A first in front line immunity research

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Monash University researchers have gained new insight into the early stages of our immune response, providing novel pathways to develop treatments for diseases from multiple sclerosis to cancer.

In a study published today in *Nature Immunology*, a team of researchers led by Professor Paul Hertzog, of the Monash Institute of Medical Research (MIMR) and Professor Jamie Rossjohn, of the School of Biomedical Sciences, have characterised for the first time how interferon beta (IFN?) proteins bind to cells and activate an immune response.

Produced when viral and bacterial infections are detected, interferon proteins are vital to the body's defences. They activate immune cells, such as macrophages, can interfere with virus replication, and can boost cells' resilience to infection. They also enhance later immune responses to cancers and other stresses.

There are at least 20 subtypes of interferons that are produced at different stages of the immune response. They appear to have different functions, but these functions and their triggers are generally not well understood. The mapping of INF? - cell interaction is a breakthrough in the field.

Professor Hertzog of MIMR's Centre for Innate Immunity and Infectious Diseases said interferon function was vital for developing and refining therapies for incurable diseases such as lupus and multiple sclerosis.

"Interferon therapy is useful in treating a number of diseases; however these treatments have dose-limiting side effects. Further, interferons appear to drive some autoimmune diseases, raising the prospect of interferon blockers as treatment," Professor Hertzog said.

"The more refined our understanding of interferon function, the more we can tailor treatments to optimise effectiveness - whether by boosting or blocking their actions."

Lead author on the paper, Dr Nicole de Weerd, also of the Centre for Innate Immunity and Infectious Diseases, said the research provided new pathways for rational drug design.

"We found that when IFN? binds to a cell, it transmits an unusual signal that seems linked to some of the toxic side effects of interferon therapy, like sepsis. This provides a promising avenue to pursue more selective activation of interferon action," Dr de Weerd said.

Professor Rossjohn and Julian Vivian from the Department of Biochemistry and Molecular Biology collaborated closely on determining the IFN? interactions at the molecular level.

"During this seven-year study, we have had great support from the Australian Synchrotron," Professor Rossjohn said.

More information: *Nature Immunology* DOI: 10.1038/ni.2667

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