MONASH University

Media Release

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Immune system's fat problem solved

Monash and Melbourne University scientists have helped unlock a 15-year mystery and advanced understanding of how the human immune system fights disease.

The findings, published today in the international journal *Nature*, could ultimately lead to the development of drugs that strengthen the response to harmful microbes and cancer cells.

Typically, when the body is threatened with bacterial or viral infection, molecules called T-cell receptors that are found on the surface of T-cells (white blood cells that play a critical role in the immune response) interact with molecules known as major histocompatibility complex (MHC) that present a protein fragment (called a peptide) from the bacterium or virus, triggering the immune response. This process has been widely studied and leads to the killing of microbes and certain types of cancer cells.

The team of researchers has discovered how T-cell receptors recognise certain fats called glycolipids, which are found in several types of bacteria and some cancer cells, thereby initiating an immune response.

The interaction has been unravelled by Dr Natalie Borg, Mr Kwok Soon Wun and Professor Jamie Rossjohn at Monash University in collaboration with Professor James McCluskey, Dr Lars Kjer-Nielsen and Associate Professor Dale Godfrey at the University of Melbourne.

Professor Rossjohn said the discovery was also relevant for many significant diseases because glycolipid recognition by T-cells has been implicated in allergy, atherosclerosis, graft rejection and autoimmune diseases such as Type-1 diabetes.

"The immune system normally recognises peptide fragments of viruses or bacteria presented by MHC molecules but also presented by the immune system are glycolipids that are presented by MHC-like molecules called CD1," Professor Rossjohn said.

"Until now it was not known how the immune system interacted with molecules that present glycolipids - it's very different to the mechanism underlying peptide-mediated recognition," Associate Professor Godfrey said.

The Monash-Melbourne collaboration studied the interaction between T-cell receptors, a member of the CD1 family called CD1d and a lipid that is being independently investigated for its anti-cancer activity. Using synchrotron radiation, the team deduced how T-cell receptors recognise foreign lipids presented by CD1d molecules.

Professor McCluskey said the work would help understanding of how a range of different glycolipids are recognised by specialised T-cells.

"Glycolipids are potent regulators of the immune response. By understanding how the immune system responds to them, there's potential to make them more potent by subtly altering their structure," Professor Rossjohn said.

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