

Understanding kiss of death for some improves outlook for others

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Although we don't realize it, almost all of us are exposed to Epstein Barr Virus (EBV), often through kissing. Around 10-20% of those exposed will develop glandular fever, known colloquially as "kissing disease". A very small number will develop blood cancers* later in life. For the unfortunate few born with the rare immunodeficiency known as X-linked lymphoproliferative disease (XLP), infection with the saliva-borne virus can be fatal.

Australian immunologists have discovered exactly why EBV is so catastrophic for people with XLP. While their finding does not point to an immediate cure for XLP, it does give us the insight we need to enhance normal immunity to EBV in the future – with vaccines or prophylactic medicines.

The team, led by Dr Umaimainthan Palendira and Associate Professor Stuart Tangye from Sydney's Garvan Institute of Medical Research, asked themselves why the mutation of a single gene should make people with XLP so acutely sensitive to EBV, but no other viruses. The reason, they found, lay in EBV's choice of host cell.

Viruses cannot exist outside a host cell. HIV infects 'T cells', hepatitis infects liver cells, EBV infects 'B cells', a type of white blood cell. Ordinarily, when a B cell becomes infected with EBV, it 'alerts' the immune system's killer T cells, which spring into action.

The research team found that the 'SAP' gene, which is missing from XLP patients, is critical for allowing killer T cells to 'see' B cells. When the SAP molecule is missing, T cells have no way of knowing that B cells are infected.

If other viruses were exclusively 'housed' by B cells, XLP patients would also be acutely sensitive to them. Had EBV evolved to live in skin cells, XLP patients would not feel its effects any more than the next person.

This insight into a key aspect of our immune system is published in *PLoS Biology*, now online.

“Rare conditions can tell us a lot about normal biology, and this finding shows how the immune system has evolved to deal with EBV, and how EBV has evolved to exploit the immune system,” said Dr Tangye.

“We can now see what you need to get a really good immune response against EBV. This is useful information, given that some people develop cancers as a result of exposure – particularly if their immune systems are suppressed. Our finding could help find ways to enhance immunity against EBV-induced lymphoma.”

“We’ve now identified the SAP molecule as a critical T cell receptor for the EBV immune response – and that will now operate as a therapeutic target.”

* EBV was the first virus recognized as capable of causing cancer.

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 over 500 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation and Neuroscience. 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.

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