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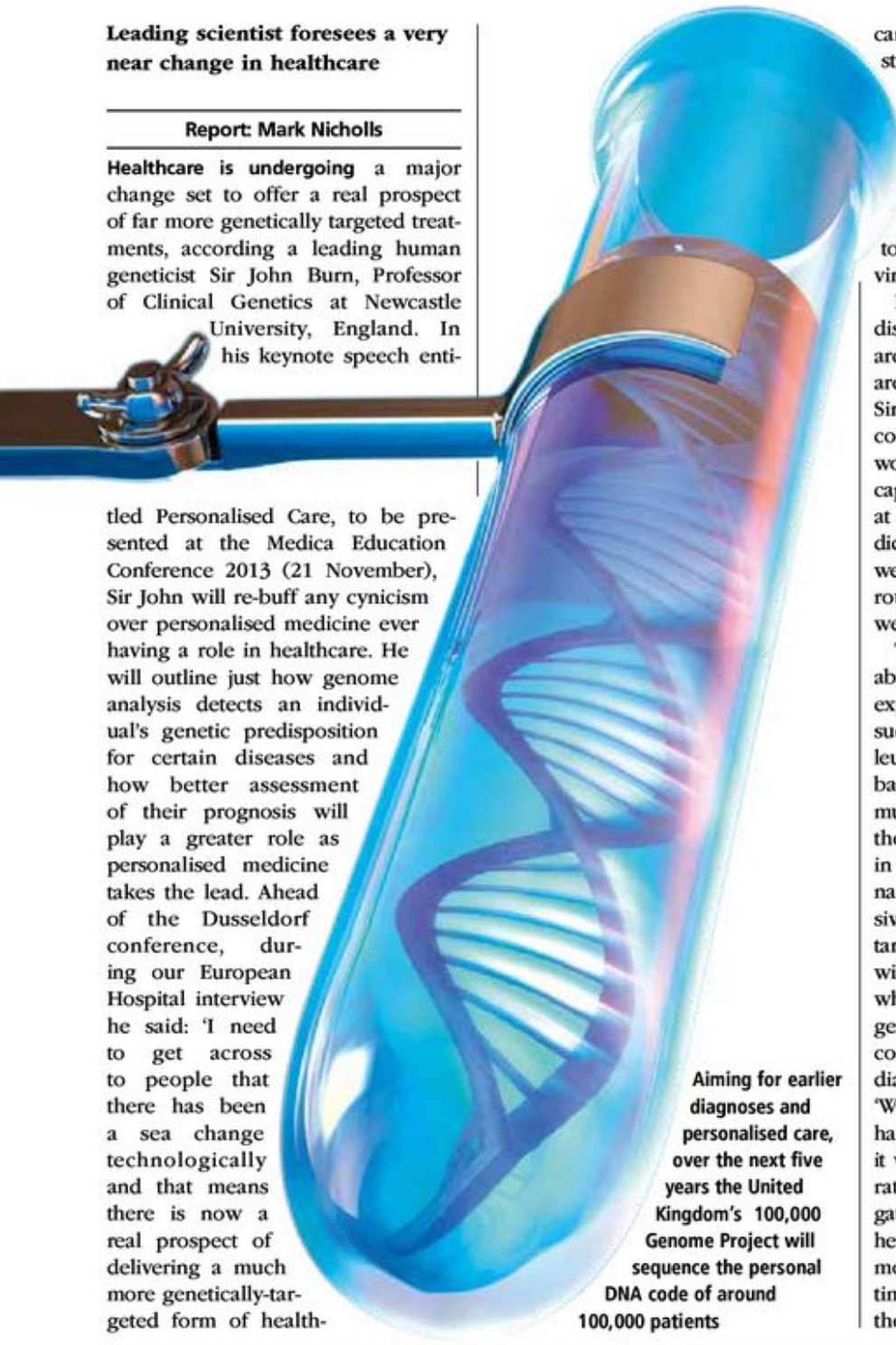
Genetically targeted medicine forges ahead

Leading scientist foresees a very near change in healthcare

Report: Mark Nicholls

Healthcare is undergoing a major change set to offer a real prospect of far more genetically targeted treatments, according a leading human geneticist Sir John Burn, Professor of Clinical Genetics at Newcastle University, England. In his keynote speech entitled Personalised Care, to be presented at the Medica Education Conference 2013 (21 November), Sir John will re-buff any cynicism over personalised medicine ever having a role in healthcare. He will outline just how genome analysis detects an individual's genetic predisposition for certain diseases and how better assessment of their prognosis will play a greater role as personalised medicine takes the lead. Ahead of the Dusseldorf conference, during our European Hospital interview he said: 'I need to get across to people that there has been a sea change technologically and that means there is now a real prospect of delivering a much more genetically-targeted form of healthcare.' There is now better understanding of the molecular level of the diseases, particularly cancer, he explained, pointing out that scientists and clinicians can now find the explanation for rare genetic syndromes and identify people's genetic predispositions to anyone of a myriad of disease virtually at will.



Aiming for earlier diagnoses and personalised care, over the next five years the United Kingdom's 100,000 Genome Project will sequence the personal DNA code of around 100,000 patients

Doctors have to recognise that diseases once considered common are now rare and that rare conditions are 'in relative terms more common', Sir John said. 'Rare diseases are now collectively a large chunk of our workload and now that we have the capacity to understand those diseases at a much more precise level and predict which ones will run in families, we are duty bound to get our heads round this in a way that collectively we have avoided before.'

This is being driven by the availability of targeted medication, he explained, and cited early examples such as treating chronic myeloid leukaemia by targeting the molecular basis of the tumour, and with B-raf mutation in melanoma, which opened the way for dramatic improvements in prognosis for patients with malignant melanoma. 'These very expensive but highly effective drugs are targeted to individual patients, which will change the whole ground on which we operate. Up to now most genetic testing has been done in rare conditions and at the end of a long diagnostic chain,' he pointed out. 'What is happening, and is going to happen even more extensively, is that it will become the first thing you do, rather than the last thing, to investigate the genetic make-up.' The shift, he continued, will also see geneticists move from looking at one gene at a time to capturing the fragments of all the genes they think are relevant to a specific disease and on to exome sequencing to capture fragments of all the genes in the coding sequences.

The ultimate step was to move to whole genome sequencing which has now fallen in price to a few thousand euros, Sir John said. Problems that he plans to identify during his address include incidental findings that suggest an individual is at risk of a genetic disorder and knowing how to tell them about it; and the need to acknowledge that subtle variations in gene expression – an area he believes is grossly under-estimated even by experts in the field – may be very important. 'Subtle variation in gene expression in many of the common diseases will not be about gross loss of gene function but will be about a particular set of genes being slightly dis-regulated and causing a discord, which is very difficult to demonstrate unless you have the most subtle understanding of gene expression,' Sir John emphasised. The professor also stated that interventions need not be expensive. For many years he has pioneered the use of Aspirin as a means of preventing cancer. 'We proved in people at the highest genetic risk that taking two aspirins a day for two years cuts their risk of cancer by 60%,' he pointed out.

His keynote speech will conclude with a focus on the UK's 100,000 Genome Project, which will sequence the personal DNA code of 100,000 patients over the next five years to help lead to better and earlier diagnoses and personalised care. He believes a major challenge is to encourage the European Union to embrace the initiative.

'Personalised medicine is so important that it won't be called personalised medicine,' he said. 'It will just be called medicine. It will be so integral to what we do.'

Sir John Burn, Professor of Clinical Genetics at Newcastle University, England, was knighted in 2010 for services to medicine and healthcare. An Honorary Consultant Clinical Geneticist at Newcastle Hospitals NHS Foundation Trust, he was Lead Clinician NHS North East until March 2013 and chairs the Genetics Speciality Group (NIHR). He is also a Director of the Collaborative Group on Genetics in Healthcare (NIHR and Department of Health), a member of the UK Human Genomics Strategy Group, Chair of the British Society for Human Genetics (2011-13), Medical Director QuantuMDx Ltd and a current member of the National Health Service (NHS) Genomics Strategy Board.

NB: Professor Sir John Burn's keynote lecture on Personalised Medicine will be delivered at the Medica Education Conference 2013, in Dusseldorf, on 21 November 2013, at 1 p.m. in CCD South, Room 3.

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CONTENTS

System analyses smoke to inform surgeons which tissue is cancerous

Scientists develop an intelligent knife

Scientists at Imperial College in London, United Kingdom, have developed an 'intelligent knife' that instantly informs surgeons whether the tissue they are operating on is cancerous.

Report: Mark Nicholls

The *iKnife* is based on electrosurgical knives that use an electrical current to rapidly heat tissue to cut through it. Smoke generated by vaporised tissue is normally sucked away by extraction systems, but iKnife inventor Dr Zoltan Takats realised the smoke was a rich source of biological information. As different types of cell produce thousands of metabolites in different concentrations, he connected an electrosurgical knife to a mass spectrometer and was able to profile the chemicals in a biological sample to reveal information about the state of a specific tissue sample.

In cancers involving solid tumours, surgeons normally take out the tumour with a margin of healthy tissue but acknowledge it is often impossible to tell by sight which tissue is cancerous. For example, one in five breast cancer patients who have surgery need a second operation to fully remove the cancer. With a high level of accuracy reported, the iKnife gives surgeons an immediate answer rather than having to wait up to 30 minutes for laboratory tests results – while the patient is still under general anaesthetic – to know whether tissue is cancerous or not.

'This is a unique tool because the tissue identification element is built into the cutting device, giving surgeons real-time information about exactly what type of tissue is being cut,' Dr Takats explained. 'The intelligent knife will give them an immediate answer, enabling them to continue the operation without interruption.'

Studies showed the iKnife was 100% accurate when diagnosing tissue samples from 91 patients and matching the post-operative diagnosis based on traditional methods.

Researchers have also used the iKnife to analyse tissue samples collected from 302 surgery patients, recording the characteristics of thousands of cancerous and non-cancerous tissues - including brain, lung, breast, stomach, colon and liver tumours - to create a reference library. The iKnife works by matching its readings during surgery to the reference library to determine what type of tissue is being cut, producing a result in less than three seconds.

Dr Takats, an analytical chemist at ICL, said: 'These results provide compelling evidence that the iKnife can be applied in a wide range of cancer surgery procedures. It provides a result almost instantly, allowing surgeons to carry out procedures with a level of accuracy not possible before. We believe it has the potential to reduce tumour recurrence rates and enable more patients to survive.'

He added that the benefits to patients include improved accuracy, meaning that resection is kept to a minimum, as well as reduced exposure to anaesthetic.

The iKnife is not commercially available at this stage. Whilst its accuracy has been proven in trials, Dr Takats said the next step is for a clinical trial to see whether giving surgeons access to the iKnife can improve patient outcomes.

Although the current study focused on cancer diagnosis, Dr Takats says the iKnife can identify other features, such as tissue with an inadequate blood supply or types of bacteria present in the tissue.

The National Institute for Health Research (NIHR) Imperial Biomedical Research Centre, the European Research Council and the Hungarian National Office for Research and Technology funded the study.

Lord Darzi, Professor of Surgery at ICL and the study's co-author, said: 'In cancer surgery, you want to take out as little healthy tissue as possible, but you have to ensure that you remove all the cancer. There is a real need for technology that can help the surgeon determine which tissue to cut out and which to leave in. This study shows that the iKnife has the potential to do this. The impact on cancer surgery could be enormous.'

A former post-doctoral research associate at Purdue University in Indiana, USA, as well as Director of the Cell Screen Research Centre and Head of Newborn Screening and Metabolic Diagnostic Laboratory at Semmelweis University, Budapest, **Dr Zoltan Takats** later became a Junior Research Group Leader at Justus Liebig University, Giessen, Germany. In 2012 he moved to the United Kingdom where he is a Reader at Imperial College, London. He has pioneered mass spectrometry research and is one of the founders of Ambient Mass Spectrometry, as well as primary inventor of six mass spectrometric ionisation techniques and the founder of several companies that pursue analytical and medical device development..

The Starled5 surgical LED lamp

Part of the Starled series incorporating LED (light emitting diodes) technology, produced by Italian firm ACEM Medical Company, the surgical lamp Starled5 is reported to produce light intensity of 160.000 lux, yet ensure low consumption.

'Starled5 grants optimal performances producing a light beam without infrared rays, with a CRI value of 95 and a colour temperature of 4900 °K reproducing the exact colour chromatic scale of the human body,' the manufacturer reports. 'Its ergonomic design takes into consideration the needs of operating rooms. It is comfortable and light to move thanks to its lateral handles assuring stability and constant illumination – even during its movement.'

Acem also points out that its smooth, resistant material makes cleaning quick and thorough, and also, 'The lamp shape assures visual comfort and is particularly suitable for laminar flows. Its structure has been studied to avoid obstructing airflows inside the operating room reducing considerably the turbulence areas.'

Functions are managed via the digital I–Sense control system. A simple touch adjusts light intensity, and can activate the ENDO (Light for Endoscopy) and DOF (Depth of Field) functions as well as the SYNC mode (optional), which enables the use of a control panel that is synchronised with the other lamps combined – all managed by just one operator.

'In order to achieve a correct illumination according to the different needs Starled5 can produce a Focused and Ambient light. Simply rotating the lamp's central handle controls the focusing system of the light field. Removable and sterilisable, the handle can also host (on demand) a fixed focus or zoom video camera.

Due to the particular light beams from the lamp's upper part, a diffuse lighting is produced that is particularly suitable for minimally invasive surgery and preparation/monitoring of a patient during the operation.

Acem S.p.A, based in Bologna, Italy, will be in Hall 10, at Stand D31 during Medica 2013 in Düsseldorf.

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