

Embargoed until 23.01 UK time Monday 26 September 2011

Researchers uncover gene associated with blood cancers New genetic insights could facilitate screening for mutation

A genomic study of chronic blood cancer – a precursor to leukaemia – has discovered gene mutations that could enable diagnosis using only a blood test, avoiding the need for an invasive and painful bone marrow biopsy.

Researchers at the Wellcome Trust Sanger Institute identified the *SF3B1* gene as being frequently mutated in myelodysplasia, one of the most common forms of blood cancer. Myelodysplasia is particularly prevalent among people over the age of 60, and often the only symptom is anaemia, which makes it a challenge to give a positive diagnosis. Patients with mutations in the *SF3B1* gene frequently had a specific abnormality of red blood cells in their bone marrow, called ring sideroblasts.

The findings have significant potential for clinical benefit, as the disease is often under-diagnosed. It is hoped that patients will soon be able to be screened for mutations in the *SF3B1* gene through a single blood test.

“This discovery illustrates the promise of genome sequencing in cancer,” says Dr Elli Papaemmanuil, lead author from the Sanger Institute. “We believe that by identifying *SF3B1*, and working to characterize the underlying biology of this disease, we will be able to build improved diagnosis and treatment protocols.

“Significantly, our analysis showed that patients with the *SF3B1* mutation had a better overall chance of survival compared to those without the mutation. This suggests that the *SF3B1* mutations drive a more benign form of myelodysplasia.”

In order to piece together the genomic architecture of myelodysplasia, the team sequenced all genes in the genome of nine patients with the disease. To their surprise, six had mutations in the *SF3B1* gene. To expand their analysis, the researchers sequenced the *SF3B1* gene in 2,087 samples across many common cancers.

In myelodysplasia, *SF3B1* mutations were found in 20.3 per cent of all patients, and in 65 per cent of those patients with ring sideroblasts, making it one of the most frequently mutated genes so far discovered in this disease. Researchers found mutations of the same gene in up to 5 per cent of a range of other common cancers, such as other leukaemias, breast cancer and kidney cancer.

“Anaemia affects 1 in 10 people over the age of 65, and we cannot easily find a cause for the anaemia in a third of cases,” says Peter Campbell, senior author, from the Sanger Institute and a practicing Haematologist at Addenbrooke’s Hospital, Cambridge. “To diagnose myelodysplasia, we often have to resort to an invasive and painful bone marrow biopsy, but we hope this and future genetic insights will provide more straightforward diagnosis for patients through a simple blood test.”

“Ever since I first saw these unusual and damaging blood cells – ring sideroblasts – down the microscope while training to become a haematologist, I have been fascinated by them and determined to find a cause. To discover a major genetic clue to their origins is very exciting, and I look forward to piecing together how the mutations cause these curious cells to develop and lead to this disease.”

The *SF3B1* gene encodes a core component of RNA splicing, an important editing mechanism that controls how the genome's message is delivered to the cell. The team discovered a strong association between the gene and the presence of ring sideroblasts, making it the first gene to be strongly associated with a specific feature of the disease. Ring sideroblasts are abnormal precursors to mature red blood cells with a partial or complete ring of iron-laden mitochondria (energy generators) surrounding the nucleus of the cell. Their presence is frequently associated with anaemia.

"These genetic discoveries are very important and could potentially assist clinicians when diagnosing blood cancers in patients, avoiding the need for invasive bone marrow biopsies. Myelodysplasia is becoming increasingly prevalent in people over 60, and cases will continue to rise with our increasing ageing population, particularly among those who suffer from anaemia," says Dr David Grant, Scientific Director at Leukaemia & Lymphoma Research. "We are delighted to have supported research into the genomic architecture of myelodysplasia which will contribute towards making a difference for the diagnosis and treatment for patients."

The study was a project for the International Cancer Genome Consortium, a forum for collaborations among the world's leading cancer and genomic research.

###ends###

Notes to Editors

Publication Details

Papaemmanuil *et al.* (2011) Somatic mutation of *SF3B1* in myelodysplasia with ring sideroblasts and other cancers. *New England Journal of Medicine*, published online Wednesday 28 September 2011

Funding

A full list of funding agencies can be found at the *New England Journal of Medicine* website. The research was supported principally by the Wellcome Trust and the Kay Kendall Leukaemia Fund.

Participating Centres

A full list of participating centres can be found at the *New England Journal of Medicine* website.

The **Wellcome Trust Sanger Institute** is one of the world's leading genome centres. Through its ability to conduct research at scale, it is able to engage in bold and long-term exploratory projects that are designed to influence and empower medical science globally. Institute research findings, generated through its own research programmes and through its leading role in international consortia, are being used to develop new diagnostics and treatments for human disease.

<http://www.sanger.ac.uk>

The **Wellcome Trust** is a global charitable foundation dedicated to achieving extraordinary improvements in human and animal health. We support the brightest minds in biomedical research and the medical humanities. Our breadth of support includes public engagement, education and the application of research to improve health. We are independent of both political and commercial interests.

<http://www.wellcome.ac.uk>

Contact details

Don Powell Press Officer
Wellcome Trust Sanger Institute
Hinxton, Cambridge, CB10 1SA, UK
Tel +44 (0)1223 496 928
Mobile +44 (0)7753 7753 97

Email press.office@sanger.ac.uk

End of Notes to Editors