For Dr Massimo Mariani, becoming a heart specialist was a case of continuing the family tradition. His father, Mario Mariani, MD, is a cardiologist at the cardiac and thoracic department at the University of Pisa, Italy, and is also a past president of the Italian Society of Cardiology. Born in Italy and now living in the Netherlands with his wife and 3 children, Dr Mariani traces his desire to get into medicine not only to his family’s influence but also to a natural passion for the discipline. His aspirations became focused further during his pregraduation internship at the University of Pisa, when he had the opportunity to attend some cardiac surgical procedures. “I was impressed and inspired by what I saw,” says Dr Mariani.

After his undergraduate studies in Pisa finished in 1989, Dr Mariani went on to fulfil part of his training in Italy and part in the Netherlands. He began his career at the San Raffaele Hospital in Milan, Italy, and then he moved to the University Hospital of Siena, Italy.

For his next, unusual step, he went to Rosaria, Argentina, where, he says, “I had the privilege of training with Federico Benetti, MD, PhD, one of the pioneers of beating-heart surgery.” From there, Dr Mariani moved to the Netherlands to the University Hospital of Groningen in 1996. He became assistant professor of cardiac surgery at the University of Pisa in 2000, where he stayed until 2004, when he took up his current position at the Thoraxcenter, Twente.

He says, “I have been interested from the very beginning in innovative techniques and new technologies, either for diagnostic tools or for surgical devices. In my view, the results of cardiac surgery are very much influenced by the technology. These aspects have conditioned my interests and my choices from the beginning of my career.”

Areas of particular interest include general adult cardiac surgery (see Figure), particularly beating-heart surgery, mitral valve plasty, atrial fibrillation, heart failure, and aortic and aortic arch surgery. But, he adds, “I have abandoned robotic surgery because I believe that current robotic systems need to be further developed.” He hopes to focus more on the surgery of atrial fibrillation and heart failure because of the epidemiological growth of these diseases. Dr Mariani also would like to work toward further improving the short- and long-term results of coronary artery surgery; he says, “Coronary artery bypass grafting still remains the procedure of choice for multivessel coronary artery disease. The results so far from the use of drug-eluting stents for patients undergoing percutaneous coronary intervention are not leading to the promised land that many cardiologists expected.”

Reflecting on those who were most influential in his career, he comments, “It’s a long list. I try to learn something from everyone I work with. This includes the bad teachers,

On other pages...

**Spotlight: Massimo Mariani, MD, PhD, FECTS**

At the age of only 41, Dr Massimo Mariani already has a high profile as a teacher and as a consultant at the Thoraxcenter, Twente, Enschede, the Netherlands. He specialises in beating-heart surgery, atrial fibrillation, surgery to the aorta, and aortic arch surgery. He speaks with Mark Nicholls about his work.

---

**Centres of Excellence: A New Project in Spain**

Valentin Fuster, MD, PhD, FESC, discusses his latest venture, the Centro Nacional de Investigaciones Cardiovasculares, a development that he hopes will profoundly influence cardiological research in his home country.

Page f104

**Viewpoint: Frank Enseleit, MD**

Dr Frank Enseleit does not want to leave Europe, but he recognises that he will inevitably need to go to work in the United States at some point to further his career. He reflects on his journey so far and the rewards of research.

Page f106
because I could learn from their mistakes.” He points out that it ultimately involves endeavouring to be a better man and a better surgeon. “Learning never stops,” he says. The people who have inspired and motivated him, he says, “were excellent surgeons and good men.” They include Dr Benetti, Tjark Ebels, MD, PhD, FECTS, and Jan Grandjean, MD, from the University Hospital of Groningen.

Dr Mariani finds motivation in helping people and in getting them back to leading normal lives, saying, “Their gratitude keeps pushing me ahead. I want to do better every day for my patients.” When it comes to advice for young surgeons aiming to follow a similar path into cardiac surgery, he considers it crucial to stay focussed on the task but also to have respect for your own body. “You must be physically and mentally 100% if you are going to help other people,” he says. “Above all, respect your patients and take your time to listen to them.”

For the future, he wants to keep training young doctors to become surgeons. “It’s really rewarding for me to see young talented doctors growing up through the various difficulties and becoming professionals who can make the difference.” His proudest personal achievement to date—like that of so many parents—is being a good father to his 3 children. “But, professionally speaking,” he adds, “I am proud to be chosen, together with my colleague Dr Grandjean, as a training centre for off-pump coronary surgery. I am proud to regularly receive colleagues from all over the world and to be able to teach them tips and tricks about off-pump surgery. It’s rewarding, and it gives me the opportunity to get to know colleagues who are coming from far away and to help them improve their practice.”

Looking to the future of cardiac surgery, Dr Mariani sees the comeback of coronary artery surgery, emphasising that stenting is not living up to expectations in the long term, and he believes that valvular surgery will increase. “In other words, even if most of my colleagues are worrying for their own future, I see a growing need for cardiac surgery.” The key challenges, concludes Dr Mariani, lie in the realms of gene therapy, stem cells, regeneration of scar tissue, and the search for the ideal valve that will be long lasting and have no need for anticoagulation.

However, it is not all work for Dr Mariani. He has his family, and away from work he enjoys cycling, jogging, sailing, and skiing.

Mark Nicholls is a freelance medical writer.

Centres of Excellence: A Spanish Cardiovascular Research Initiative

A Major European Research Project Gathers Momentum

Valentin Fuster, MD, PhD, FESC, president of the scientific and external evaluation committee of the Centro Nacional de Investigaciones Cardiovasculares, discusses his latest venture—a development that will profoundly influence cardiological research in his home country—with Jennifer Taylor, BSc.

Dr Valentin Fuster, director of Mount Sinai Heart, New York, NY, has been based in the United States for 36 years, but he has never lost touch with the cardiovascular community of his home country, Spain. His latest venture has been setting up the research activities of the new national centre for cardiovascular investigations, the Centro Nacional de Investigaciones Cardiovasculares (CNIC), where he is president of the scientific and external evaluation committee, a project that will involve him in spending increasing amounts of time in Spain.

Dr Fuster agreed to the post only under certain conditions. He wanted funding from the federal government to
be matched by private enterprise, with this joint funding used in 2 ways: first, to discover young researchers of the future, and second, for research to translate findings in the laboratory into clinical applications.

He wanted money to come in from banks, real estate, and so on, rather than from the pharmaceutical industry. “I didn’t want at that time to have any bias,” he says. “I didn’t want research projects to be bound to relating to particular drugs.”

It just so happened that 5 private enterprises that knew Dr Fuster in one way or another decided to support the venture. The companies involved, the Spanish Ministry of Health and Consumer Affairs, and Dr Fuster signed an agreement on December 15, 2005. This agreement ensured stable funding for the CNIC by committing contributions until 2012 of €166 million from public funds and almost €100 million from private sources. Now, 16 private companies, through the ProCNIC Foundation, have contributed significant amounts of money to subsidise the federal funds.

CNIC is already giving grants to young people through 6 programmes. The organisation aims to identify potential researchers from people younger than 17 years of age, people starting careers in biology or in medicine, cardiologists in training or who have just finished their studies, and students who want to study abroad for up to 3 years at any stage in their degree. The research teams are led by a principal investigator who is associated with the national Spanish health system. The teams may be made up of several research groups from public or private centres, and such groups may be from overseas.

Visits to high schools to look for creative people have already identified 8 secondary school students younger than 18, who have received grants to stay in Madrid and to spend time in the laboratory at the cardiovascular research centre.

“I’m beginning to get feedback from a number of these students who want to be investigators,” says Dr Fuster. “It’s interesting because they are picked up at a very young age, but they have been in touch with what investigation is all about, particularly in the laboratory, and they are quite intrigued by and excited about it. CNIC will continue to support them in their studies.”

On the research front, projects will be undertaken across the cardiology spectrum in 6 departments. The development and embryology department will look at how the human body and the heart develop from the very beginning, to increase understanding of the aspects of embryology that lead to disease on a genetic or congenital basis. The regenerative biology department will investigate how to make new tissue, new organs, and new hearts through research into stem cells and genetic therapy. The vascular biology and inflammation department will take steps toward understanding vascular disease, whether it affects the coronary arteries or arteries in the brain.

Imaging will be a technical department cutting across all subspecialities. The epidemiology and outcomes department will use population studies to investigate certain disease pathways and will look at proteomics and genomics as they apply to epidemiology. Finally, the department for translation research will unify research at the very basic level with clinical applications. The prospects for this activity clearly excite Dr Fuster.

CNIC is now calling for grant applications. The idea is to have programme projects, where 4 or 5 research groups will look at 1 research question from different angles. The groups will initially come from Spain, but eventually will involve researchers from the rest of Europe and the United States.

CNIC is establishing links with the Johns Hopkins University and Mount Sinai so that researchers from Spain can work in these institutions, or, alternatively, researchers from US institutions can work with Spanish colleagues on particular projects. “We are really opening the scenario internationally,” says Dr Fuster, “because the research is then much more effective. If you begin to think on a basis of international organisation, there are things that can be done in one country better than in another. I think today we are much more global and international in the research questions we try to answer.”

Dr Fuster emphasises that CNIC’s work will involve a collaborative effort with the other institutes of research in the country. Many of the research projects will involve teams who belong to other cardiovascular research organisations. “This is not like an isolated entity,” he says. “I believe that although this is going to be, in a way, a new
way of doing things, we believe that the whole research enterprise has to be integrated in some way.” He intends to develop very high-quality research with investigators at the tops of their fields. For this reason, Dr Fuster requested an external committee of top investigators to monitor him and the system. An external international committee of eminent experts will scrutinise all the senior and junior investigators being recruited, their research, and their publications. This monitoring will continue throughout their tenure.

The committee contains a mix of scientific people from the government and some from private enterprise who are supporting the CNIC’s activities. “This, to me, has been very important because there’s no such thing as a short cut here. We’re all under surveillance, and it is a healthy system in that regard. At the same time, you create an incentive to the people to be investigators of the highest quality because you really support them.”

Right from the start of his scientific career, German cardiologist Dr Frank Enseleit recognised the challenges he would face in a scientific world dominated by English speakers. “All the important journals are from English-speaking countries,” he says. And during his medical training at the Johannes Gutenberg University, in Mainz near Frankfurt, Germany, Dr Enseleit first came to understand the special limitations of a Eurocentric career in cardiology, under the inspirational guidance of his teacher and mentor, the nitric oxide specialist Ulrich Forstermann, MD, professor at the department of pharmacology, Johannes Gutenberg University, Mainz.

Recognising the young Dr Enseleit’s ambitions in cardiology, Dr Forstermann told him that to advance in science, he would have to move. “One coffee break, he asked me what I wanted to do after medical school. I said I was interested in cardiology, because you can put the nitric oxide science together with the physical aspects.” Dr Enseleit explains. “He told me that to do this it would be necessary to go to another country first.” He had 2 options: choose another European country, or move to the United States. Having already spent some time in the United States as a student in 1997, Dr Enseleit chose Europe and, taking the recommendation of his mentor who had contacts in Switzerland, applied for a postgraduate position at Zurich University, which houses one of the best cardiology research departments in the world. Although happy with his current residence and appointment—“I have a good quality of life, and from a scientific point of view, there is good funding in Zurich”—Dr Enseleit has resigned himself to the fact that his later career will include a move to the United States. “If you want to become a renowned scientist or clinician, you have to go abroad. All of us who want to move on have to go there,” he says.

How does Dr Enseleit explain this US bias in the cardiological sciences? During his student year at Albert Einstein College of Medicine, New York, NY, he had the opportunity to compare science, careers, and attitudes between Germany and the United States. “From a clinical point of view, it is the same. For example, you prescribe the same ACE inhibitors in both countries, and you have the same clinical possibilities,” he says. “So, this bias has less to do with the quality of scientific experience or conduct and more with language.”

Dr Enseleit, who speaks excellent English, says, “Becoming fluent is essential for communicating research, and that’s not something you can achieve in Switzerland.” Language skills also ensure that a wider audience will read your work. “There are some good journals in France, Germany, and Italy, but the pace is set by the English-speaking journals... and if you look in the US journals, most of the study groups are not from Europe; they are

---

**Viewpoint: Frank Enseleit, MD**

**From Tako–Tsubo Syndrome to Percutaneous Heart Valve Implantation, His Research Maintains Its Appeal.**

Dr Frank Enseleit does not want to leave Europe, but he recognises that he will inevitably need to go to work in the United States at some point to further his career. He reflects, with Hannah Brown, BSc, on the journey so far and on the rewards of research, despite the fact that it can sometimes take years to reach fruition.

Over the past few months, Dr Fuster has spent 25% of his time in Spain and the remainder in the United States, but he expects this to rise to at least 75% as the centre develops. He says, “This is the best way to do things, particularly when you are developing a situation that takes time.”

He sees the CNIC as critical to the future of cardiology in Spain because it aims to produce the best quality of research that can be applied to patients and to foster the young investigators of the future. “Knowing that cardiovascular disease is the number one killer, it is obvious that this is the way to create an infrastructure that will be positive for the future of cardiovascular research and clinical activity in the country.”

*Jennifer Taylor is a freelance medical journalist.*
So, at some point, I want to go where these studies are done,” he says.

For now, however, Dr Enseleit is making the most of his European roots under a second inspirational mentor, Thomas F. Lüscher, MD, FRCP, of the University Hospital in Zurich, Switzerland. “He has that great ability to motivate people and to train them for science, and that is a great talent,” Dr Enseleit says of his head of department.

Since moving to Zurich, Dr Enseleit has nurtured his interest in vascular biology and carried out research into slow vessel dilation in patients with inflammation. Dr Enseleit feels he has made his biggest scientific contribution so far in this field of inflammation research. “During the 1990s, it became well known that atherosclerosis was an inflammatory disease, so we thought we should do more research in patients with inflammation and work out cardiovascular risk and how to manage it,” he explains.

This work has led him to look outside cardiology and find connections with other areas of medicine. Dr Enseleit and his colleagues wrote an often-cited article in 2002 about treating patients with rheumatoid arthritis (Figure 1), using inhibitors of the inflammatory mediator tumour necrosis factor-alpha, showing that endothelial function improved. “People with rheumatoid arthritis don’t die of their condition; they die of heart disease and stroke. That shows a very interesting connection between 2 different fields of medicine—rheumatology and cardiology,” says Dr Enseleit.

Taking this logic a step further, his group went on to test the effect on endothelial function of inhibition of COX-2 in patients with coronary artery disease. They concluded after a small study that selective COX-2 inhibition with celecoxib “improved endothelial function in patients with cardiovascular disease, thus indicating a potential for benefit through a reduction of inflammation and increased nitric oxide bioavailability, as well as for harm via the reduction of prostacyclin.” But the withdrawal of the COX-2 inhibitor rofecoxib from the market in 2004 after concerns about cardiovascular side effects has, says Dr Enseleit, made it difficult to pursue this idea. “It is an important issue to have a look at, to see how the inflammation story develops in atherosclerosis. The other issue is to find out whether these analgesics are harmful for patients or not.”

Dr Enseleit has other diverse research interests—including the so-called Tako–Tsubo syndrome of left ventricular apical ballooning (discovered by Japanese scientists who named it because its shape resembles a traditional octopus trap), echocardiography, and imaging—but he thinks the most interesting area of research at the moment is cardiac valve replacement (Figure 2). “Some groups are trying to implant cardiac valves percutaneously, and we are working on a different type of graft in sheep,” he explains.

Proving the concept in patients who need pulmonary valve replacement has been fairly simple, says Dr Enseleit; researchers are now focusing on replacement of the mitral and aortic valves, because most patients have problems with those valves. “These valves are the great challenge, especially if they are calcified. But if you can remove the valve without fear of stroke, as in carotid stenting, then it could be very beneficial,” Dr Enseleit predicts.

When the first results from this work will start to benefit patients depends on the progress of experiments. “From
now, I think it will take another 2 years to have the first results in humans,” says Dr Enseleit. But having to wait years for clinically applicable results is not something that frustrates him. “Science is not a very fast thing, but it is continuously moving on,” he explains, “and it is that continuous progress that maintains my motivation.”

Dr Enseleit says he turned away from a clinical practice career in favour of research because he wanted to improve treatment for future patients. But the process of science really excites him. “You see that you can bring the field a little forward, and that is what makes it interesting,” he says. “You can reflect on the fact that you did the experiment and published it, that others read it and then, based on your findings, did more experiments. That is the way things move on. That is what makes it interesting for me.”

Hannah Brown is a freelance journalist based near Cambridge, United Kingdom.

References

The opinions expressed in *Circulation: European Perspectives in Cardiology* are not necessarily those of the editors or of the American Heart Association.
Circulation. 2007;115:f103-f108
doi: 10.1161/CIRCULATIONAHA.107.184354
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 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/115/21/f103.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/