FROM BENCH TO BEDSIDE, & BACK

King’s Health Partners (KHP) is a pioneering collaboration between King’s College London, as one of the world’s leading research-led universities, and three of London’s most successful NHS Foundation Trusts. It unites world-leading research, medicine, healthcare and education in order to bring about improvements in health and well-being for patients, in London and world-wide.

A major focus of KHP is on ‘translational research’: enabling research discoveries to be effectively converted or translated into new treatments for patients as quickly as possible – and ensuring that the outcomes for patients feed back into further research and into the education of future clinicians and researchers.

The Cardiovascular Clinical Academic Group (CAG) of King’s Health Partners is one of the country’s leading centres for the study and treatment of heart and circulatory disease and shows translational research in practice.
Professor Ajay Shah is a clinician scientist whose busy working life provides an example of the close relationship between the development of academic research, the treatment of patients, and the education of the next generation of students, researchers and clinicians.

A major part of his time is taken up with his role as Director of the British Heart Foundation Centre of Research Excellence at the Denmark Hill Campus of King’s College, but one or more days a week may also see him on call to treat heart attack patients at King’s College Hospital, next door.

Another day may catch him in the laboratory at the James Black Centre, close to the Hospital, carrying out his own research into the causes of heart failure; and the remaining days may find him lecturing to students, supervising PhD candidates or planning future courses.

The establishment of King’s Health Partners means two important things to Professor Shah. ‘One is that it is enabling us to develop the UK’s leading high-quality environment for research, education, and clinical care and innovation in heart disease’, he explains. ‘We aim to be THE place that people come to when they want the best in heart treatment, research or teaching.

‘The other is that it reinforces the cycle that links basic scientific research with translational research and with clinical research, innovation and care, which then connects back to basic education and research. In this way important clinical questions can be addressed by academic research, and our students can be taught by people whose research and clinical expertise is making a real difference to patients.’

Patients from south-east London and beyond who suffer heart attacks are rushed to King’s College Hospital or St Thomas’ Hospital to be treated by Professor Shah and his clinical colleagues, using a new technique called primary angioplasty.

‘We were the first centre in the UK to establish primary angioplasty for all heart attack patients’, Professor Shah explains. ‘It has already saved hundreds of lives and revolutionised the outcome for these patients, and it is now spreading to hospitals all around the country.’

Angioplasty involves a half-hour keyhole procedure, under local anaesthetic, in which a small balloon is inserted and inflated to unblock the artery whose narrowing or closure caused the heart attack. The re-opened artery is then reinforced with a stent. Most patients can be back at home again within three days of treatment. ‘This treatment is vastly superior to the old therapy with clot-busting drugs, which often failed to re-open blocked arteries’, Professor Shah says.

Professor Shah’s experience in the operating theatre and by the bedside feeds directly into his own research on fundamental questions about why heart failure still occurs after a heart attack in many patients, even after successful treatment by angioplasty, or in patients whose aortic valve has been blocked or narrowed. His research aims to develop new drugs to further improve the outcome for patients at risk of heart failure.

Meanwhile other researchers in the King’s Cardiovascular Division and BHF Centre are using many innovative technologies such as those involving proteomics, stem cells and imaging, to make further advances in treating heart disease. ‘And beyond that, we are working hard to bring in knowledge from other disciplines, such as bioinformatics, maths, physics and engineering, to develop new treatments. Recruiting bright PhD students with expertise in these areas is an important part of our strategy.’
How can one be certain that a cell really is a stem cell?

The researcher’s story

Dr Manuel Mayr is Head of Proteomics at the BHF Centre at King’s. He is analysing proteins – the molecules of life – to find better ways of using stem cells to improve the success rate of heart bypass operations by growing new sections of blood vessel to replace or repair damaged arteries.

‘Stem cells are already used in clinical trials for treating patients after heart attacks’, he explains. ‘But how can one be certain that a cell really is a stem cell? In practice, scientists and clinicians tend to infer that a cell is a stem cell if it tests positive for particular protein markers that are thought to be indicative of their stem cell potential. According to our latest research, some of these markers are not reliable.

The advent of novel technology allows us to screen thousands of proteins and this “proteomics”-led approach contributes towards a better classification of stem cells. ‘Our results suggest that cells used in some clinical trials may have been masquerading as stem cells, but were actually a different type of cell. We need to develop new ways of purifying stem cells and be sure that they are actually able to contribute to the repair of heart tissue before they are tested in trials on people. Within the King’s BHF centre, we are very fortunate to have state-of-the art proteomic equipment and funding possibilities that allow us to utilize the latest technologies for our research.’

A diagram showing a typical proteomic workflow: proteins are prepared from cell cultures and cleaved into peptides. These peptides are separated by liquid chromatography and sprayed into a mass spectrometer. The mass spectrometer first records the mass of the intact peptide (MS) and then induces a fragmentation process (tandem MS). The peptide fragments unambiguously identify the protein.
Introducing King’s Health Partners

King’s Health Partners was one of the UK’s first five Academic Health Science Centres (AHSCs) to be accredited by the Department of Health in March 2009. It brings together King’s College London with the NHS Foundation Trusts of Guy’s and St Thomas’, King’s College Hospital, and the South London and Maudsley, which between them include seven hospitals and over 150 community-based services, and have a joint annual turnover of some £2 billion. It has access to around 60 per cent of London’s population, or around five million people, and serves a larger number of patients than any other AHSC. The diversity of its population base provides a microcosm for studying world health issues and developing treatments of international benefit.

Strengths in neuroscience, psychiatry and mental health, together with complementary disciplines such as medical and molecular genetics, public health sciences and imaging, enable King’s Health Partners to deliver better health and well-being for the mind and body, for the whole person. This combination of strengths helps to attract significant support from a wide range of partners, including many of the world’s leading pharmaceutical companies and biotech industries.

The funder’s story

Professor Peter Weissberg is Medical Director of the British Heart Foundation, which funds the BHF Centre of Research Excellence at King’s.

‘Every year heart and circulatory disease causes more than one in three deaths in the UK’, he points out. ‘Our mission is to play a leading role in the fight against cardiovascular disease so that it is no longer a major cause of disability and premature death. Our investment in four Centres of Research Excellence is helping us towards that goal, and we were delighted to award King’s £9 million over six years from 2008.

‘King’s has brought together a team of scientists and clinicians from a wide variety of scientific disciplines to focus on different aspects of heart disease and to train a new generation of researchers. In particular their strengths in structural and cellular biology provide a real opportunity for “bench-to-bedside” translational research into new treatments for heart disease. The BHF believes that the Academic Health Sciences ethos at King’s can only add value to the BHF Centre of Research Excellence and facilitate the interaction between laboratory science and patient care.’
The clinicians’ story

Transcatheter Aortic Valve Implantation (TAVI) is another new and highly innovative operating technique pioneered in the King’s Health Partners Cardiovascular CAG.

‘TAVI offers a new treatment option for high risk patients with aortic stenosis – a narrowing of the aortic valve which connects the heart to the major blood vessel carrying oxygenated blood to the body’, says Mr Olaf Wendler, Clinical Director for Cardiac Services and Consultant Cardiothoracic Surgeon at King’s College Hospital.

‘The TAVI programme at King’s started in August 2007 as part of the largest European feasibility trial for this technique, and so far more than 140 implantations using the Edwards Sapien™ valve have been performed at King’s and St Thomas’ hospitals, making the King’s Health Partners programme the largest in the UK.’

Instead of open-heart surgery, keyhole surgery is performed through a leg artery (the so-called ‘transfemoral’ approach) or through the apex of the heart (the ‘transapical’ approach). ‘This avoids the opening of the patient’s breast bone and the temporary by-passing of their own heart and lungs by a machine’, explains Dr Martyn Thomas, Clinical Director for Cardiac Services and Consultant Cardiologist at St Thomas’ Hospital. ‘TAVI has therefore the potential to reduce the side effects of the operation and can be a particularly helpful treatment for patients – such as those who are older and have other health conditions – for whom conventional surgery would be very high-risk.’

‘The excellent interaction between cardiac surgeons with a particular expertise in aortic valve surgery and interventional cardiologists with a track record in driving innovative technique brought our Centre into the spotlight when this technique was introduced in the UK’, Olaf Wendler comments. A larger multidisciplinary team, including cardiologists with a particular interest in imaging; cardiac anaesthetists; research nurses; technicians and specialised nurses for pre- and post-operative care was formed and this guaranteed that strengths from all different areas could contribute to the programme.

‘We are convinced that this is the reason we were able to achieve excellent results and shorten our learning curve’, Wendler adds. In addition to successful contribution to the first trials, the academic side of the programme is analysing impact on heart function and patient outcomes, supported by research fellows, and clinical and academic data has been presented at national and international meetings.

King’s Health Partners is currently seen as a centre of excellence for TAVI treatment. ‘In our centre we facilitate teaching for other clinical groups who develop new programmes’, points out Martyn Thomas. ‘We act as supervisors in other centres to assist with their first implantations and have been invited to become primary investigators in forthcoming trials and European registries. This is enabling us to pursue further development of this technique at our campuses and also to offer these new techniques to our patients.’

‘Our experience at King’s Health Partners shows that, with the adequate support of a multi-disciplinary team, excellent clinical and academic results can be achieved.’
The patient’s story

Bernie Irvine describes how angioplasty treatment from Professor Shah saved his life.

“Because of my heart attack, I developed diabetes and angina. I’ve also gained weight due to the steroids, and find I get breathless because of this. I’ve been on diets to bring my weight down, without much success. But I have successfully stopped smoking as a direct result of the attack.

“My life is good. I got married in March this year, and have recently started back to work as a self-employed driver. I also dabble in buying and selling antiques.

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Ignat Drozdov is a PhD student supervised by Professor Shah and Professor Christos Ouzounis, Head of the Centre for Bioinformatics at King’s. With first degrees in physics and music from American University, Washington DC, he is one year into his PhD on Redox signalling networks in cardiac response to stress.

‘Rapid and ubiquitous genome sequencing allows scientists to monitor expression levels of thousands of genes in conditions such as cancer, diabetes, or heart disease’, he explains. ‘When applied to the study of cardiac response to stress (eg hypertension), these technologies make it possible to explore how genes interact with each other and identify key mechanisms that either protect the heart or lead to heart failure. The end product of such studies will not only result in molecular understanding of heart function, but may also elucidate novel treatments that could be tailored to individual patients – a much more effective alternative to a one-treatment-fits-all approach.’

Ignat’s knowledge of physics and ability to model a real-world system using mathematical concepts is a valuable adjunct to experimental biology. ‘In my research I study the function of more than 20,000 genes and 20 million potential interactions during cardiac response to stress.

‘I integrate mathematical modelling of this system with validated biological data (eg transcript/protein expression levels, gene sequences, and known protein-protein interactions) to create a reliable overview of heart failure. Further assessment of this model may lead to identification of novel drug targets, assessment of patients’ response to treatment, and more thorough understanding of molecular signalling cascades in the heart.

‘I feel very privileged to be working with multi-disciplinary experts to help understand why heart failure occurs and how it can be prevented. The thrill of experiencing the genomic era in medical research first-hand, on more than one occasion has placed me at the centre of a fast-paced science fiction story rather than the reality of modern day research.’