Inside INSERM: An English Researcher in France

An English Cardiovascular Researcher Talks About His Experience Working for the French National Medical Research Organisation

Collaboration between cardiovascular researchers in different countries has yielded huge rewards, according to John Chapman, PhD, DSc, who has worked in France for the past 20 years and is currently the director of Unit 551 (Dyslipidaemia and Arteriosclerosis) at l’Institut National de la Santé et de la Recherche Médicale (INSERM) at l’Hôpital de la Pitié, Paris. He speaks to Barry Shurlock MA, PhD.

In 1964, the French government created l’Institut National de la Santé et de la Recherche Médicale (INSERM) as the successor to the French National Institute of Hygiene, originally founded in 1941. In the hands of its Director General, Christian Bréchot, MD, PhD, professor of hepatology at l’Hôpital Necker, Paris, INSERM now has a network of 350 research groups, or unités, and 31 clinical research centres distributed throughout France. It also has other unités outside France, in Germany, Canada, Scotland, and Japan, as well as one on the French dominion of Réunion, an island in the Indian Ocean.

Like its counterparts elsewhere, such as the US National Institutes of Health and the British Medical Research Council, INSERM carries out research in all major areas of medicine. It currently participates in >600 clinical trials, and its Web site (www.inserm.fr) shows that during 2006 alone, its researchers made significant contributions in more than 50 clinical and scientific areas. It would be surprising if INSERM did not employ mainly French nationals, but its organisation also includes a substantial number of non-French researchers who have taken root in Gallic soil.

Gaining an appointment as a researcher at INSERM is a considerable achievement in itself, as the recruitment process is equally rigorous for junior and senior researchers, and only 1 tenured position is awarded for every 10 to 20 candidates.

One such researcher is Dr John Chapman, director of INSERM Unit 551 at l’Hôpital de la Pitié, Paris. He originates from the Wirral, a part of the English county of Cheshire, near the city of Liverpool. He went to the same state school as Harold Wilson, a former British prime minister. But he has come a long way since then, and he now works with a group that includes >40 people and has a strong international flavour, with a potent mix of scientific and medical staff. The group includes 6 investigators, 8 support staff tenured by INSERM, 12 clinicians, 8 doctoral students, 2 postdoctoral fellows, 10 students on short-term projects, and 5 technician-engineers funded from outside sources. The clinicians include the hospital’s head of endocrinology and head of diabetology, 4 junior clinical investigators, and 4 senior investigators who have the status of professeur d’université or professeur hospitalier.

Unit 551 has links with 5 outpatient clinics that cover endocrinology, dyslipidemia, nutrition, obesity, diabetology, and the prevention of cardiovascular disease; the unit focuses its activities strongly on the structure, metabolism, function, and therapeutic modulation of high-density lipoproteins (see Figures 1 and 2). The success of the unit is due to its competitiveness and originality for almost 20 years in the field of lipoproteins and atherosclerosis. This area remains a major problem for public health as cardiovascular disease presently...
contributes the main cause of morbidity, not only in France, but in most European countries.

Since 1985, Dr Chapman has worked exclusively in Paris, after a career that started at the University of Aberdeen, Scotland, and that found him in the mid-1970s studying for a PhD at Middlesex Hospital Medical School, London, United Kingdom. He recalls that during that time, basic research on dyslipidemia was moving from the bench to the clinic, and he wanted to work in a centre that enabled close links between researchers and clinicians.

He contacted a number of centres in the United States, and, he says, he “Greyhounded around” them all until he found himself on the 15th floor of the Cardiovascular Research Institute of the University of California Medical Centre in San Francisco, Calif, with fog rolling in under the Golden Gate Bridge and a job offer in his hand from the head of the institution, Richard Havel, MD. He finished his PhD in London before moving to San Francisco, where he worked for 5 years.

The next stage of his career demonstrates the key role that serendipity and networking have played. “It so happened that there was a researcher from Paris in the lab, and he had a sister who worked at the French Consulate in San Francisco. It was the late 1970s, and Michael S. Brown, MD, and Joseph L. Goldstein, MD, had just discovered the low-density lipoprotein receptor, a discovery that was to lead to them sharing the Nobel Prize for Physiology and Medicine in 1985. They were about to go to a major meeting in Graz, Austria, followed by a lecture tour of Europe. The consulate needed someone to help with arrangements for their visit to Paris, and I obliged.”

As a result of this involvement, Dr Chapman explains, “I subsequently met Philippe Laudat, PharmD, the then Director General of INSERM, and I was offered an INSERM international fellowship at l’Hôpital Henri Mondor, Paris. They called it a poste vert—the idea was to fund foreign researchers for a short period to bring in new ideas and techniques. I was quite privileged, as there were not many people of Anglo-Saxon descent around!”

Between his poste vert and settling permanently in France, Dr Chapman worked again in San Francisco from 1982 to 1985, this time at the Gladstone Institute of Cardiovascular Disease. He shuttled back and forth between California and Paris until some French scientific colleagues suggested he apply for a tenured position with INSERM. “With my first application, I got within range of an appointment, and a second application brought success,” he says. “This is normal for tenure in France—it’s exceedingly rare to succeed at the first attempt, though in the last 2 to 3 years some researchers have been sought by INSERM to further develop specific biomedical areas. My decision to settle in France was almost subconscious—I had always been a Francophile, I enjoyed French culture and gastronomy, and was equally interested in languages.”

INSERM works in a less hierarchical way than some American institutions, and it provides a higher degree of continuity in research funding, according to Dr Chapman. New INSERM units receive funding for two 4-year periods, with an interim assessment, and INSERM often maintains funding to allow researchers breathing space to move into new areas. He comments, “We don’t have to worry that someone somewhere has cut off the grant because we haven’t published enough papers. It allows time to invest in the medium term in new projects.” He explains that they recently successfully completed a novel project involving the creation of a genetically modified mouse model. “And if you can make a case for a project, INSERM is quite likely to take you up on it,” he continues. “INSERM has not in the past focused on highly targeted areas and has been open to new biomedical themes, though over the last 2 to 3 years it has been more targeted, a change attributable to the influence of the Agence Nationale de Recherche, the French national research agency created in 2005.”

Dr Chapman says, “Throughout the early part of my career in San Francisco, I was stimulated by a whole series of congresses—including the American Heart Association meetings and the Gordon Conferences on Lipid Metabolism and Atherosclerosis.” He explains, “I didn’t realise it at the time, but the networking was very helpful later in Paris. A major plus for our lab is that the friends and colleagues I have made will take promising young French researchers for 1 or 2 years, such as in the United States, Australia, or the United Kingdom, and, to a lesser degree, elsewhere. Hopefully, they do not phagocytose them! Their track record is very good or excellent. Last week, for example, one of our young researchers presented a paper on dendritic cells at the Arteriosclerosis, Thrombosis, and Vascular Biology meeting in the United States and received 3 postdoctoral offers.”
Although he acknowledges the shortage of junior registrar posts in France and the difficulty of inserting young clinicians into academic research, Dr Chapman feels enthusiastic about the internships for clinical research that INSERM has created, whereby young clinicians can spend 2 to 3 years doing original research. “We need more clinical investigators and more translational research to convert basic findings into pharma targets,” he says. “Dr Bréchot has had the insight and foresight to identify a weakness and convert it into a strength. In 2003, he created the contrat d’interface, which complements the salaries of basic researchers or clinicians to encourage collaborative research spanning the spectrum from basic to clinical research with an emphasis on therapeutic innovation. It has been a great success, and, to date, 300 contracts have been awarded.”

Unit 551 has a strong international profile, with researchers from the Netherlands, Italy, Brazil, and the United Kingdom. Joint arrangements now exist for tutoring between 2 universities, called the co-tutelle system, which allows doctoral students to start their research in one country and then move to another, to acquire complementary techniques and ideas. “New opportunities are also coming from a major reorganisation by the Assistance Publique—the French national health service—of the 9 university hospitals in Paris,” says Dr Chapman. The changes, claimed to be in the interests of patient care and efficiency, involve a regrouping of the various clinical departments, generally but not always from the same hospital, into major divisions, or pôles. L’Hôpital de la Pitié is reorganising 77 departments into 7 pôles, with Dr Chapman’s INSERM Unit 551 and another housed alongside 6 clinical departments. It will form the first centre of metabolic disease to be established in France, and it should open in mid-2009.

Cardiology has its own pôle, centred around the Institute of Cardiology that was opened in 2003. Dr Chapman clearly feels excited about the changes, which are opening new horizons for clinical research.

“A major obstacle to carrying out medical research in France is the cumbersome bureaucracy that has to be endured without appropriate clerical support,” says Dr Chapman. “Health and safety regulations, with myriads of forms and dossiers, are especially irksome for relatively routine studies with radioisotopes, genetically modified organisms, and the like.” Also, the French system often moves slowly. Grant money may be slow to appear, and spending it requires time-consuming procedures. “As an example,” says Dr Chapman, “we recently wanted to buy a gas chromatography–mass spectrometry system, but had to go through a complex process to select the best supplier—things like that can lose us 6 months.”

Whatever the future holds in France under its newly elected president, Nicolas Sarkozy, Dr Chapman believes that the government recognises that the country spends too low a percentage of its gross national product on biomedical research, and he hopes it will act to increase the amount by the half percent required to bring it in line with other industrialised countries. He reflects, however, that 2 years ago, in 2005, when INSERM staff and others went on strike and resigned their posts, the government of President Chirac made hollow promises. “It was publicly stated that there would be an increase in funding and the number of research positions, but what was given was only a drop in the ocean,” Dr Chapman says. “One serious problem in France—not just in biomedical research but in academic research in general—is that there is a serious shortage of technicians and engineers. We need them particularly in our sort of work, which is very technically demanding and labour intensive.”

Dr Chapman, whose career has included a stint as President of the French Atherosclerosis Society, received the title of Distinguished Fellow of the International Atherosclerosis Society earlier this year. He was also recently nominated by his election to chairmanship of the Gordon Conference on Atherosclerosis in 2011, and in June this year the American Heart Association nominated him to be a European Associate editor for their journal, *Arteriosclerosis, Thrombosis, and Vascular Biology*.

Having lived in France for more than 20 years and now married to a British international civil servant working in Paris, he does not envisage ever moving back to the United Kingdom. He comments, “We miss some of the great national events, like Wimbledon, the Derby, the Grand National, and the FA Cup Final. But we don’t find British culture as attractive as we find it here in France.”

*Barry Sharlock is a freelance medical writer.*

**References**


Dr Tomasz Siminiak is Head of the Catheterisation Laboratory at the Cardiac and Rehabilitation Hospital, Kowanówko, Poland

The first in his family to go into medicine, Dr Siminiak has continued to break new ground ever since. He talks to Joanna Lyford, BSc, about his pioneering work in the field of cell-based myocardial repair, his current enthusiasm for percutaneous mitral valve repair and his belief that independent academic researchers in Poland get more freedom as permission to undertake research is based on trust in the individual.

Dr Tomasz Siminiak, head of the catheterisation laboratory at the Cardiac and Rehabilitation Hospital, Kowanówko, Poland, grew up in postwar Poland in the southwestern city of Poznań, an ancient city steeped in academia and culture. Even as a young boy, Dr Siminiak wanted to be a doctor, believing medicine to be a “magical area.” With the encouragement of his “strongly anticomunist” parents, he became the first in his family to enter medicine, qualifying at Poznań’s University School of Medical Sciences in 1985.

After a stint at a rural state-run polyclinic, he decided to specialise in cardiology. “I think that cardiology as a specialty is one of the most effective and fruitful in terms of saving human lives,” he says. “Recent progress has borne out what was hoped for years ago—that cardiology really has enormous potential for saving human lives, and this is what always encouraged me.”

Dr Siminiak’s time spent as a research fellow included posts around the world, sparking a lifelong passion for travel. His work led him to the University of West Berlin, just across the border in Germany, then to the University of Nagoya in Japan, and finally to a British Heart Foundation-funded position with the Academic Cardiology Unit of Imperial College, based at St Mary’s Hospital, London, United Kingdom.

At St Mary’s, under the supervision of Desmond Sheridan, FRCP, Dr Siminiak studied the pathogenesis of ischaemic heart disease, work that underpinned many of his subsequent achievements. “Mainly I was focused on the role of inflammatory processes in the development of myocardial injury,” he explains, “free oxygen radicals, cell response, and other inflammatory mediators and their role in myocardial ischaemia and myocardial infarction.”

On his return to Poznań in 1995, Dr Siminiak took up his current post as consultant in the cardiac catheterisation laboratory at the J. Struz Hospital and began probing the potential of stem cells to regenerate damaged heart muscle. “I always felt enthusiastic about restoring function to a supposedly irreversibly damaged organ,” he says. “In fact I was very excited about it before it became fashionable.”

Dr Siminiak believes that he and his colleagues were at the forefront of stem cell research because Polish medical education stresses the value of basic scientific knowledge and techniques. “Polish cardiologists are relatively well-educated in basic research,” he says. “For example, I work in interventional cardiology, but in the past I was involved in projects that included cell technology, biochemistry, and cell culture. That’s why clinical cardiologists from Poland are very keen to be involved in projects that need an understanding of basic biology and biological techniques.”

This firm belief in the value of basic research is reflected in Poland’s regulatory framework, which is relatively relaxed toward academic research. “Regulations are very strict regarding industry-sponsored research,” Dr Siminiak says. “By contrast, independent academic researchers get more freedom, and permission is based on trust in the individual.”

With funding from the Polish Ministry of Science, Dr Siminiak’s group became the second worldwide to transplant autologous skeletal myoblasts in postmyocardial infarction patients. For ethical reasons, the initial procedures were performed in patients undergoing coronary artery bypass grafting. Having demonstrated the feasibility of the approach, Dr Siminiak progressed to myoblast transplantation as a sole procedure, using a catheter system to deliver cells via the coronary veins (see Figure). His other pioneering work in this field includes autologous bone marrow stem cell transplantation in the setting of acute myocardial infarction and the use of radionuclide imaging to trace the fate of transplanted cells.

After nearly a decade of experimental work, however, the entire field of stem cell research is facing a funding crisis. “We’ve proved that the technique is feasible and safe with positive signs of efficacy,” Dr Siminiak says. “Now large-scale clinical trials have to follow.” But large trials cost large sums of money. “Typically several million Euros,” he says, “and private companies are wary about investing. The industry is unsure of the profits to be made in cell culturing, and European companies are afraid to invest in case the product is not patentable.”

In the United States, the situation is more encouraging. Transatlantic differences in patent rights mean that several US companies are now active in the cell technology market and are trying to implement their products in the clinical arena. But in Poland, as in many countries, public funding for clinical trials is relatively weak, and Dr Siminiak expects his country’s contribution to come to an end.
“We’ve got nothing to be ashamed of,” he says. “We’ve done a lot of good work here, but now we’re facing the same problems as the rest of Europe.”

Dr Siminiak believes the greatest hope for stem cell research lies with the European Commission (EC), which funds research and technological development within so-called Framework Programmes. “Under previous programmes, I coordinated a project focused on cell transplantation for myocardial regeneration, but the grant was too small to fund real research; it was more about the exchange of information and networking,” he says.

“In the future, I hope the EC will find a way to fund a really large pan-European program on stem cell research. This field is very important for the future of the whole of medicine.”

Meanwhile, Dr Siminiak is nurturing a number of new “hobbies,” as he calls them, such as testing Polish-made coronary artery stents and investigating the genetics of restenosis, atherosclerosis, and hyperlipidaemia. But the project he is most excited about is a minimally invasive technique for repairing the mitral valve, which involves accessing the valve via the coronary veins and inserting a device to narrow the mitral ring. At present, the only option for mitral valve repair is open-heart surgery, but Dr Siminiak says that his earlier experience in delivering stem cells via the coronary veins was invaluable in developing this new approach.

“Percutaneous methods for repairing cardiac valves are very exciting because we can treat patients without opening their chests,” he says. “This is especially useful in patients who would be high-risk candidates and those with very severe heart damage due to valve disease.”

Dr Siminiak’s team has already treated 12 patients using the new technique and a controlled clinical trial is now under way. If past successes are anything to go by, Dr Siminiak’s work should help keep Poland at the forefront of scientific innovation and ensure that cardiology continues to inspire young doctors to save lives.

Joanna Lyford is a freelance medical journalist.

References
European Meetings Update

August–October 2007

20 August–1 September
40th World Heart Federation Teaching Seminar on Cardiovascular Disease
Sommarøy, Norway
For further information, contact
kk101@medschl.cam.ac.uk

1–5 September
European Society of Cardiology Congress 2007
Vienna, Austria
For further information, visit
www.escardio.org/congresses/esc_congress/esc2007

13 September
7th Cardiovascular MRI Workshop
Athens, Greece
For further information, contact
soma@aias.gr

15–18 September
The 46th National Congress of Cardiology of the Romanian Society of Cardiology
Sinaia, Romania
For further information, contact
rscardio@rscardio.ro

16–19 September
International Workshop on Regulation of Transport Phenomena in Biological Systems
Antalya, Turkey
For further information, visit
www.ichmt.org/upcoming-meetings/tpbs-07/index.html

17–21 September
43rd European Association for the Study of Diabetes Annual Meeting 2007
Amsterdam, the Netherlands
For further information, contact
easd@eurocongres.com

20–22 September
XI International Congress of the Polish Cardiac Society
Wroclaw, Poland
For further information, contact
zarzad.glowny@ptkardio.pl

3–5 October
Bleeding Complications in the Treatment of Acute Coronary Syndrome
Lund, Sweden
For further information, contact
info@malmokongressbyra.se

4–6 October
XII Congress of the Slovak Society of Cardiology
Bratislava, Slovak Republic
For further information, contact
ssc@susch.sk

7–10 October
Venice Arrhythmias 2007–10th International Workshop on Cardiac Arrhythmias
Venice, Italy
For further information, contact
info@venicearrhythmias.org

7–10 October
7th International Congress on Coronary Artery Disease–From Prevention to Intervention
Venice, Italy
For further information, contact
coronary@kenes.com

9–11 October
National Cardiology Congress of the Society of Cardiology of the Russian Federation
Moscow, Russian Federation
For further information, contact
oganov@gnicpm.ru

10–12 October
Annual Autumn Meeting of the Finnish Cardiac Society
Helsinki, Finland
For further information, contact
fcs@fincardio.fi

11–14 October
European Conference on Myocardial and Pericardial Diseases With Focus on Heart Diseases in Women
Marburg, Germany
For further information, contact
ecmr2007@med.uni-marburg.de

11–13 October
Annual General Meeting of the Irish Cardiac Society
Holywood (County Antrim), Ireland
For further information, contact
secretary@irishcardiacsociety.org

17 October 2007 20 October 2007
Annual Meeting of the Spanish Society of Cardiology
Madrid, Spain
For further information, contact
sec@secardiologia.es

Editor: Thomas F. Lüscher, MD, FRCP, FACC
Managing Editor: Keith Barnard, MB, BS, MRCS, LRCP
We welcome your comments. E-mail the managing editor at
Keith.Barnard@wolterskluwer.com
European Perspectives

Circulation. 2007;116:F19-F24
doi: 10.1161/CIRCULATIONAHA.107.185705
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/116/4/F19.citation