'Copy-and-paste DNA' more common than previously thought

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Researchers at the University of Leicester have demonstrated that movable sequences of DNA, which give rise to genetic variability and sometimes cause specific diseases, are far more common than previously thought.

In a paper published in the leading journal *Cell*, Dr Richard Badge and his collaborators examined L1 (or LINE-1) retrotransposons: DNA sequences which can 'copy and paste' their genetic code around the genome. By breaking up genes, L1s can be responsible for some rare instances of genetic disease.

Working in collaboration with colleagues from the Universities of Michigan and Washington and the HHMI, the researchers developed an innovative technique to find L1s, using short sequences of DNA called fosmids. These are free-floating loops of DNA, which can be easily transported into bacterial cells, and can carry pieces of human DNA.

Each fosmid can hold only a specific amount of DNA, approximately 40,000 bases. So by comparing the two ends of a piece of human DNA held in a fosmid, against their known positions in the human genome sequence*, the scientists were able to quickly and easily spot differences in size.

"We're just looking at each end of the sequence and seeing if they're the right distance apart."explains Dr Badge. "This shows us the existence of insertions (which we're interested in) and also deletions. This technology

is completely unbiased - it doesn't care what the insertion/deletion actually is, just whether it's there."

Having identified the insertions, the next step was to see if they could 'jump' in cultured human cells and how common they are - which is where the research team found something completely unexpected.

"Previous studies suggested that lots of L1s should jump - but don't," says Dr Badge. "But about half of the L1s we found jump really well, which was very surprising. We found about 65 elements, which had not been previously identified.

"This tells us that active human retrotransposons are much more common than we expected. Individual active L1 retrotransposons are quite rare - but there are a lot of them."

The paper 'LINE-1 Retrotransposition Activity in Human Genomes' by Beck et al is one of three L1 studies published in the 25 June 2010 issue of Cell. A commentary in the journal describes the team's results - 37 of the 68 elements studied being very active or 'hot' - as "incredible."

Because of the mistaken belief in their rarity, active retrotransposons have not been as closely studied as other sources of genetic variation, but this study and the others in the journal signify a developing acceptance of their significance.

"In this field, we are constantly fighting the perception that these bits of DNA are 'junk'," observes Dr Badge. "Actually they're very active and some of them have disease relevance. They are big bits of DNA so when they jump into a gene they disrupt the gene sequence and this can cause genetic disease."

More information: www.cell.com/

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