Talking the language of genes

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(PhysOrg.com) -- The majority of hospital cases of Clostridium difficile at the John Radcliffe Hospital in Oxford are not caused by transmission of the bug within the hospital, so early results of a new project suggest.

It was one example used by Professor Peter Donnelly last night, in giving the first Oxford London Lecture at Church House in Westminster, to illustrate how the modern revolution in genetics is already beginning to affect healthcare for us all.

The research, carried out jointly by researchers at the University and the Oxford Radcliffe Hospitals through the Oxford Biomedical Research Centre, uses the latest genomic screening technologies to identify DNA variations present in the C difficile bugs causing the infection.

It works as a kind of 'genetic fingerprinting for germs', explained Peter Donnelly, allowing the researchers to trace whether the same bug has been transmitted between patients.

C. difficile can cause infections that lead to diarrhoea and fever, often after antibiotics have been used to treat other health conditions, and can be serious or life-threatening. Significant efforts have been made by the NHS to reduce cases in hospitals and numbers have come down.

The research, taking place after these changes have been made in the NHS, are reassuring in showing most cases are from C. difficile bugs with different genetic profiles. That means these cases can't have been down to the same bug being transmitted between patients in the hospital

wards.

In his overview of recent advances in genetics for the Oxford London Lecture, Peter Donnelly looked at what we have learned since the human genome was decoded 10 years ago, and the research it had facilitated.

In particular, he outlined how technologies have allowed the identification of genetic variants –single changes in the DNA code – that are associated with increased risk of common diseases like diabetes, heart disease and many types of cancer.

Peter Donnelly has played a large role in these efforts himself as director of the Wellcome Trust Centre for Human Genetics at Oxford University.

The approach involves scanning the whole genomes of a large group of people with a condition at around 0.5m positions along the 3bn DNA letters in their genomes, and comparing these to the DNA letters found at the same positions in the genomes of a large number of healthy people. Any DNA variations that occur a lot more frequently in those with the condition can be considered to confer some kind of increased susceptibility to the condition.

The first genetic variant (associated with age-related macular degeneration) was discovered in this way in 2005. By 2007, only two years later, there had been an explosion in the genetic variants linked to different diseases, and by summer 2010 there were around 1000 variants known to be associated with 200 different diseases and conditions.

‘We know remarkably little about the biological causes of disease,’ said Peter Donnelly. ‘[Identifying these genetic variants] has given us a whole new set of clues about what is happening in the disease processes.’

The hope is that this will lead to new treatments and drugs targeted

against the disease processes, and possibly new interventions to reduce someone's risk of that disease.

Peter Donnelly noted the technological challenge in managing the huge amounts of data generated by this research (a new project the Wellcome Trust Centre for Human Genetics is beginning to sequence the whole genomes of 2700 people with and without type 2 diabetes will create an incredible 50 Tb of data). But he said 'the bigger challenge will be to translate [these new discoveries] into medical care'.

The real hope, he explained, is to be able to transform information about an individual's genetic profile into a tailored treatment for them – personalising their medical care.

Our genetic profiles can influence how we react to drugs, including the side-effects we might experience, he said. Knowing these connections would mean clinicians could get the right dose or avoid drugs that would give that particular patient nasty side-effects.

'Cancer is fundamentally a disease of the genome,' explained Peter Donnelly. Underlying the development of any cancer are disruptions in the DNA in individual cells, allowing them to escape normal controls and grow without restriction to form tumours.

Just in the last year or two, it has been possible to catalogue the genetic changes found in cells taken from patients' tumours. These early pictures of the large number of genetic changes that can build up in cancerous cells are also showing something else. Breast cancers in different people, for example, can look entirely different at the level of the genome – even though the cancers are of the same part of the body.

It may be possible soon to be able to classify patients' tumours by their genetic profiles, suggested Peter Donnelly, enabling clinicians to make

better decisions about the treatments that will work best for them.

And finally, Peter Donnelly illustrated what knowing more about our genetic profiles might mean for us as individuals. You can now send off samples of your DNA to various companies who will send back information, based on current understanding, on your relative personal risk of different diseases according to your genes.

Peter has done this himself and shared some of the results, as well as what is needed to interpret what the findings mean.

His results showed he was around 6 times more likely to suffer psoriasis during his lifetime than the general population. That's a large increase in risk, but he pointed out that only around 2% of the population get psoriasis. If he is then at a 12-13% risk of the condition, there's still a 90% chance of not getting it.

His risk of type 2 diabetes is a little bit greater – 1.2 times more – than the population as a whole. But he explained that this effect was more serious, as he was then at a 31% lifetime risk of diabetes because so many more people in the population develop diabetes. This finding, however, does allow him to take steps to reduce this genetic risk by making healthy lifestyle choices, something he said he is trying his best to do.

'We live in exciting times,' he concluded. 'There's a good chance that we'll look back at the first part of the 21st century as the time when we started to understand ourselves by learning the language of genes.'

Provided by Oxford University

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