Rheumatoid arthritis breakthrough

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Rheumatoid arthritis is a painful, inflammatory type of arthritis that occurs when the body's immune system attacks itself. A new paper, published in this week's issue of *PLoS Biology*, reports a breakthrough in the understanding of how autoimmune responses can be controlled, offering a promising new strategy for therapy development for rheumatoid arthritis.

Normally, immune cells develop to recognise foreign material – antigens; including bacteria - so that they can activate a response against them. Immune cells that would respond to 'self' and therefore attack the body's own cells are usually destroyed during development. If any persist, they are held in check by special regulatory cells that provide a sort of autoimmune checkpoint. A key player in these regulatory cells is a molecule called Foxp3. People who lack or have mutated versions of the Foxp3 gene lack or have dysfunctional immune regulation, which causes dramatic autoimmune disease.

Scientists at the Medical Research Council's Laboratory of Molecular Biology in Cambridge, and funded by the Arthritis Research Campaign, have genetically engineered a drug-inducible form of Foxp3. Using this, scientists can 'switch' developing immune cells into regulatory cells that are then capable of suppressing the immune response.

Dr. Alexander Betz, Group Leader at the MRC laboratory, explains: "We have generated a modified form of Foxp3 which can be introduced into immune cells using genetic engineering techniques and then activated by a simple injection. When administered to and activated in

animal models of arthritis, the modified cells inhibit or even reverse the disease process."

Further work is now aimed at elucidating the detailed molecular mechanisms involved in Foxp3 function, and transferring the experimental approach to human cells.

"First, we will develop a human Foxp3 factor and then assess its function in human arthritis models," said Dr Betz. "To be viable as a therapeutic option, the regulatory cells must fulfill certain criteria; they must be tissue matched to the patient for compatibility; they must only block the targeted disease and not the whole body immune response; and they have to home correctly to their target tissue. Establishing these criteria will be the key focus of our research.

"If Foxp3 functions as a key developmental switch in human immune cells, there is potential for a new avenue of therapy development that could transform arthritis treatment is substantial," he added.

Citation: Andersen KG, Butcher T, Betz AG (2008) Specific immunosuppression with inducible Foxp3-transduced polyclonal T cells. PLoS Biol 6(11): e276. doi:10.1371/journal.pbio.0060276
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