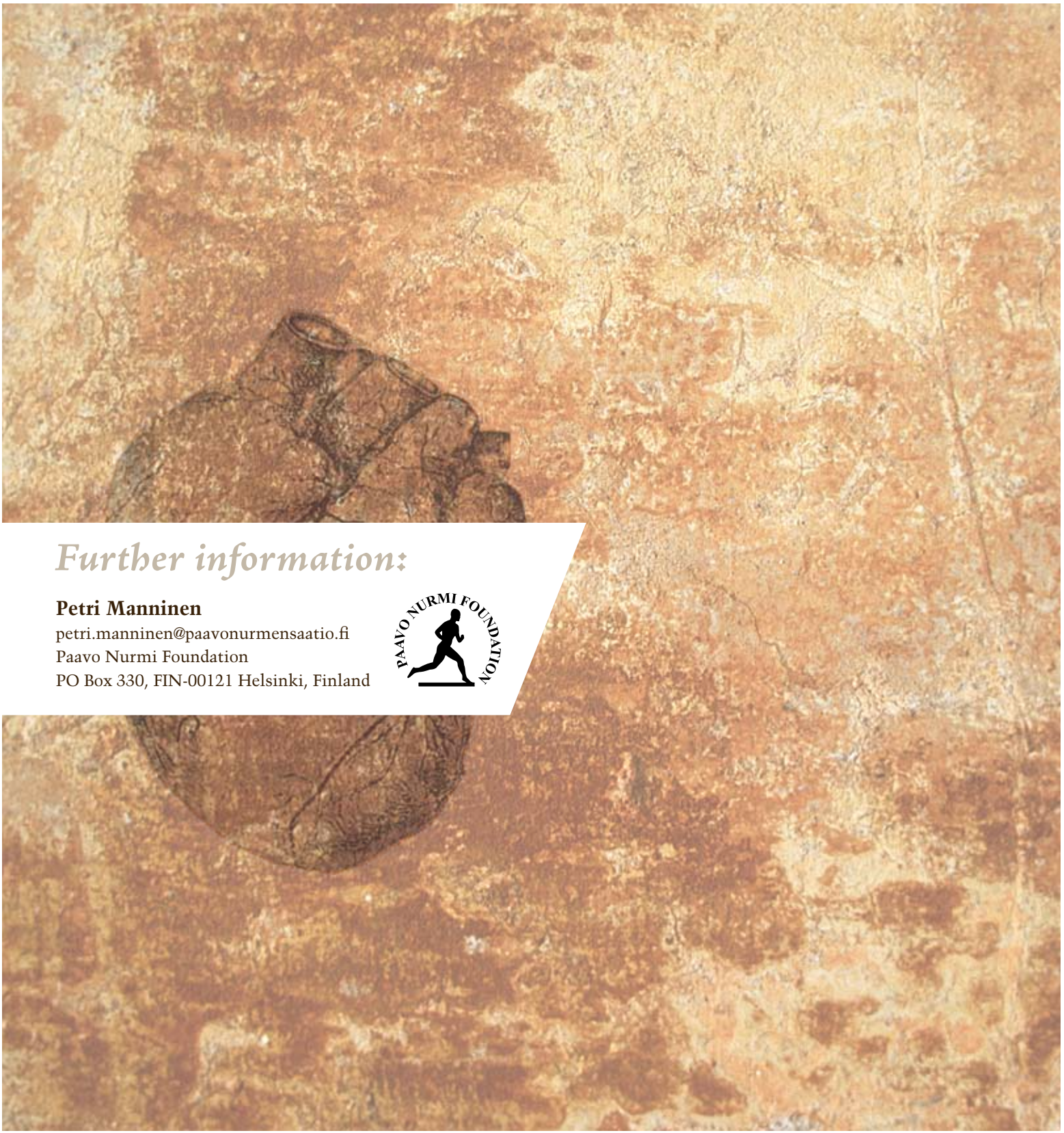
I was born in Helsinki in 1944. I obtained my Licentiate in Medicine in 1969 and defended my doctoral thesis in Medicine and Surgery in 1972 at the University of Helsinki. My thesis concerned the influence of the cell wall structure of salmonella bacteria on their pathogenicity. Later on, in the 1970s, I specialised in Internal Medicine and Infectious Diseases at Helsinki University Central Hospital (HUCH). I became a Docent in Clinical Microbiology in 1976, and in Internal Medicine in 1987. I have held several posts at HUCH and at the University for over 38 years, the last ten years as Chief Physician of the Division of Infectious Diseases. I was awarded the title of professor in 1998.

My researcher training was good, first in my doctoral research under the supervision of academician Pirjo Mäkelä, and later on as a researcher at Harvard Medical School, Boston from 1977 to 1978. My main area of research over the past 30 years has been the importance of infections in the aetiopathogenesis of cardiovascular diseases. My enthusiasm for the subject first arose when I saw in clinical work young patients with no known risk factors suffering a cerebral or myocardial infarction after an acute infection.

I have been fortunate to work with many famous researchers; let me name Pekka Saikku and Maija Leinonen, with whom I have investigated the role of chlamydia pneumonia in the aetiopathogenesis of atherosclerosis. I have studied the role of infections in the pathogenesis of myocardial infarction for decades with Markku Nieminen, and in the pathogenesis of ischaemic stroke with Markku Kaste. Pirjo Mäkelä and Jussi Huttunen have supported me from the beginning. I have had the pleasure of supervising the doctoral research of many young researchers, including Kimmo Mattila and Jaana Syrjänen, both investigating (particularly dental) infections as risk factors for cardiac and cerebral infarction in the late 1980s.

Over the last ten years, I have worked with Juha Sinisalo, Marja-Liisa Lokki and others. In this connection I would like to single out the doctoral thesis of Anil Palikhe, which demonstrated that certain HLA types protect against coronary disease while other types act as risk factors. Infections have proved to be an important risk factor in the pathogenesis of cardiovascular diseases. However, experiments with antibiotic therapy have yielded partly conflicting and negative results in the secondary prevention of cardiovascular diseases, one exception being influenza vaccination, which has turned out to be an important means of reducing cardiovascular mortality. At the moment, the potential of pneumococcal vaccination in the reduction of cardiovascular diseases is being investigated in other countries, because it seems that pneumonia quite often precedes myocardial infarction.

One of the most important events of my career as a researcher was the opportunity I got in 1992 to arrange with the support of the Paavo Nurmi Foundation an international conference in Hanasaari, Helsinki, at which the world's leading researchers discussed the role of infections in the pathogenesis of cardiovascular diseases. I am deeply grateful to the Paavo Nurmi Foundation for this support.



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