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Family may hold clue to killer diseases

A genetic mutation discovered by chance in the South Island descendants of a Cornish tin miner may be a vital clue in finding cures for killer diseases from Alzheimer's to cancer.

New research by Otago University scientists, which has just been published in the journal *Nature Genetics*, has identified a genetic mutation in the family that triggers premature death in blood platelets, the cells that aid clotting. Researchers say if they can pinpoint what causes "cell suicide", they may be able to better target treatment for diseases involving abnormal cell death - such as Alzheimer's, in which cells die too early, and cancer, when the cells do not die when they should.

Otago University haematologist Ian Morison began his hunt for the mystery gene more than 10 years ago, after being approached by a woman whose surgery had been cancelled because of low blood platelet levels. Her mother also had low platelets, and the woman, who worked in the university's science faculty, suspected the condition was hereditary, Dr Morison said. "Some blood tests later, we knew we had found a condition that had never before been described."

Dr Morison and his team spent the next five years sifting through three billion letters of dna within the genome that was shared by family members. Their job was made a lot easier by the work of a family genealogist, who had already traced the family tree.

The gene arrived in New Zealand with Cornish tin miner William Cargeeg, who emigrated in 1875 aged 44, with his family. Two branches of the family have inherited the gene, though it appears some of them knew nothing about the other side till researchers reunited them. Researchers got blood samples from 80 family members, of whom 30 had low platelets, and narrowed the site of the mutation to a single gene, which affected a protein called cytochrome c.

Otago biochemist Liz Ledgerwood said one of the surprising things about the mutation was it affected part of the protein that had "remained unchanged for two billion years across a range of living organisms, from yeast to the grey whale". Dr Ledgerwood found the mutation made cytochrome c better at triggering cell death, a natural process for maintaining the correct number of cells in the body.

She said she would have expected the mutation to have caused premature cell death in other parts of the body, such as the brain. "But apart from a tendency to bruise easily, they [family members] are generally a very healthy, long-lived lot."

If scientists can find out what keeps the carriers healthy, it could open up exciting new avenues for "modifying the death process", she said. "I wouldn't go as far as to say we've found the cure for all known diseases, but it does give us a completely new way of thinking about the process of cell death."

UNKNOWING VICTIM

Nigel Stanger, 40, who is descended from the Cargeegs through his mother, has become "a virtual pincushion" over the last couple of years because he happens to work in Otago University's IT department. "I was a handy person to have on site whenever they needed a blood sample." He "didn't have a clue" that he had low platelets till he tested positive. "Obviously it hasn't affected me at all, but it's exciting to think we could play a small role in medical history."