

Researchers find more uses for immune system's 'Swiss army knife'

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Oxford University research has found that a little-studied and relatively unknown part of the human immune system could be twice as important as previously thought.

Mucosal Associated Invariant T-cells (MAIT cells) were first identified in 1993 but largely ignored until recently. Australian researchers recently found that they had an important role in fighting bacterial infections. Now, the Oxford team, led by Professor Paul Klenerman, say that they also fight viruses. Their results are in the journal *Nature Communications*.

Researcher Bonnie van Wilgenburg said: 'MAIT cells are unlike any other part of the immune system because they are multipurpose, rather than responding to particular pathogens - the various bacteria, viruses and other microorganism that can cause disease.'

All T-cells recognise and destroy infected <u>human cells</u> to prevent them spreading the infection. Standard T-cells possess specific receptors on their surface, each of which allows them to recognise a different pathogen. Most T-cells have a large range of such receptors to cover all pathogens. One receptor can recognise one particular pathogen infection, while another will be activated by a different pathogen.

MAIT cells have only a few receptors because they do not recognise specific pathogens. Instead they recognise a chemical made by many different pathogens. Researchers in Melbourne identified this chemical:



a small molecule called 5-A-RU, which is made by the majority of bacteria. In effect this makes MAIT cell receptors multi-purpose - spotting a whole category of bugs rather than just a set of individual ones.

Now, the team have discovered that MAIT cells are even more multipurpose than that.

Professor Paul Klenerman explained: 'We found that MAIT cells are readily activated by cytokines, chemical messengers released by the human body in response to infections.'

Cytokines are key parts of the immune system. When released by cells, they trigger certain behaviours in other cells, regulating the body's immune response to match the threat of a pathogen.

Prof Klenerman continued: 'Most human T-cells require their specific receptor to be triggered in order to react, but MAIT cells can bypass this and will be strongly and specifically activated in response to a combination of cytokines.

'In our latest study we discovered that viruses, not just bacteria, can activate the immune system to produce this specific mix of cytokines that activates MAIT cells. By studying people with different viral infections, including flu, dengue and hepatitis C, we found evidence that MAIT cell activation occurs during human viral infection.

This is the first time that MAIT cells have been observed having a role in the immune response to viruses. This opens up the exciting possibility that MAIT cells could be involved in the defence against viruses or reduce their damaging effects.

'The discovery suggests that MAIT cells are a 'Swiss army knife' for the



immune system - useful against all sorts of bacterial and viral infections.'

The discovery may also have implications for vaccine and treatment design. Traditional vaccines stimulate B-cells to produce antibodies that can attack pathogens directly. T-cell vaccines, a focus of current research, are designed to stimulate the production of standard pathogen-specific T cells, which attack <u>infected cells</u> in the body to destroy them and the infection they harbour. But MAIT cells offer another possible treatment route.

However, the Oxford researchers say that we first need to understand more about these unique cells and they will continue to play a key role in that.

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