

Australian marsupials challenge gene theory

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Scientists studying the kangaroo genome have cast doubt on the credentials of a gene thought to be crucial to the process of inactivating one sex chromosome in women.

The finding challenges a whole field of research that has developed around the XIST gene since its discovery in the early 1990s. Scientists had expected that the gene – which was thought to direct the switching off of a surplus X chromosome during embryonic development – would inform our understanding of how genes are controlled in normal development, and how control goes awry in genetic diseases such as cancer.

The sophisticated genetic process of switching off one X gene is necessary to equalise the dosage of genes in females (which have two X chromosomes) and males (with only one). It occurs in all placental mammals including humans and mice, as well as in marsupials, which diverged from placentals 180 million years ago.

But Professor Jennifer Graves, the Head of the Comparative Genomics Group at the ANU Research School of Biological Sciences (RSBS) and director of the multi-university ARC Centre for Kangaroo Genomics, and RSBS PhD student Tim Hore, showed that the XIST gene is absent from the genomes of marsupials, as well as the platypus (which diverged even earlier), leading them to conclude that the gene must have evolved more recently in placental mammals. This means that XIST probably isn't critical to the basic X inactivation mechanism after all.

“We thought that if XIST really was so critical, we should have been able to find a copy of this gene in kangaroos. We’ve been looking since 1995, but found no trace of it. But this wasn’t absolutely convincing because we could never be sure that it wasn’t hiding out somewhere, or had changed so much in evolution we couldn’t recognise it,” Professor Graves said.

Thorough work by Mr Hore isolated kangaroo and platypus copies of the genes that lay close on either side of XIST in the mouse and human genome. “To my surprise, these genes mapped far apart on the marsupial X. I sequenced the DNA containing these flanking genes and found neither contained anything like the gene XIST. XIST just does not exist in marsupials.”

The research, published recently in the international journal *Chromosome Research*, indicates that XIST evolution may correlate to some of the molecular changes regarded as slight evolutionary improvements in stabilising the X inactivation process, according to Professor Graves.

“So marsupials have done it again. Just like our work of two decades ago showing that the favoured candidate for sex determination was the wrong gene, this finding challenges a favoured hypothesis - in this case a whole field of research – and shows us how complex control systems are built up out of simpler elements of evolution.”

Source: Australian National University

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