Alison Heather
Tel: +61 (2) 9295 8128

GARVAN INSTITUTE

B cell mutations that may cause cancers and autoimmune diseases

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Scientists at the Garvan Institute of Medical Research have taken a significant step towards demystifying a critical process within our immune system.

B cells, the white blood cells that produce antibodies, form a key part of our 'immune response'. We must maintain exactly the right number of B cells to remain healthy. If there are too many, we risk developing cancers or autoimmune diseases. If there are too few, we are prone to infection.

The team from Garvan's B cell Immunobiology research group, led by Dr Robert Brink, has identified two proteins made inside B cells, TRAF2 and TRAF3, that are essential for controlling this important balance. The group's findings are published online today in the prestigious international journal, *Immunity*.

"A healthy person regulates the number of B cells in their body with a substance called BAFF," said Dr Brink. "If you don't have enough BAFF, B cells die soon after you make them. Conversely, if you have too much BAFF, then you too many B cells survive."

"We've demonstrated that when B cells have defective TRAF2 or TRAF3 they no longer require BAFF to survive. Once released from their dependence on BAFF, B cells live much longer than they should and accumulate in the body in large numbers. It is very likely, therefore, that a B cell which picks up a mutation in either its TRAF2 or TRAF3 gene is going to cause trouble."

"B cells that lose their normal survival controls like this are predisposed to turning cancerous and causing B cell tumours such as Hodgkin's lymphoma, follicular lymphoma or multiple myeloma. They also are prone to producing antibodies that attack the body itself, the process that occurs in autoimmune diseases like lupus, haemolytic anaemia, and myasthenia gravis."

"The take home message is that TRAF2 and TRAF3 are the gatekeepers for the survival of B cells. If they're perturbed, the mechanism for B cell survival goes out the window – a possible step on the road to cancer or autoimmune disease."

Dr Brink believes his team has uncovered an important clue as to how these diseases may be treated in the future. "When we examined the genes expressed in the long-lived B cells, we noticed that mutations in the TRAF2 or TRAF3 gene cause major changes to other genes within the B cell. We found around 20 genes whose expression went up dramatically in these cells. We believe these genes may hold the keys to certain cancers and autoimmune diseases, so we intend to target them in our research."

ABOUT GARVAN

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Arthritis & Immunology, Osteoporosis, and Neuroscience. The Garvan's mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

All media enquiries should be directed to:

Alison Heather 02 9295 8128 or Jackie Crossman 0402 218 662