Spotlight:
David Eisner, MA, DPhil, FRCP (Hon), FMedSci
A “Basic PhD Scientist” Who Is Happy in the Lab Interacting With Researchers and Whose Studies Over the Past 20 Years Have Increased Understanding of Cardiac Contractility in Health and Disease

David Eisner, British Heart Foundation professor of cardiac physiology, University of Manchester, Manchester, England, talks to Judy Ozkan, BA.

While working for a DPhil in physiology in the late 1970s in the lab of Professor Denis Noble, CBE, FRS, FMedSci, at Oxford University, Oxford, England, David Eisner, MA, DPhil, FRCP (Hon), FMedSci, British Heart Foundation professor of cardiac physiology, University of Manchester, Manchester, England, investigated the properties of the sodium–potassium pump in the heart with Jonathan Lederer, MD, PhD, now professor of physiology at the University of Maryland, Baltimore, Md, then a visiting postdoctoral fellow. Together with Richard Vaughan-Jones, now professor of cellular physiology at Oxford University, Eisner and Lederer also characterised the dependence of contraction on intracellular sodium concentration. This work led to an appreciation of the importance of sodium–calcium exchange in controlling cardiac contractility and also to the interactions controlling intracellular calcium, sodium, and proton concentrations.

These early influences proved enormously important for Professor Eisner’s career, and he is grateful for the “light touch” of his mentors and supervisors, in contrast to the proliferation of bureaucracy that PhD students face today. He says, “I’m happy with what I’ve done, but I accept that some of it has been down to pure chance. I don’t believe you can plan a career entirely, and I believe that if I’d done something else, I’d probably also be happy with that.”

“We Unravelled How Calcium Release From the Sarcoplasmic Reticulum Controls Calcium Fluxes Across the Surface Membrane”
Professor Eisner was born in Manchester, England, in 1955 into an academically oriented family. With a physicist father and an economist mother, he and his 3 siblings grew up in a household where learning, education, and academia were the norm. During secondary school in Manchester, Professor Eisner’s interest in physics emerged, mostly driven by a fascination with early 20th-century discoveries in areas such as relativity, and he subsequently chose to study physics at Cambridge University, Cambridge, England. He entered King’s College in 1973 but found that the subject was not quite what he had expected. He explains, “When I arrived, I found there were people who could look at equations a mile long and know what they meant. I wasn’t one of them. My math wasn’t quite good enough for that. However, the advantage of being at Cambridge was that, no matter what you wanted to do, you had to take 3 or 4 different subjects, and 1 of my subjects was physiology. At that time, physiology in Cambridge was dominated by studies on ion movements across cell membranes, basically physics applied to life.”

Eisner’s interest in physiology was encouraged by his first-year supervisor, Dr Arieh Lew, whom Professor Eisner
describes as “my first real mentor.” Dr Lew continues to carry our research on red blood cell physiology and pathology in Cambridge. Under his influence, Eisner pursued his studies into physiology and later went on to specialise in the subject. Professor Eisner recalls, “I remember him telling me that the most important reason for embarking on a research career is to enjoy it.”

Eisner emerged from Cambridge with a degree in natural sciences in 1976, and he went to Oxford University to complete his DPhil in physiology in 1979. A brief postdoctoral period back in Cambridge followed in the lab of Professor Ian Glynn, FRS, working on the kinetics of the red blood cell sodium pump before he took up his first academic post in 1980 as a lecturer in the Department of Physiology of University College London, London, England. He is grateful to the then head of department, Tim Biscoe, DSc, FRCP, for smoothing the transition from post-doc to independent faculty member. Professor Eisner is concerned that the present trend to combine departments into many larger structures results in the loss of this important mentoring role.

At University College London, Eisner found himself in a lab next to that of David Allen, PhD, now professor of physiology, University of Sydney, Sydney, Australia, who had recently made the first measurements of intracellular calcium in the heart. Together with Clive Orchard, now dean of the Faculty of Medical and Veterinary Sciences, Bristol University, Bristol, England, Allen and Eisner performed the first studies characterising the control of diastolic calcium in cardiac muscle and also made the first measurements of intracellular calcium waves. Isabelle Baro, PhD, now a National Institutes of Health and Medical Research team leader in Nantes, France, was one of Professor Eisner’s first PhD students in London.

Between 1990 and 1999, Eisner worked as a professor of veterinary biology at the University of Liverpool, Liverpool, England. During this time, he collaborated extensively with Stephen O’Neill, PhD. Andrew Trafford (a veterinary graduate) then joined him as a graduate student, and together they made measurements of the calcium content of the sarcoplasmic reticulum and studied how sarcoplasmic reticulum calcium content is controlled. He says, “We unravelled how calcium release from the sarcoplasmic reticulum controls calcium fluxes across the surface membrane. These changes of calcium fluxes, in turn, control sarcoplasmic reticulum calcium content leading to a feedback loop regulating sarcoplasmic reticulum content. This has major consequences for understanding inotropic interventions.”

In 2000, Eisner was appointed British Heart Foundation professor of cardiac physiology at the University of Manchester, where his first PhD student was Luigi Venetucci, MD, PhD, with whom he studied the factors that influence calcium waves in cardiac myocytes and how such waves might be treated. He says there is likely to be more involvement in clinical applications as the research group becomes increasingly more involved in translational research with clinicians in Manchester.

Professor Eisner describes himself as a “basic PhD scientist” who is happy in the lab interacting with his researchers. Mentoring emerging new talent is 1 of the more rewarding aspects of his role, but he says that the unrelenting growth in bureaucracy and administration is a downside that can be quite draining. He also enjoys editing scientific journals and is editor-in-chief of the Journal of Molecular and Cellular Cardiology and a senior consulting editor of Circulation Research. Until July 2000, he was chair of the editorial board of the Journal of Physiology.

Despite publishing in the region of 150 articles, Professor Eisner is wary of putting too much emphasis on number crunching. He says, “When I first started my work, no one seemed worried about where their articles were published or citation records, but now in the United Kingdom, there is a worrying emphasis on citation figures and other metrics.” He suggests that this is a retrograde step because people who need to assess other scientists for appointments and promotions are not reading the articles.

As an active member of numerous international and national societies, Professor Eisner has held many roles, including chair of the working group of cardiac cellular electrophysiology of the European Society of Cardiology, and he is president-elect of the Federation of European
Physiological Societies. He was awarded the Pfizer Prize for Biology in 1985 and the Wellcome Prize in Physiology in 1988, and he has given a number of named lectures. He was elected to the Fellowship of the Academy of Medical Sciences in 1999, and he was recently (2010) elected as an honorary fellow of the Royal College of Physicians, which he describes as a great honour.

Professor Eisner’s advice for young fellows is, “Follow your own instincts and seize every opportunity even if at first you can’t predict where it will lead.” He has particularly enjoyed his interactions with other scientists (with just a couple of exceptions) and has found them cooperative rather than unpleasantly competitive.

In Europe, in addition to those mentioned already in this article, Professor Eisner has benefited enormously from discussions and interactions with Karin Sipido, MD, PhD, from the University of Leuven, Leuven, Belgium, and Godfrey Smith, PhD, from the University of Glasgow, Glasgow, Scotland.

One investigation that Professor Eisner would most like to have done himself is the seminal study by Cheng, Cannell, and Lederer,11 which, he says, “revolutionised how we think about calcium signalling and is a beautiful study.”

Professor Eisner’s wife is Sue Wray, PhD, professor of physiology at the University of Liverpool. They met at University College London in the 1980s, celebrated their silver wedding anniversary in 2008, and still collaborate scientifically.12,13 Although they share similar career paths, their 3 children have forged their own careers in a variety of roles as a police officer (Emily), an events manager (Thomas), and a medical student (Mark). Away from the demands of his work, Professor Eisner enjoys walking, travel, and photography, including photographing colleagues during conferences.

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Spotlight:
Nilesh J. Samani, BSc, MD, FRCP, FACC, FMedSci

Raising the Profile of the University of Leicester, Leicester, England, on the International Map for Cardiovascular Research

Nilesh J. Samani, British Heart Foundation professor of cardiology, University of Leicester, Glenfield Hospital, Leicester, England, head of the Department of Cardiovascular Sciences, University of Leicester Medical School, and director of the Leicester National Institute for Health Research Cardiovascular Biomedical Research Unit talks to Judy Ozkan, BA.

Born in Kenya in 1956, Nilesh J. Samani, BSc, MD, FRCP, FACC, FMedSci, British Heart Foundation professor of cardiology, University of Leicester, Glenfield Hospital, Leicester, England, head of the Department of Cardiovascular Sciences, University of Leicester Medical School, and director of the Leicester National Institute for Health Research Cardiovascular Biomedical Research Unit, had his future mapped out at an early age by his paternal grandfather. Having arrived almost penniless in Africa from India in 1928, Samani’s grandfather and father worked hard to establish a profitable printing business from scratch. They had a burning ambition for the next generation in the family to become professionals. Professor Samani explains, “My grandfather’s best friend was a senior doctor in the small town of Kitale where we lived. His doctor friend provided good clinical care and was so well respected that he was also asked to give advice in many other ways. My grandfather wanted his grandchild to have the same respect from and influence on a community.”

With the decision made, the family left behind their comfortable lifestyle in Kenya and moved to the United Kingdom in 1971 for educational reasons. Professor Samani says, “Education in Kenya at the time was very good to the secondary school level but not beyond.” As a teenager, Samani worked hard at secondary school to fulfill family expectations. Luckily, he enjoyed science, and when he finished school, in 1975, medicine was his first choice. When the question of where to study medicine came up, the answer appeared almost on his doorstep in the newly opened Leicester University Medical School. Samani thus began an association with the medical school, which has endured >30 years. He was 1 of the first doctors and, later, the first professor to graduate from Leicester University Medical School. He recalls, “The first medical school intake was privileged. All the lecturers knew us by name and wanted feedback about the course and teaching methods. We were enthusiastically welcomed into the clinical environment.”

When Samani graduated with distinction in 1981, he took a house officer position under the late, inspirational John Swales, MD, FRCP, then the highly regarded professor of medicine at the University of Leicester and an expert in hypertension. This was followed by a 3-year postgraduate rotation at Guy’s and Hammersmith Hospitals, London, England, where Samani enjoyed working with high-calibre academics, so whetting his appetite for an academic career. When he returned to Leicester in 1985 as Professor Swales’ registrar, he investigated possible areas of research. Professor Swales was prescient enough to recognise the likely impact of molecular biology on medicine and encouraged him to pursue this field. It was sound advice, and there was no shortage of support from Bill Brammar, PhD, then professor in the Department of Biochemistry at Leicester University, whose group had recently cloned the renin gene, a key molecule regulating the cardiovascular system.

“Recognition of the High-Quality Cardiovascular Research Being Done by My Academic and Clinical Colleagues in Leicester”

Under Professor Brammar’s guidance, Samani was awarded a 3-year Medical Research Council clinical training fellowship in molecular biology. He says, “This was an exciting time for molecular biology and its application to medicine. Almost everything we worked on provided novel and interesting insights.” Samani was then keen to continue research in combination with clinical training in cardiology. This was not a common practice at the time, certainly not in Leicester.

A solution came along in the shape of the late David de Bono, FRCP, who arrived at Leicester from the University of Edinburgh, Edinburgh, Scotland, in 1989 as the British Heart Foundation professor of cardiology. Professor Samani says, “He was very supportive and under his mentorship and the continued guidance of John Swales, I was able to complete clinical training in cardiology and continue with research. I was fortunate to be one of the few people at that time in cardiovascular medicine in the United Kingdom working in molecular biology.” Professor Samani was subsequently appointed as a senior lecturer and consultant in 1993 at Leicester University Medical School, and became the first graduate of the medical school to become a professor in 1997. He was appointed British Heart Foundation professor of cardiology in 2003 and, in the same year, was asked to head the newly formed...
Looking back, Professor Samani says, “I was very lucky that the medical school opened in Leicester in 1975, just as I finished school, and that David de Bono moved to the University in 1989 just as I was seeking a clinical academic training post in cardiology.”

An exciting development that will further facilitate research in Leicester is the establishment of a UK National Institute for Health Research Biomedical Research Unit in Cardiovascular Disease at Glenfield Hospital in early 2009. Professor Samani says, “The purpose of Biomedical Research Units is to promote translational research and we are proud that we have been awarded such a unit. It is recognition of the high quality cardiovascular research being done by my academic and clinical colleagues in Leicester.”

“The British Heart Foundation Family Heart Study and the British Genetics of Hypertension Study Have Contributed Significantly to Our Understanding of the Genetic Basis of Hypertension and Coronary Disease”

Having “stumbled” into molecular biology, Professor Samani’s early work focused on the genetic regulation of the renin-angiotensin system, and he recognised the potential for using genetic markers to investigate the genetics of cardiovascular diseases. Initially, he looked at experimental models of hypertension to locate some genes that influence blood pressure. In the mid-1990s, he helped set up a UK-wide collaboration to identify families with multiple members with high blood pressure, the British Genetics of Hypertension (BRIGHT) study. Then, in the late 1990s, together with colleagues from the University of Leeds, Leeds, England, he set up a similar study of coronary artery disease, the British Heart Foundation Family Heart Study. Both studies have proved extremely valuable in improving understanding of the genetic basis of these diseases.

Professor Samani says, “What is remarkable is that when we first set up these studies our ambitions were modest—we only planned to study ≈400 genetic markers. But as technology has improved we can now study more than 1 million variants. The key here was to assemble excellent cohorts to take advantage of new technologies as they became available and we have not finished yet with realising the full potential of the BRIGHT and British Heart Foundation Family Heart studies. The genes we have identified that are associated with risk of hypertension and coronary artery disease are providing completely new insights into the pathophysiology of these diseases, which we believe will translate into better and more targeted approaches to their prediction, prevention and treatment. One of the great joys of this work on tracking genes for heart disease has been the opportunity to work collaboratively with many bright and wonderful colleagues not only in the United Kingdom, but also in Europe and the United States. This has resulted in lasting friendships.”

Professor Samani’s research priorities in the short and medium term are, “To understand how the new genes we have identified work and affect risk of coronary artery disease and how best to translate this novel information into clinical use. This will require a range of research approaches from basic work in the lab all the way to large-scale epidemiological studies and we are gearing up for the new challenges.”
"Coronary Disease May Be a Disease of Premature Biological Ageing"

Another important strand of work that Professor Samani started with Professor de Bono is the link between coronary artery disease and biological ageing. He explains, “We know coronary artery disease is a disease connected to ageing, yet we often see people in their 70s and 80s whose arteries are clear. We wondered why some people seem to be protected from coronary artery disease, whereas others get it at a much younger age than one would anticipate from their risk profile. We developed the concept that some people age biologically quicker than others. Using telomere length as a marker of biological ageing, with shorter telomeres indicating more advanced biological age, we showed that there is an association between shorter telomeres and the occurrence of coronary artery disease. This small initial study has sparked a huge interest in this field from many researchers worldwide. Whether the association has any causal basis remains to be established. Our own further work has shown for example that benefits from statin treatment are only seen in people with shorter telomeres.”

“Although There Are Often Multiple Demands on My Time, I Wouldn’t Want to Stop Seeing Patients”

Professor Samani spends his leisure time focusing on active parenting and family life, as well as playing sports, especially tennis and golf, when time allows, but he regrets that his family has sometimes seen a lot less of him than he would have liked. He is married with 2 teenage boys, aged 14 and 17. He comments, “Despite my efforts to make the older I do something else, he seems keen to embark on a career in medicine. I know that both of them see the workload I carry around, so it is a pleasant surprise that at least one of them wants to go into medicine. Half of my ‘official’ time is spent in clinical duties as an interventional cardiologist. The other half involves academic duties. I have my own British Heart Foundation research group of 25 people to look after, and as head of the Department of Cardiovascular Sciences and director of the Leicester National Institute for Health Research, I administer more than 200 other people and 15 professors. My wife says I do 3 full-time jobs.”

Although keeping so many plates spinning simultaneously creates pressure, dropping the clinical duties is not an option for Professor Samani. He says, “I entered medicine to help people, and although there are often multiple demands on my time, I wouldn’t want to stop seeing patients.” He attributes his success to support from not only his immediate family, who have had to contend with heavy demands on his time, but also to his wider family, who gave up a privileged lifestyle in Kenya so that he and his 3 sisters could access a better standard of education. Colleagues and mentors have also played their part. "I have been lucky to have had some excellent mentors and academic and clinical colleagues over a 35-year association with the University of Leicester, and I feel privileged to have had an opportunity to work in such a supportive environment.”

Professor Samani’s grandfather lived to see his grandson graduate, start his research, and achieve senior lecturer status. He was immensely proud, though it was not quite the leisurely life of the family doctor he had known in small-town Kenya. Professor Samani says, “He was puzzled that I had to get up in the middle of the night and at weekends to see patients, even when I became more senior. His vision of being a doctor was based on something entirely different.”

Professor Samani is a fellow of the UK Academy of Medical Sciences, the American College of Cardiology, and the European Society of Cardiology. In 2007, he was appointed as a senior investigator by the UK National Institute for Health Research. He is proud to have helped to put the University of Leicester on the map of cardiovascular research, and he advises his students to “Get the question right and focus on an area. Provided you’ve got the big question right, then opportunities will come along.”

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European Perspectives

Circulation. 2010;122:f13-f18
doi: 10.1161/CIR.0b013e3181e8eb7f
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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/122/3/f13.citation

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