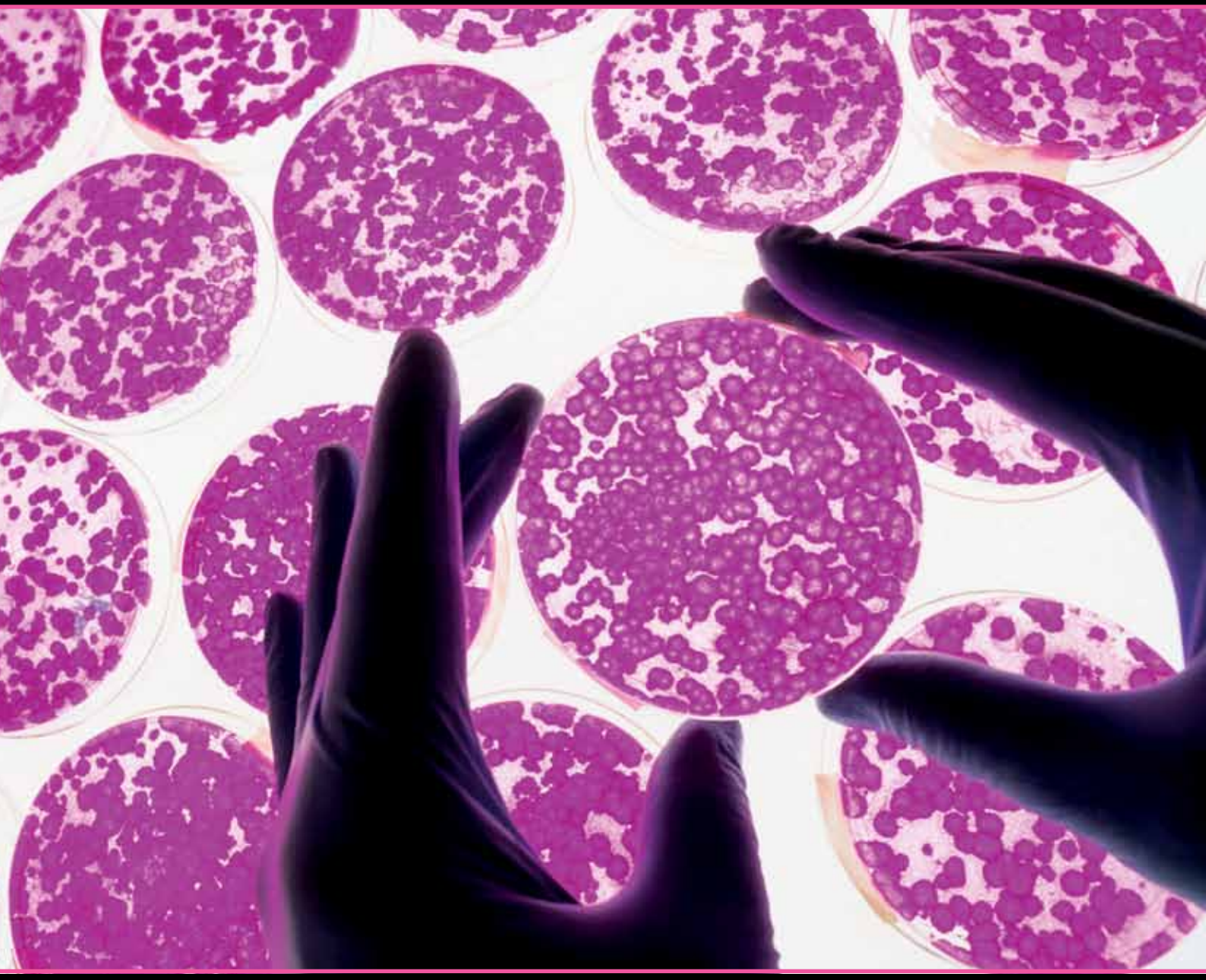
UNIVERSITY OF BIRMINGHAM

Autumn/Winter 2011

# Medlines

A biannual publication from the College of Medical and Dental Sciences



## Taking control of our genes

– Birmingham's expertise in epigenetics

Inside this issue: **Ecstasy holds promise for blood cancer treatment; Pharmacy comes to Birmingham; Screening test identifies heart defects in newborns**

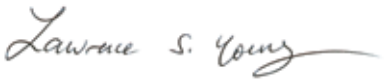
# Welcome

We've recently completed this year's round of graduations and, as ever, it was extremely uplifting to see the assembled group of MBChB students receiving their degrees and reciting the duties of a doctor.

One can't help but be moved by the ceremony surrounding graduation in the University's Great Hall, by the inspiring addresses of our honorary graduates and by the outstanding achievements of our students – yet again two of our MBChB students received the Chancellor's and Vice-Chancellor's prizes for their scholarship, leadership and contribution to the general life of the University. At a time when changes to higher education funding are rightly focusing the sector on the primacy of the student experience and on the widening participation agenda, it is worth remembering that we have always been dedicated to giving our students a distinctive, high quality experience and to ensuring that we provide opportunities for students from all backgrounds.

As a leading research-intensive university, it is imperative that our students tangibly benefit from the world-leading research that is undertaken here by being exposed to 'state-of-the-art' developments taught by internationally-recognised research leaders. We are doing much to ensure that the experience of our medical students is enriched by being in such an environment and this is being achieved through early exposure to our star researchers and by increasing the opportunities for students to get directly involved in research projects. In this way we hope to equip our students for clinical practice in the 21st century, to promote the value of continued learning through practice and to encourage the development of the next generation of clinical academics.

This edition of *Medlines* testifies to the richness of the student environment in the College and to our continued research success. It highlights how close collaborative working with our NHS partners is generating real patient benefit and opening new avenues to take basic research breakthroughs from 'campus to clinic'. Changes in HE funding and structural reforms in the NHS may be challenging but we remain confident and proud, as I hope you are, in our premier position as leaders in the training of tomorrow's healthcare professionals and as an internationally-recognised centre of excellence in research that improves health.



Pro-Vice Chancellor and Head of College of Medical and Dental Sciences

Front cover shows stem cell research. Cultures of stem cells growing in petri dishes. Stem cells are pluripotent, they are able to differentiate into any of the cell types of the body. Stem cell differentiation can be initiated in the laboratory by the use of biochemical growth factors. Stem cells are a potential source of cells to repair damaged tissue in diseases such as Parkinson's and insulin-dependent diabetes.

## Modified Ecstasy holds promise as potent blood cancer treatment

Scientists at Birmingham have discovered a modified form of the drug MDMA – commonly known as Ecstasy – which has 100 times more cancer-busting properties than the popular recreational drug itself and which they hope may be able to be produced in a safe form to treat patients.

Research results show significant success in redesigning the 'designer drug' for potential use as a cancer-killing agent in the treatment of leukaemia, lymphoma and myeloma.

The new work builds on the Birmingham scientists' discovery six years ago that more than half of the cancers of white blood cells they looked at responded in the test tube to the growth-suppressing properties of psychotropic drugs. These include amphetamine derivatives such as Ecstasy and weight-loss pills, and antidepressants such as fluoxetine (Prozac).

At the time, the team stressed that translating their laboratory findings into a useable clinical compound would present significant problems, not least because the dose of MDMA required to treat a cancerous tumour would have proved fatal to the patient. They aimed to break down the actions of the drug to isolate its cancer-killing properties from its general toxicity.

Working with researchers from the University of Western Australia, who produced the new compounds for them, the Birmingham scientists found specially modified forms of Ecstasy boosted their ability to attack and destroy cancerous cells by a factor of 100. Importantly for the future, they believe they understand the mechanism behind this.

Professor John Gordon, from the School of Immunology and Infection, says: 'This is an exciting next step towards using a modified form of MDMA to help people suffering from blood cancer. While we would not wish to give people false hope, the results of this research hold the potential for improvement in treatments in years to come.'

The team now hopes to go on to develop pre-clinical studies.

# Simple screening test identifies heart defects in newborns, say researchers

A simple test to measure blood oxygen in newborns has been shown to identify babies with life-threatening congenital heart defects, a major cause of infant mortality in the developed world. Research from the University and Birmingham Women's Hospital has now been published in *the Lancet*.

The PulseOx study is the largest UK investigation into screening newborns for congenital heart defects, which occur in 1 in 160 births in the UK. More than 20,000 mothers and babies from throughout the West Midlands took part in the trial. Midwives used pulse oximetry to measure oxygen levels in newborns' blood via a small sensor placed on the skin of hands or feet. Babies with low oxygen levels soon after birth may be at increased risk of heart defects.

Current screening for heart defects involves ultrasound before delivery and routinely examining all newborns in the first 24 hours after birth. However these examinations often miss babies with serious heart defects. PulseOx is an additional test which is carried out on the postnatal ward, before discharge from hospital and can be life-saving.

Babies who failed the PulseOx test were given a heart ultrasound. Of 195 babies with an abnormal result following the test, 26 had a major congenital heart defect and a further 46 had other important problems which required urgent treatment brought to attention by the test.

'It's usually performed within 24 hours of birth and is simple, painless and non-invasive,' explains lead investigator Dr Andrew Ewer. 'A small probe is put on the baby's hand and then on the foot, the machine is switched on and you obtain a reading. That's it. It takes longer to undress the baby than it does to do the test.

'This study has shown conclusively that this test is advantageous,' he continues. 'We would like to see all babies being routinely tested. In this way the test will pick up additional babies who might otherwise have become very ill or even died. I think we now have enough evidence to say that pulse oximetry screening should be incorporated into everyday clinical practice.'

The research was carried out in six NHS trusts covering an area including Birmingham, Wolverhampton, Warwickshire and Shropshire.

# *Pharmacy* comes to Birmingham

Birmingham is laying the foundations for a brand new exciting Pharmacy programme. Headed by Professor John Marriott, the new course will form an integral part of the College of Medical and Dental Sciences' teaching and research agenda.

Since October, students have been able to enrol on the University's postgraduate DPharm course and there are plans to develop an undergraduate MPharm course starting in 2013.

Professor Marriott says: 'This is a flagship investment into pharmacy by the University which will have wide impact in prescribing, medicines optimisation and research being able to augment clinical pharmacology and translational research providing novel drug delivery systems and medicines formations.

'Pharmacy will complement existing programmes in the College and across the University. There are already parallels in some of the teaching on the Medical Science course and Pharmacy can also work with the MBChB and nursing programmes, experiencing patient care and stimulating inter-professional learning.'
The new programmes are being developed under guidance from the General Pharmaceutical Council and follow the principles of the Department of Health's Medical Education England's Modernising Pharmacy Careers, which proposes a new approach to pharmacist undergraduate education and pre-registration training. The five-year integrated course will also include the pre-registration year and by working with pharmaceutical partners to deliver the pre-registration element, the University plans to maintain a seamless educational experience providing the very best teaching and learning experience possible both within the University and in professional practice. There will also be the added option for students to intercalate and do study exchanges abroad.

In contrast, the DPharm is a mixed taught and research professional doctorate designed for registered pharmacists who are experienced practitioners. The flexible four-year programme will focus on work-based research and is ideal for the next pharmacist consultants of the future.

There is already some collaborative pharmacy research happening within the College and

Professor John Marriott

Professor Marriott, who has active research groups examining a variety of aspects of clinical pharmacy, also plans to develop this further. John concludes: 'There is a national need and patient need for more pharmacists. The beauty of Birmingham is that we are centrally placed within a network of large hospital Trusts and dynamic General Practices making it an ideal setting.

'Ultimately this will have a significant impact on patients and students on a number of programmes and will pave the way for vibrant, well qualified pharmacists of the future.'

# University to be national blood cancer trials hub

Birmingham is to be the hub of a unique national network of clinical trial centres being set up by the blood charity Leukaemia & Lymphoma Research. The network will have access to up to £50 million worth of new lifesaving drugs, in response to current poor survival rates for many types of leukaemia, lymphoma and myeloma.

The University will be home to a clinical trials unit which will co-ordinate the 13 centres in the national network. The move is central to the charity's vision to deliver 'Tomorrow's Treatments Today'.

Leukaemia & Lymphoma Research says the number of people dying from blood cancers, which have traditionally been seen as rarer cancers, is now slightly higher than breast and prostate cancer. Blood cancers are the most common cause of cancer deaths in the under 35s, with new figures released by the charity showing that more than 12,000 people still die of blood cancers each year.

With some notable exceptions, survival rates have improved very little for most forms of blood cancer in the last decade.

Leukaemia & Lymphoma Research Clinical Trials Adviser, Professor Charlie Craddock, Director of the Centre for Clinical Haematology run by the University of Birmingham and University Hospitals Birmingham NHS Trust, says: 'Every doctor will tell you that they are routinely turning down promising new drugs because they don't have the resources to conduct early stage clinical trials. We have a moral case for getting new drugs out there as soon as possible – if you have a relative with a blood cancer, you don't want life-saving treatment available in ten years, you want it now.

'Being part of this clinical trials network will increase the access of blood cancer patients in Birmingham to potential life-saving drugs and treatments. It offers hope to those patients who do not respond to current treatments.'

## Famous Birmingham graduates give students sound support through one-to-one mentoring

Twelve lucky final year undergraduate students from the University of Birmingham will get a once-in-a-lifetime opportunity to gain first-hand career insight and guidance from famous Birmingham graduates at the top of their field, in a new initiative. The Alumni Leadership Mentoring Programme will see a number of high profile Birmingham alumni – reading like a who's who spanning business, health, consumer, charity, arts and media sectors – providing one-to-one mentoring to selected students throughout their final year.

Top leadership mentors signed up so far from the health related fields include:

- Sir Liam Donaldson – former Chief Medical Officer (MSc, Anatomy 1976; DSc, Honorary Degree, 2005)
- Baroness Doreen Massey – Chair, The National Treatment Agency for Substance Misuse (PGCE, Education, 1962; BA, French Language and Literature, 1961)
- Sir Charles George – Chairman, The Stroke Association (Interc BSc, Anatomy, 1962; MBChB 1965; MD, Medicine, 1974; DSc Honorary Degree, 2003)
- Andrew Vallance-Owen – Bupa Group Medical Director and Bupa Foundation Deputy Chair (MBChB, Medicine, 1976)

All mentors will offer their time for free.

Leadership mentors will offer practical advice on employability and support to students as they prepare to enter the workplace.

## Alastair Campbell visits centre

Former Downing Street communications supremo Alastair Campbell made a special visit to the Centre for Clinical Haematology in July.

Mr Campbell, who is chair of fundraising for the national charity Leukaemia & Lymphoma Research, which funds the centre, spent an hour touring the facility – headed by leading haemato-oncologist Professor Charlie Craddock – and talking to Professors Michael Sheppard and Lawrence Young about the ground-breaking work that takes place there.

Best known for his role as press spokesman for Prime Minister Tony Blair and as one of the architects of New Labour, Mr Campbell was in Birmingham to deliver the 2011 Baggs Memorial 'Happiness' Lecture in the University's Great Hall.


From left: University Provost and Vice-Principal Professor Michael Sheppard, MDS College Head Professor Lawrence Young and Professor Charlie Craddock flank Alastair Campbell outside the Centre for Clinical Haematology.

# *Childhood cancer survivors* ‘at greater risk in middle age’

Scientists at the University have found that survivors of childhood cancers are four times more likely than the general population to develop a new cancer. The results are published in the *Journal of the American Medical Association*.

The researchers, funded by Cancer Research UK, followed the health of over 18,000 childhood cancer survivors** for an average of 25 years. They found that in middle age, survivors were at greater risk of developing certain types of new cancers, particularly of the digestive or genitourinary systems, such as bowel and kidney cancers.

Among the survivors there were 837 new cancers, almost four times the 216 that would be expected in the same number of people in the general population.

They also found that five per cent of survivors had developed a new cancer by the age of 38, while in the general population it took until 54 years to reach this same figure.

Study author Dr Raoul Reulen, of the School of Health and Population Sciences, said: ‘We know that survivors of childhood cancer are at increased risk of developing new cancers, but we didn’t know what the long term risks were as they reached middle age. By knowing the cancers that survivors are most at risk of we can focus attempts to prevent or pick up cancers earlier hopefully helping them to be treated successfully.’

Most of the increased risk of developing further cancers can be attributed to the treatments used for the original cancer. Cancer Research UK is already exploring ways to minimise these effects in its many research programmes. The researchers found that survivors treated with radiotherapy to the abdomen and pelvis 20 to 30 years ago were three times more likely to develop a new cancer of the digestive system.

As the risk for developing bowel cancer among this group was similar to those who have a strong family history of the disease the researchers have questioned whether they should be offered colonoscopy screening to detect possible bowel cancers earlier.

Dr Reulen added: ‘The increased risk of developing new cancers in survivors is still relatively low overall, but we encourage survivors to take part in the existing screening programmes for bowel, cervical and breast cancer.’

The study also showed a changing pattern in the cancers being seen among survivors as they got older. Digestive and genitourinary cancers are relatively rare among survivors younger than 20 years, but they become more common over time.

Overall, five-year survival rates for childhood cancer patients have made great improvements over the last 40 years and today almost 80 per cent survive. Due to this success there is now an urgent need to reduce the late side-effects of some of these treatments.

**British Childhood Cancer Survivor Study (BCCSS)

# Iodine deficiency findings prompt calls for diet change

Collaborative research involving scientists from the University of Birmingham has revealed that more than two-thirds of UK teenage girls are iodine deficient, leading to calls for a simple diet change to combat the most common cause of mental impairment worldwide.

Iodine is an important component of thyroid hormones and deficiency has substantial effects on growth, development and cognition. Solving this potentially major public health problem can be helped by increased milk intake, with the research, published in *The Lancet*, highlighting a link between low iodine levels and a decline in milk consumption.

The World Health Organisation (WHO) recommends a daily intake of iodine of 150µg. Seventy per cent of the 14–15-year-old girls assessed during the study had median urinary iodine concentrations of less than 100µg/l, indicative of mild iodine deficiency. It is especially important for women of child-bearing age to have sufficient levels as even a mild iodine deficiency can harm unborn babies, causing stunted growth, reduced IQ and mental impairment.

Co-author of the paper, ‘Iodine status of UK schoolgirls: a cross-sectional survey’, Dr Kristien Boelaert, from the School of Clinical and Experimental Medicine, explains: ‘We found that median urinary iodine concentrations in 737 pre-pregnancy female participants, whose offspring will be most susceptible to the adverse effects of iodine deficiency in the short-medium term, were indicative of mild iodine deficiency.

‘Lower iodine concentrations were recorded in Belfast and lower urinary iodine content was independently associated with lower milk intake. Our findings emphasise an urgent need for a comprehensive investigation of UK iodine status and evidence-based recommendations on the need to implement a policy of iodine prophylaxis.’

The team concludes that the UK is now iodine deficient which is at least in part caused by a reduction in the amount of milk consumed by the population.

The researchers are calling for increased milk intake as well as looking to the successful model used in Australia and New Zealand to reverse iodine deficiency by implementation of the use of iodised salt; a cost-efficient method of increasing a nation’s iodine levels.

# PIONEERING new University centre open for business

Professor Janet Lord

After months of meticulous planning and preparation, the University of Birmingham's brand new Centre for Translational Inflammation Research is now up and running at the city's Queen Elizabeth Hospital (QE).

Headed by Janet Lord, Professor of Immune Cell Biology, the state-of-the-art laboratories bring together staff from a multitude of specialist areas, including rheumatology, ageing, respiratory medicine, nephrology, ophthalmology, immunity and trauma to work on major collaborative research programmes.

Sitting within the facility is the NIHR Centre for Surgical Reconstruction and Microbiology, a ground-breaking, multi-partner £20 million trauma care initiative which opened in January under the interim directorship of Professor Sir Keith Porter OBE, Honorary Professor of Clinical Traumatology and a QE consultant.

'...many people now survive the early stages of trauma who would have died just a few years ago.'

Bringing together military and civilian trauma experts to provide cutting-edge care at the earliest stages of injury, the NIHR Centre is a collaboration between the University, the NHS, the MoD and UHBFT, and is the first and only research facility in the UK to focus on military as well as civilian trauma care. The University and Trust will each contribute £5 million towards its work over the next five years.

With all returning injured UK Army personnel receiving treatment at the QE, the University's world-leading scientific expertise will help to fuel novel treatments for a wide range of challenging injuries and push the boundaries of current understanding in areas including burns and blast wounds.

Professor Lord and colleagues said they were delighted to be starting work in the University's new laboratory space. 'Trauma is the commonest cause of death before the age of 45 years,' Professor Lord explains. 'But additionally, many people now survive the

early stages of trauma who would have died just a few years ago. Moreover, the types of trauma that have hitherto been rare are now frequently encountered in modern warfare or as a result of terrorist activity – blast injury is an example.

'The NIHR Centre unites basic researchers and trauma surgeons to examine the body's response to trauma, with the aim of developing an in-depth understanding of the most appropriate response to maximise survival through the acute stage following injury and to ensure optimal wound healing, prevent infection and ensure good physical and mental rehabilitation.'

Microbiology at the labs is led by Professor Mark Pallen and is supported by the University's high-throughput sequencing capability which was funded by the Birmingham Science City project.

'Just as a soldier needs to know who the enemy is, where he is and how he got there,

Up and running: Laboratory staff carry out work in the NIHR Centre for Surgical Reconstruction and Microbiology within the University of Birmingham's Centre for Translational Inflammation Research at the Queen Elizabeth Hospital.

so healthcare professionals need not only to identify the organisms that cause infection but track their spread in the hospital environment,' says Professor Pallen. 'This new technology means we can now determine the entire genetic blueprint of individual bacterial isolates relatively quickly, easily and cheaply, enabling us to distinguish bacteria that differ by as little as a millionth of a genome.'

Professor Richard Lilford, who led the bid for the Centre for Surgical Reconstruction and Microbiology and serves on its management and executive committee comments: 'This centre was brought together under the Protocol Development Service of the Birmingham Clinical Research Academy and represents an example of working across boundaries.

'The centre is outward looking and is building on extensive national and international links so that our researchers have access to the world's best brains and greatest expertise.

'In addition to the three organisations mentioned above, three colleges within the University have contributed to its development, along with collaborators from other universities. We have also been awarded a network grant by the Medical Research Council to promote basic science relevant to trauma research across the country and, more recently still, a competitive grant from a major charity, details of which will be announced imminently.

'The centre is outward looking and is building on extensive national and international links so that our researchers have access to the world's best brains and greatest expertise. Working with a diverse range of disciplines to pull the application together has been enormous fun. I also perceived a sense of purpose that exceeded my expectations and suspect there may have been an additional motivating factor at work, in the form of commitment to the country's injured service men and women.

'In the spirit of the icons of military surgery such a Larrey and Pare, one of the tasks of the centre will be translation of knowledge from the battlefield to civilian surgery.'

Professor Lord has previously studied how the immune and endocrine systems respond to both physical trauma, such as hip fracture, and emotional trauma, like bereavement, in older people. Her work has shown that an excess of the stress hormone cortisol, coupled with a lack of the counter stress hormone DHEAS is associated with infection. Analysis of the same hormones in Vietnam war veterans has shown the same imbalance was associated with poor health in later life, including higher rates of diabetes, heart disease and depression.

Her team is now going to explore whether these hormones also play a role in determining recovery from major trauma and, if so, to carry out a clinical trial giving patients DHEAS and monitoring whether this aids recovery in the short and longer term.

# Expertise in epigenetics

Birmingham's ability to incorporate basic science into clinical trials is paying early dividends in an emerging area of treatment, reports Jenni Ameghino.

The University of Birmingham's global reputation for excellence in cancer research is being further enhanced by pioneering translational work being carried out in the fledgling biotechnological field of epigenetics.

Explained simply as the process by which the DNA within the nucleus of cells is packaged by proteins – known as histones – to turn genes on or off, epigenetics is only just beginning to yield tangible results in the treatment of disease. But cutting-edge research at Birmingham is bringing remarkable early success in this competitive arena, most particularly in the treatment of blood cancers such as leukaemia and lymphoma where our work is already showing positive bench-to-bedside effects.

'It is now clear that acquired epigenetic changes, or abnormalities in how DNA is packaged, is a common cause of abnormal gene expression, leading to cancer,' explains Charlie Craddock, Professor of Haemato-oncology and Director of the Centre for Clinical Haematology run by the University and University Hospitals Birmingham NHS Trust. 'We originally assumed it was acquired changes in the DNA code that entirely drove the acquisition of a neoplastic phenotype or that made a cell cancerous, but we now know you can have a patient whose cancer arises because of changes in how the DNA is put together.'

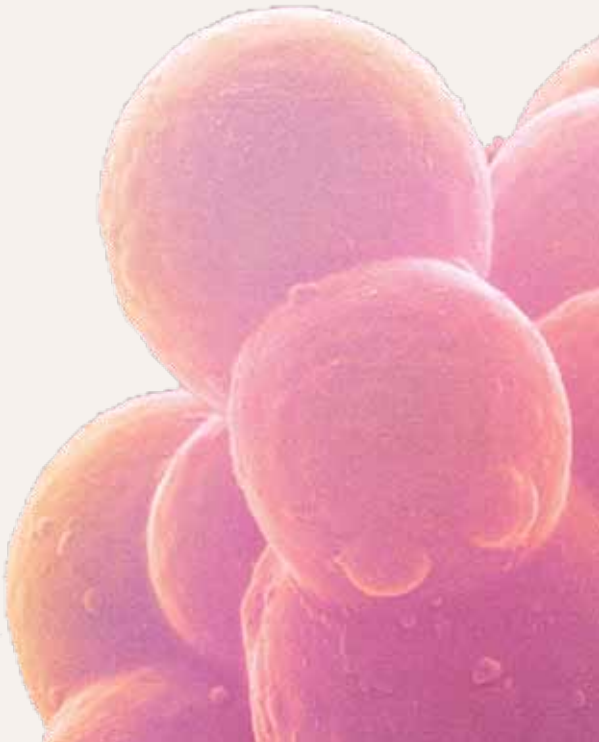
Epigenetic drugs that can reverse such abnormalities and repackage DNA have been found to increase the expression of genes which were previously switched off, selectively killing leukaemic and other cancer cells, he explains.

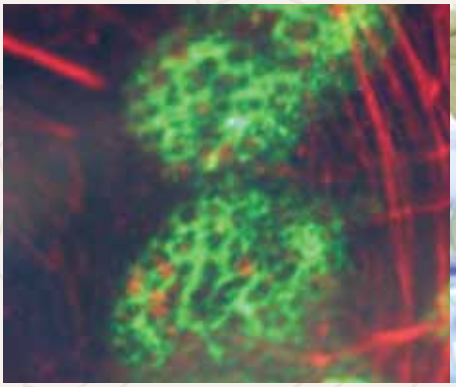
Birmingham's clinical trials programme in epigenetic therapies started seven years ago. Several drug treatments developed here are showing promising results, particularly in the treatment of patients with Acute Myeloid Leukaemia (AML), one the most common, and most difficult to treat, blood cancers.

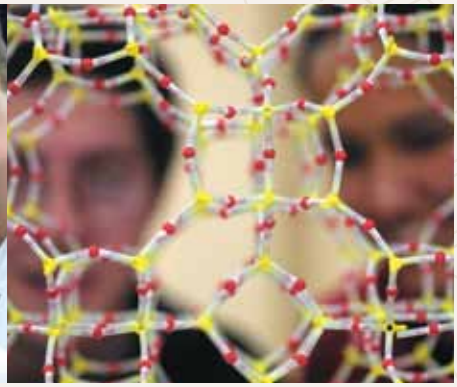
> 'We have observed remarkable activity in about a third of patients who were either too old for chemotherapy or resistant to other treatments'

'There are two challenges in improving outcomes for patients with AML,' says Professor Craddock. 'One is to develop more effective drug and (bone marrow) transplant therapies but a second is that because AML is common in older people, who cannot tolerate drug treatments such as chemotherapy, we need to develop therapies that are less toxic and have fewer side effects so they can be delivered in comparative safety in older patients.'

One ground-breaking phase two trial, run by the Cancer Research UK Clinical Trials Unit at the University has involved giving a combination of four drugs to patients with AML or high risk Myelodysplasia (MDS). Known colloquially as Val/Aza* it included using the popular anti-epileptic drug sodium valproate combined with the DNA methyltransferase inhibitor azacitidine in 79 older patients, in the first trial of its kind in the world.







All of the patients had failed other treatments and were left with no other options other than supportive care.

'We have observed remarkable activity in about a third of patients who were either too old for chemotherapy or resistant to other treatments,' says Professor Craddock.

Senior Trial Co-ordinator Shamyla Siddique adds: 'Some patients, who were predicted to survive no longer than a matter of weeks, lived to see the birth of a grandchild, or survived long enough to see another Christmas or birthday, and even long enough to get married for one particular patient. In addition, four patients were able to proceed to a potentially curative transplant following treatment on the trial.'

A total of 21 patients survived for more than 12 months after entering the trial, with some living longer than three years. 'This prolonged survival was remarkable in the group of patients enrolled, who were expected to survive for no longer than six months at most.'

A significant number of participants suffered from side effects including somnolence and fatigue, reports Professor Craddock. 'So we are now in an advanced stage of planning a randomised trial between azacitidine given alone and azacitidine combined with a new epigenetic agent, which we believe will be better tolerated.' The team hopes to begin this national clinical trial early next year.

> 'We have shown, for the first time, that we induce an immune response against the cancer in these patients...'

Collaborating with the University of Oxford, Professor Craddock's team has been exploring how leukaemic stem cells, believed to represent a reservoir of the cell of origin in AML, are not eradicated in patients treated with epigenetic therapies. 'Since it appears that most of these patients don't achieve durable benefits and subsequently relapse, this suggests we need to develop therapies that specifically target this population,' he says.

Another strand of the team's work is a collaboration with Professor Paul Moss and Dr Tatjana Stankovic, which has shown for the first time that epigenetic drugs not only alter the expression of genes that may be related to why a cell becomes cancerous, but also upregulate antigens on the tumour which can be recognised by the patient's immune system.

'We have shown, for the first time, that we induce an immune response against the cancer in these patients, and so this offers insight into a novel mechanism by which epigenetic therapies might have anti-tumour activity,' Professor Craddock concludes. 'We are therefore now in the final stages of recruiting to the first study in Europe using epigenetic drugs to improve stem cell activity in bone marrow transplants. We believe that within five to ten years there is every prospect that these therapies will be established as an important part of new treatment in leukaemia'

* Phase II study of the tolerability and efficacy of the histone deacetylase inhibitor sodium valproate administered in conjunction with 5-acazitidine, theophylline and ATRA (all trans retinoic acid) in patients with Acute Myeloid Leukaemia (AML) and high risk Myelodysplasia (MDS).

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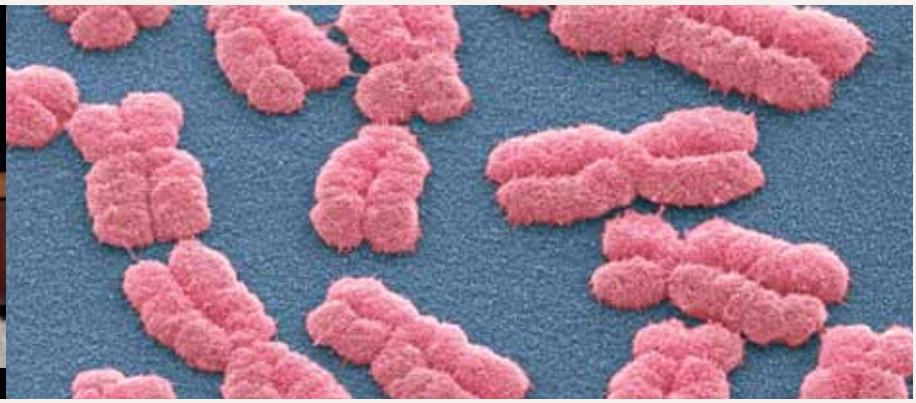
**Expertise**
in epigenetics

# Taking control of our genes

Professor Bryan Turner



We are all now familiar with the idea that many aspects of our lives are influenced by our genes, writes University of Birmingham epigenetics expert Professor Bryan Turner. We all have essentially the same set of genes (we're all members of the same species after all), but most genes exist in human populations as several variant types and the selection of variants that we inherit from our parents helps determine our individual characteristics. For example what colour our eyes are, how soon our hair falls out or how likely we are to get diseases such as diabetes or some types of cancer.

Human genome (DNA sequencing) projects are providing us with the ability to know what variant genes we have inherited and thereby predict what is likely to happen to us later in life. This information can be useful, but genes are like a hand of cards dealt in a game of bridge; you play it to the best of your ability, but you can't change it.

So genes are very powerful, but what is not generally appreciated is that genes themselves don't do very much. Genes are made of DNA and DNA is an enormously long, chemically quite simple and very stable molecule whose job is to carry all the genetic information required to make the proteins and other molecules of which our bodies are made. It is these other molecules (mostly proteins) that actually build our bodies and make things happen.

The second important point, often overlooked, is that all the various cells and tissues in our bodies carry the same set of genes, even though they are so very different. Think of a long, thin skeletal muscle cell or a small white blood cell. As an even more dramatic example, consider a caterpillar pupa (chrysalis) and the butterfly that finally emerges. They too have the same set of genes, but their body shapes could not be more different. How does this happen? The answer is that in each of these different stages of development, or cell types, a different set of genes is expressed (ie, switched on or off). It is the proteins and other molecules encoded by these different sets of genes that form the different cell types or body shapes.

The study of the mechanisms by which gene expression is regulated so as to generate different cell types and body shapes is called epigenetics, and it is arguably the most exciting, and certainly the most rapidly developing, area of biomedical research.

The reason for the excitement is easy to see. Gene expression is regulated by families of proteins and enzymes, all of which are themselves influenced by environmental agents such as drugs, toxins and dietary components. In other words, as we begin to understand these control processes, we can start to change how our genes operate by selective drug therapy, or even a change in diet. Such epigenetic therapies are already being used to address some of the health problems caused by inappropriate gene function (which can be genetic, ie, inherited, or acquired).

As a final metaphor, it is useful to think of DNA as an (old fashioned) audio tape. It contains all the information needed for a piece of music, but is useless without a tape player. Epigenetic processes are the workings of that tape player. If the tape encodes Beethoven's fifth symphony, that is all that can be played, but by adjusting the volume, tone, balance etc, of the player, we can dramatically alter the quality of the music that emerges. We may even be able to disguise faults (mutations) in the original tape (DNA). Epigenetics is an empowering science that allows us to take control of our genes by understanding the delicate and complex interactions between our bodies and the wider environment.

* Bryan Turner is Professor of Experimental Genetics at the Institute of Biomedical Research, University of Birmingham.

**Expertise** in epigenetics

# On trial: one man's Val/Aza journey

Ian Smith took part in the Val/Aza clinical trial at Birmingham as a precursor to undergoing a bone marrow transplant in 2010.

Having being diagnosed with acute myeloid leukaemia in November 2008 he spent his 70th birthday undergoing chemotherapy. 'On January 30, 2009, we were told by a doctor at Stoke Mandeville Hospital that there was little more they could do for me. I had only a five per cent chance of seeing another Christmas.'

But with characteristic zest for life, the retired father of four from Buckingham wasn't about to let blood cancer get the better of him. 'It was against my nature to accept the prognosis, though I could appreciate how some other people might. I was reasonably fit from running and jogging so I was conscious that I had to make my own case for continuing treatment.'

> 'He told me that with a transplant I would have a 20 per cent chance of mortality and a 25 per cent chance of survival. Those were good enough odds for me.'

Ian responded well to the chemotherapy and, after much lobbying, he and his wife Mary were put in touch with an Oxford-based consultant specialising in bone marrow transplantation. 'He told me that with a transplant I would have a 20 per cent chance of mortality and a 25 per cent chance of survival. Those were good enough odds for me.'

Unfortunately, shortly before the transplant was due to take place, Ian's leukaemia returned. 'It was a huge blow,' he recalls.

'I was told I had weeks – months at most - to live.' Refusing to give up hope, the Smiths

persisted with their treatment investigations and eventually heard about Professor Craddock's work at Birmingham. 'I was referred for treatment under him and he enrolled me into the Val/Aza trial,' says Ian.

The trial process involved having daily subcutaneous injections into the stomach. Ian spent so much time at the newly opened Centre for Clinical Haematology at the Queen Elizabeth Hospital in Birmingham that he and his wife began staying at a city hotel rather than commuting from home.

'I experienced some side effects, mainly from the sodium valproate,' remembers Ian. 'They upped the dose until, as Charlie put it, you could no longer finish *The Times* crossword in half an hour. I play keyboards in a band and I couldn't play properly, or capably drive, for some time.

> 'It felt like completing a journey. We've also travelled on the Orient Express since then. I feel very fortunate and I think I owe a lot of people a lot.'

'Just after I started the trial I was so thin that I lost my wedding ring one day while washing my hands,' he explains. 'My wife and I had been married for about four years then and so when I noticed it had gone I went out and bought another one. A close friend rang me and said, 'What a crazy thing for a dying man to do!', which made us both laugh. But there was lots of sadness too; we met trial patients who dropped by the wayside, and we are still in touch with the widow of one gentleman who never made it.'

Ian was one of the lucky ones, responding well and quickly going back into remission. Fit enough to enjoy a ski-ing holiday that Christmas, he returned to the QE on January 3 last year for his long-awaited bone marrow transplant, going on to participate in another trial, involving azacitidine alone, to improve the outcome of the transplant by targeting any residual leukaemia.

Last month, having been clear of leukaemia since last November, the Smiths travelled to stay with family in San Francisco. 'That was a milestone for me,' says Ian. 'It felt like completing a journey. We've also travelled on the Orient Express since then. I feel very fortunate and I think I owe a lot of people a lot.'

# *THE SHAPE* of things to come

Once again the health services landscape is changing. With Primary Care Trusts due to be dissolved in 2013, the controversial notion of GP commissioning consortia has given way to a new manifestation of health care organisation – Clinical Commissioning Consortia (CCC)*.

'These are going to involve a greater diversity of professionals than commissioning bodies in the past and will be more clinically led which, in my opinion, is a good thing,' says public health expert Dr Edwina Affie, director of the West Midlands Commissioning Support Unit based in the University's School of Public Health.

'One of the problems with health care commissioning previously has been that the people doing it didn't have sufficient understanding of medical and clinical services. If you want to successfully commission for population health, which is very different from providing clinical care on an individual basis, then really good intelligence, evidence and data analysis is needed to support it. Understanding what works, is cost-effective and meets the population's health care needs requires very different skills from clinical ones.'

She should know. Dr Affie has spent 30 years in the NHS, half of which was in clinical care working as a clinical histopathologist. As a health care commissioner in the London borough of Islington she had responsibility for significant budgets and led teams of professionals who supported acute commissioning and commissioned for cancer services.

While clinicians will be at the forefront of CCCs, they will be underpinned by a select group of commissioners, she says. 'These won't just be GPs, which is good because GPs don't necessarily understand the population side of things, so other clinical perspectives need to be represented.'

> It's never easy to save money and indeed it is almost impossible to do that at the same time as undergoing major structural reform.

Dr Affie predicts a much wider range of professionals being involved in commissioning, 'senior clinical people including primary care practitioners, hospital consultants and directors of nursing; a range that reflects the complex nature of community health care. There will be commissioning managers to take responsibility and do the procurement plus people from social services and local authorities, all working in close collaboration.

'Another significant point to remember is that at the same time that the government is reforming the commissioning of health care, it is expecting £20 billion of savings. That's a risky thing to do when you're trying to reorganise the landscape. It's never easy to save money and indeed it is almost impossible to do that at the same time as undergoing major structural reform. The danger is the large financial risk that will constrain the services being commissioned.'

The unit Dr Affie leads at Birmingham has several key roles, including providing intelligence on the health and care of the 5.5 million people living in the West Midlands, providing education and training for commissioning organisations and providing specialist expertise in a broad range of clinical and policy areas. The unit works closely with Professor John Glasby, director of the Health Services Management Centre in Social Sciences, and Professor David Fitzmaurice, from Primary Care Clinical Sciences.

'While I am interested in health care commissioning, the HSMC has much more experience in public health sector commissioning so it is important that we work together,' says Dr Affie.

To this end, the three academics are hoping to set up within the University a Centre for Health Care Commissioning. 'We would like to be able to develop the services we offer in a more aligned way, and for our three units to collaborate to support excellence in commissioning for the coming new landscape,' explains Dr Affie. 'We would like to develop four key themes: Intelligence, Education and Training, Research and Consultancy.

'We have a strong and historic collaborative history with the NHS in the West Midlands. We train doctors and we train public health professionals here. Research in my unit is NHS funded. We hope the University's senior management will recognise how inclusive and important this is to the institution's strategic objectives and support us in our aim.'

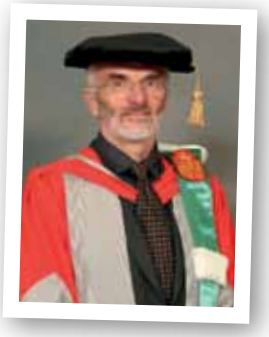
*Jenni Ameghino*

* Correct at time of going to press (September 2011)

# 2011 HONORARY GRADUATES

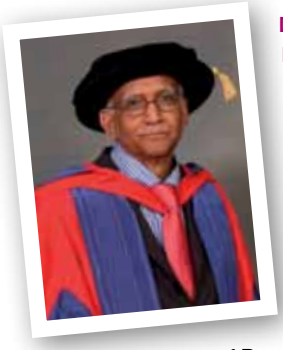
**Chris Henney – Doctor of the University**

Chris Henney is involved in all entrepreneurial aspects of the biotechnology industry. He co-founded a number of biotechnology companies, one of which developed the first immunotherapeutic vaccine approved for the treatment of cancer and the best selling drug world-wide for the treatment of rheumatoid arthritis.



**Jo Bradwell – Doctor of Science**

Jo Bradwell is Chairman of The Binding Site – a biomedical development company. He is currently involved with clinical trials with patients who have multiple myeloma and are in renal failure. He is studying immunotherapy in patients with parathyroid carcinoma and maintains strong research links with the University's Medical School.



**Dr The Hon Ahmed Rashid Beebeejaun – Doctor of the University**

Ahmed Rashid Beebeejaun (MBChB, 1962) is Deputy Prime Minister of the Mauritius Labour party, Minister of Renewable Energy and Public Utilities for the Government of Mauritius and has served as a Government Consultant in Child Health. He is also a Fellow of the Royal College of Physicians in London.

In addition to our honorary graduates, this year the Vice-Chancellor's Prize was awarded to Robert Tidswell (MBChB, 2011). This prize is awarded to a student from across the whole of the University who has obtained exceptional marks throughout their degree. Congratulations Robert!

**Sue Hill OBE – Doctor of Science**

Professor Sue Hill trained as a clinical physiologist and gained a PhD in Respiratory Sciences. She has worked for most of her career in the NHS and academia at University Hospital Birmingham and its predecessors and at the University of Birmingham. Sue was appointed as Chief Scientific Officer at the Department of Health in 2002 and is the professional head of the 50,000 strong healthcare science workforce in the NHS and related organisations. In 2005, Sue received an OBE for her services to healthcare science.

**Alumna of the year – Sarah-Jane Marsh**

Sarah-Jane Marsh is Chief Executive Officer of Birmingham Children's Hospital, a position she took up at the age of 32 making her the youngest ever Chief Executive of a Foundation Trust. In her career Sarah has worked in a number of planning, development and managerial roles for Worcestershire Hospitals, Redditch and Bromsgrove PCT, Walsall Hospitals and Birmingham Children's Hospital.

## Alumni congratulations

**Congratulations to alumnus Andrew Wilkinson** (MBChB, 1968), Consultant Paediatrician and Professor of Neonatal Medicine at Oxford University , who has won the James Spence Medal 2011 from the Royal College of Paediatrics and Child Health. This medal is awarded for outstanding contributions to the advancement or clarification of paediatric knowledge and is the highest honour the Royal College can bestow.

**Congratulations also to Nick Ruskin** (MBChB, 2001) who has won the coveted Keith Yeates medal from the Royal College of Surgeons (Urology). The medal was awarded to Nick following his outstanding performance in the Intercollegiate speciality examination in urology.

## Ever wondered where medicine and medical science graduates live in the world?

Medicine and Medical Sciences University of Birmingham graduates are represented in 79 countries across the globe.

Although 90% choose to live in the UK, 139 alumni live in Canada; 137 in Australia and 100 in the USA. There are 20 University-wide alumni international groups. See the alumni website for countries and contacts at **www.birmingham.ac.uk/alumni**

# Birmingham University Medical Society, ***the best in the UK and it's official!***

MedSoc, the students' society for Medicine at Birmingham has won the United Kingdom Medical Students' Association Student Medical Society of the Year Prize.

This prestigious prize is awarded annually to the medical society that has most improved over the previous 12 months and is accompanied by a cash prize.

The award was presented to Sophie Lumley, current MedSoc president by Professor Michael Baum, Director of UCL clinical trials group and a former Birmingham graduate himself. As Sophie readily admits however, this award was a culmination of activity from three generations of MedSoc Presidents: herself, Majd Protty (president 2010–11), Jake Mann (2009–10), and the 2010–11 Vice President (Academic), Aruna Ekanayaka.

Comprising some 3,000 members, MedSoc encompasses no less than 22 individual societies, eight charities raising approximately £7,000 each year, 16 sports teams and has hosted no less than 15 social events this year. It also provides the Dean of Medicine's team with much welcomed academic student representation and with it an improved course and welfare system.

L–R: Jake Mann, Majd Protty and Sophie Lumley

# New Student BMJ Editor

Fourth-year medicine student Neil Chanchlani has become the latest editor of the Student BMJ. He has taken a year out of his studies to concentrate on the new role.

Neil, who has always had a strong interest in creative writing, follows Birmingham graduate Pritpal Tamber (MBChB, 1998) who was Student Editor in 1996–1997. In 2010, Neil was awarded the Clegg Scholarship, which is an eight-week work placement at the BMJ aimed at medical students.


Neil Chanchali

Neil said: 'I really enjoyed the placement; having the opportunity to write and edit health copy and attend press conferences. It also demonstrates that you don't have to do a clinical placement for your elective and there are plenty of other options out there. When the opportunity came up to apply for the editor position, I decided I definitely wanted to go for it.

'Seeing the process that goes into creating the journal is fascinating. Being able to read through all the submissions, commission articles and take part in the peer review process puts you firmly at the centre of current health care issues and formulating ideas. When it all comes together it's quite exciting.'

The medical journal currently has a print run of roughly 21,000 and an online readership of up to 24,000 people per month. During his time as editor, Neil would like to see that increase further, particularly driving international readership.

In the future Neil says he would really like to become more involved in the policy side of health care and 'be part of the bigger picture'. He plans to continue with his love of writing and apply for the Academic Foundation Programme once he has finished his medicine degree.

The Student BMJ welcomes submissions from anyone up to Foundation Year 2, so if you have a submission or any suggestions, please contact the journal via studenteditor@bmj.com

## At the cutting edge...

Dr John Black (MD, 1978), President of the Royal College of Surgeons came back to the Medical School in March to talk to SurgSoc, the University's surgical society. Dr Black gave a talk entitled 'my life in surgery' which focused on the changes in surgery he had witnessed and famous surgeons, but with a very strong influence on how Birmingham based surgeons have contributed to and enhanced the discipline over many years.

The President then presented certificates and prizes to the winners of SurgSoc's National Academic Prizes Competition for this year, and the certificates and trophies to those students who have successfully completed this year's SurgSoc Anatomy Course and Lecture Series.

Founded in 2002 with the aim of promoting surgery and inspiring students to undertake a surgical career, SurgSoc has a vibrant membership of more than 350 students drawn from all years and courses in the College of Medical and Dental Sciences. The society runs many events throughout the year and it has invited an impressive array of surgical guest speakers to speak on various topics over the last few years.


Sanah Anwari, winner of the SurgSoc Anatomy Cup for the Clinical years, receives her trophy from Dr Black

# Conferences and events at the Medical School

## Conferences and events

**Research Using Human Tissue**
The aim of this course is to provide an understanding of the regulations and ethical issues surrounding the collection and use of human biomaterials for research.
Date: Tuesday 15 November 2011

**Leonard Parsons Lecture**
Speaker: Alan Lucas, Head of the Medical Research Council's Nutrition Unit at the Institute for Child Health, London
Date: Friday 4 November, 5.00pm

**Commercialising Academic Medical Research**
The course discusses the challenges concerning the identification of viable projects with guidelines concerning their evaluation, the rationale for the selection of the route to commercialisation and the mechanism of protecting the intellectual property.
Date: Saturday 19 – Sunday 20 November 2011

**John Ash Lecture: 'Birmingham, Birmingham University and the Public Health History of the Nation'**
Speaker: Professor Simon Szreter, Professor of History and Public Policy, University of Cambridge.
Date: Thursday 8 December, 4.30pm
Contact: Kiranjit Hallan on k.k.hallan@bham.ac.uk for more information

Medlines editor Michelle Morgan is now on maternity leave. Her colleagues in MDS would like to wish her well in the coming weeks and months.

## Save the date!

**Class of 1957:**
The Class of 1957 will hold its 55th reunion in Birmingham on 5 and 6 October 2012. Joy Bevan is organising.

**Class of 1966:**
The Class of 1966 will hold its 45th reunion at the Priest House Hotel Castle Donnington on 15 October 2011. David Hosking is organising.

**Classes of 1987, 1977, 1972, 1967, 1962:**
The University is hosting its annual anniversary reunions on Saturday 9 June 2012. Contact the alumni events team on +44 (0)121 414 9084 or via alumnievents@contacts.bham.ac.uk for more information.

**Class of 2011:**
Join us for a nostalgic day of catching up with old friends on Saturday 5 November 2011. At 3.00pm there will be a tour of the Medical School with Kate Thomas followed by dinner and dancing at Hornton Grange at 7.30pm. Black Tie. Tickets via Tom Bragg at twhbragg@hotmail.com



## Helping to raise funds

Sally Brooks has recently joined the College of Medical and Dental Sciences to help raise funds for health-related projects across the University. She works closely with alumni who wish to make financial gifts to the University, especially donations towards the Medical and Dental Schools.

Sally, who has worked for the past five years in the NHS, said: 'I have really enjoyed getting to know everyone here at the College of Medical and Dental Sciences, and have particularly enjoyed meeting former medical students and hearing about their time at the school. There are lots of fantastic ways that alumni can get involved, and one of the more popular ways is by supporting bursaries for students who might not otherwise come to University.'

If you would like to talk to Sally, or organise to meet with her, you can contact her on 0121 414 7957 or s.b.brooks@bham.ac.uk.

# Obituary

Sidney Montague Hilton was born on 17 March 1921 and died on 28 January 2011. Sidney Montague Hilton had been Bowman Professor and Head of the Department of Physiology at the Medical School in Birmingham from 1965–1983. He was a distinguished physiologist who made leading contributions to understanding brain control of cardiovascular changes accompanying behavioural reactions associated with sudden emergencies like the Fear-Flight-Fight reaction. These have relevance to psychosomatic disease and to chronic hypertension. Hilton was in the vanguard of thinkers who provided experimental evidence against the long held view that there is a single brain centre controlling blood pressure. He was an excellent lecturer and travelled widely.

Sidney Hilton was educated at St Paul's School, London from where he won a place to study medicine at Cambridge having gained an exhibition at Jesus College. During the Second World War he was allowed time to take the Part II Honours Tripos course in Physiology following which he did his clinical training at Guys Hospital, London where he subsequently held several house appointments. He then was required to do National Service and for this he served in the RAF at the Institute of Aviation Medicine. Here he assisted in developmental work on the design of flying equipment and carried out studies on ways to accurately measure oxygen levels in the blood, non-invasively. On leaving the RAF in 1950, Sidney returned to Cambridge to the lab of Professor Adrian a Nobel Laureate. It was here that he decided on a career in physiological research and possibly the seeds were sown for his later major contributions. He then joined the scientific staff of the Medical Research Council (MRC) where he worked on the local mechanical and chemical control of blood vessels and later studied blood flow and secretion in salivary glands. At the end of the 1950s his attention began to move to the regulation of the heart and vascular system by the brain, and it was here that arguably he made his biggest contribution. He had become fascinated by the hypothesis of Cannon concerning the Fright-Flight-Fight response so fundamental to survival in wild animals but when over-expressed in humans can lead to chronic hypertension.

He gained experience at the renowned Nenki Institute of Experimental Biology of the Polish Academy of Sciences in Warsaw and from his studies it was clear to Hilton that no longer could a single localised area in the hind brain be considered responsible for blood pressure regulation, a concept that had stood for 50 years and appeared in every textbook. It was now necessary to define a model based around discrete reflex control of parallel pattern generators for the cardiovascular responses accompanying various types of behaviour. These studies which were started at the MRC Research Institute, continued at Birmingham with his appointment to the Bowman Chair of Physiology.

Hilton was a complex perhaps egotistic person whose measure of mischief in scientific and administrative confrontations often led to acrimony and this perhaps resulted in his not receiving the full credit for his scientific contribution. However, the move to Birmingham provided an opportunity to build up a department that had lost most of its staff. Hilton built up its teaching and its research to a state where it became not only one of the strongest departments in the University but also in the UK, whilst its research quality became recognised internationally. It was also a happy department and during this time it nurtured many 'Prima-donnas' providing three Heads of Departments at other universities as well as a Director of the Army Personnel Research Establishment in Farnborough. During this time Hilton also helped to establish the Physiology Department in the new Medical School in Salisbury (Harare) Southern Rhodesia (now Zimbabwe) that had been founded in 1963 with a special relationship to the University of Birmingham. The early days of Hilton's time in Birmingham were very happy ones for budding physiologists who not only enjoyed the intense 24/7 research activity but also the social events of parties in Gerta Vbova and Hilton's home as well as other social occasions. During this time Hilton served as secretary of The Physiological Society where his irreverent sense of humour was not always enjoyed although his contribution to scholarly debate at scientific meetings of The Society were often a highlight and much missed on his retirement. In 2004 he was awarded the distinction given to only a few of being elected as an Honorary Member of The Society.

He retired in 1984 and moved with his third wife Mary to a lovely rural but somewhat remote setting on a mountain side, near Dolgellau in West Wales. Despite being quite cut off from the scholarly environment he appeared to be very happy, much enjoying the attention of Mary's children and grandchildren. Recently he had renal failure but was looking forward to reaching his 90th birthday in March of this year but this sadly was not to be. He is survived by his third wife Mary and a number of children from previous marriages.


## Medlines

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