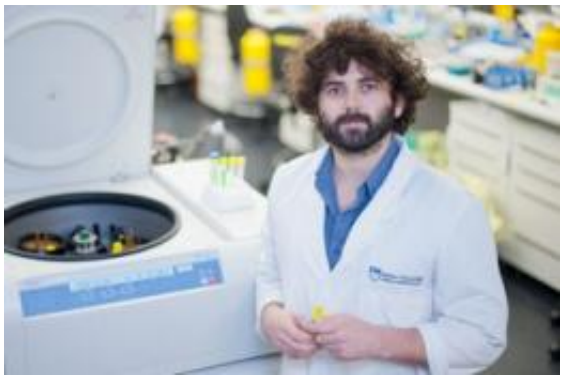
Rewiring DNA circuitry could help treat asthma

5 July 2012



Dr Rhys Allan from the institute's Molecular Immunology division, was part of a research team that found asthma-promoting immune cells could be rewired so they no longer cause inflammation.

(Medical Xpress) -- Reprogramming asthma-promoting immune cells in mice diminishes airway damage and inflammation, and could potentially lead to new treatments for people with asthma, researchers have found.

The researchers were able to reprogram the asthma-promoting cells (called Th2 (T-helper 2) cells) after identifying an enzyme that modifies the DNA of these cells. The enzyme could be a target for the development of new treatments for chronic inflammatory diseases, in particular allergic asthma , caused by an excess of Th2 cells.

Walter and Eliza Hall Institute researcher Dr Rhys Allan led the research while working at Institut Curie, Paris. The research team from Institut Curie, National Centre for Scientific Research (CNRS), France, National Institute of Health and Medical Research (INSERM), France, and Montpellier Cancer Research Institute published the study today in the journal *Nature*.

Dr Allan said the research team discovered that the enzyme Suv39h1 could switch off genes to control the function of Th2 cells, which are key to the allergic response.

“Th2 cells have an important function in the immune response, but they also play a significant role in diseases such as allergic asthma,” Dr Allan said. “People with asthma have too many Th2 cells, which produce chemical signals that inflame and damage the upper airways. In this study, we discovered that the Suv39h1 enzyme plays a critical role in programming these asthma-promoting cells, making it a potential target for new therapies to treat asthma.”

More than two million Australians have asthma – approximately one in 10 people – and the disease is even more common among Indigenous Australians. The prevalence of asthma in children in Australia is among the highest in the world.

Dr Allan said the Suv39h1 enzyme was part of the ‘epigenetic circuitry’ of Th2 cells.

“Epigenetics refers to changes or modifications in the DNA that alter how genes are switched on and off, without changing the fundamental DNA sequence. Suv39h1 effectively ‘tags’ the DNA to tell the cells which genes they need to switch on or off to promote an allergic response.”

Using agents that inhibit Suv39h1 could destabilise Th2 cells in people who have an excess of these asthma-promoting cells so they no longer cause inflammation, Dr Allan said.

“We had the idea that erasing these epigenetic tags could ‘short-circuit’ the asthma-promoting Th2 cells and diminish the inflammatory immune response. And, in fact, in mouse models of allergic asthma, blocking this pathway with an inhibitory compound did reduce allergy-related airway damage. Ultimately, our results have identified a potential target for therapeutic intervention in asthma and potentially other Th2-mediated

inflammatory diseases, which could improve outcomes for patients," Dr Allan said.

Dr Allan is continuing to study the epigenetic circuitry of asthma-promoting immune cells in the institute's Molecular Immunology division, with funding from the National Health and Medical Research Council of Australia (NHMRC).

The research was supported by Institut Curie, CNRS and INSERM. Dr Allan was funded by an INSERM-NHMRC exchange fellowship.

More information: View the journal paper at *Nature*.

Provided by Walter and Eliza Hall Institute of Medical Research