New gene sequencing technology like a high-powered microscope

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Dr. Tim Mercer, who led the development of Capture Sequencing technology, is pictured. Credit: Garvan Institute of Medical Research Dr Tim Mercer

A new gene sequencing technology allows us to explore the human genome at a much higher resolution than ever before, with revolutionary implications for research and cancer diagnosis.

Outperforming existing technologies, 'Capture Sequencing' (CaptureSeq) can accurately measure the activity of many specific genes in a sample -

even when they are expressed at minute levels. This will have immediate practical applications, including the diagnosis of many blood cancers.

Publishing today in the leading journal *Nature Methods*, an Australian team demonstrated the strengths of CaptureSeq.

Dr Tim Mercer, Dr Michael Clark, Professor John Mattick and Associate Professor Marcel Dinger from Sydney's Garvan Institute of Medical Research, who developed CaptureSeq, compared it with techniques currently in use for gene expression analysis, and found it to be much more sensitive to genes expressed at very low levels.

Until recently, it was thought that humans have around 20,000 genes - that is, the sections of DNA that are 'transcribed' into RNA molecules, then 'translated' into the proteins that perform tasks in cells.

Protein-coding genes occupy only 2% of the genome, and their number and function remains relatively constant across the animal kingdom, from worms to humans.

We now understand that the rest of the genome is made up of genes that do not code for proteins, and that these non-coding genes create the complexity that distinguishes humans from worms.

Non-protein-coding genes perform an important regulatory function in various aspects of human development and brain function. Most are expressed only in a few cells rather than whole tissues, or they are expressed at very low levels, making them difficult to study.

The new study shows that CaptureSeq will help us uncover these rare genes by allowing us to explore specific stretches of the human genome at much higher resolution than current RNA sequencing approaches.

CaptureSeq will also enable rapid detection of diseases where diagnosis is guided by gene expression, and the genes involved are known.

Diagnosis of blood cancers, for example, will immediately improve with the availability of CaptureSeq to detect the presence of 'fusion genes'.

Fusion genes (literally two genes fused together) are found in 20-30% of cancers. There are around 200 known fusion genes in leukaemia alone.

At present, patients suspected of having leukaemia are tested using existing amplification-based technology, which can search for only one fusion gene at a time. Patients would rarely, if ever, be tested for all 200.

CaptureSeq can test for all 200 known fusion genes at once - saving much time and money, and potentially saving lives.

CaptureSeq can also be used to analyse a range of solid cancers and other diseases.

More information: Quantitative gene profiling of long noncoding RNAs with targeted RNA sequencing, *Nature Methods* (2015) DOI: 10.1038/nmeth.3321

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