Faulty gene linked to depression and cardiovascular disease

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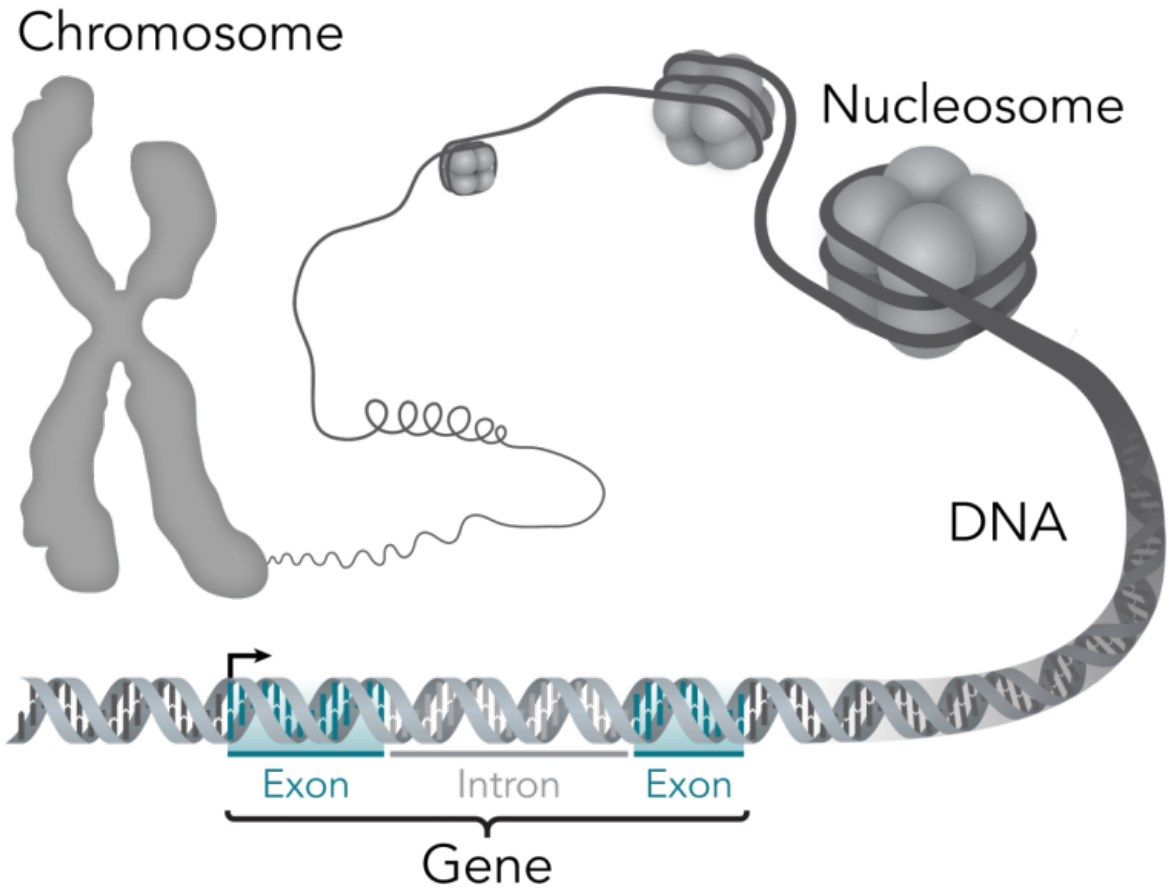

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. The diagram labels a region of only 55 or so bases as a gene. In reality, most genes are hundreds of times longer. Credit: Thomas

Researchers at the University of Adelaide say they may have discovered a new target in the fight against depression: a faulty gene that is linked to cardiovascular and metabolic conditions.

A team lead by the University of Adelaide's Discipline of Psychiatry has reviewed and attempted to replicate the findings of the growing body of research showing the types of genes expressed in the brain and surrounding tissues during depression.

The findings – published online ahead of print in the journal *Neuroscience & Biobehavioral Reviews* – have supported multiple theories of the underlying genetic causes of depression, and have highlighted one gene that until now has gone under the radar in relation to mood disorders.

"Depression is much more complex than most people think, and it includes dysfunction at multiple biological levels, from genes to brain regions, and blood circulating through the body," says Professor Bernhard Baune, Head of Psychiatry at the University of Adelaide and lead author of the paper.

"The state of depression can also change over time, it goes through various phases and it may present with a large range of symptoms.

"In those circumstances, it shouldn't be surprising that while there's a growing body of research investigating the underlying genetics of depression, so far there have been inconsistent findings in various studies throughout the world."

The team examined and re-analysed in a novel way research covering 16 brain regions and five cell types from the peripheral nervous system. Across the body of work, they identified 57 differently expressed genes in the brain and 21 in the peripheral tissues.

"What we saw was overlap in genetic expression between the brain and peripheral tissues that strongly implicated a link between depression and cardiovascular disease," Professor Baune says.

"Out of this, we identified the gene PXMP2 as a potential candidate for further investigation."

PXMP2 plays a role in the permeability of microbodies called peroxisomes, which break down fatty acids in the body and convert them to energy.

"PXMP2 is robustly expressed during depression. However, to the best of our knowledge, neither this faulty gene in particular nor its related functions in metabolism have ever been investigated in relation to mood disorders of any kind," Professor Baune says.

"With the shared pathways between cardiovascular disorders and depression, we suggest that faulty regulation of the PXMP2 gene may play a role in depressive disorders via specific metabolic pathways."

Professor Baune says he doubts that one single gene has the biggest role to play. "Our research on genetic networks also showed support for the wide range of theories that different genes may play a role in depression, including those involved in regulation of serotonin, melatonin and the immune system, among many others. Even so, PXMP2 represents a very strong, new target for future research programs," he says.

More information: Liliana G. Ciobanu et al. Differential gene

expression in brain and peripheral tissues in depression across the life span: A review of replicated findings, *Neuroscience & Biobehavioral Reviews* (2016). DOI: 10.1016/j.neubiorev.2016.08.018