Tipping the Balance: Targeting the Thymus for Production of Immune Cells Protective Against Auto-immune Disease

NI McCarthy, J Cowan, K Nakamura, A Bacon, S Baik, A White, S Parnell, EJ Jenkinson, WE. Jenkinson and G. Anderson

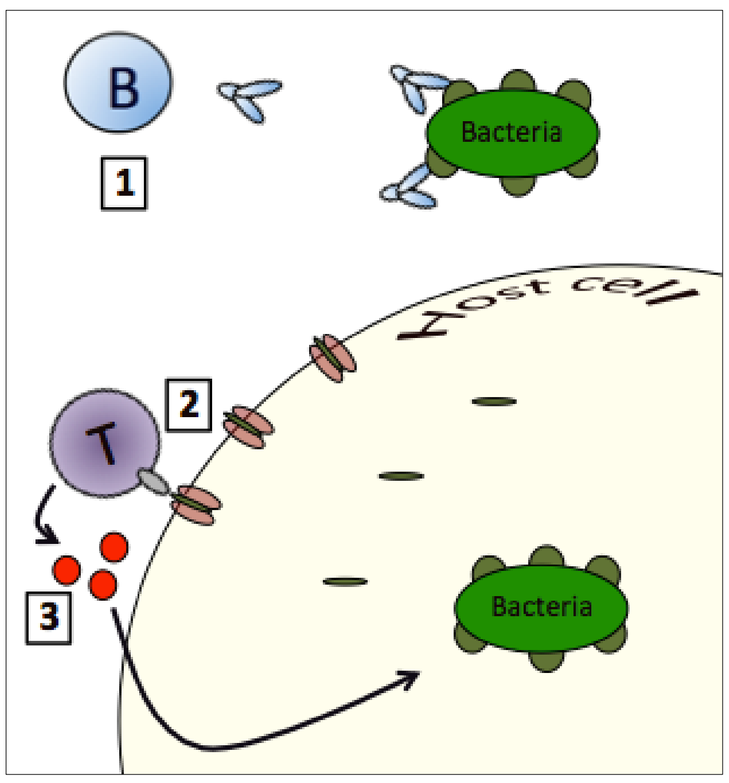
MRC Centre for Immune Regulation, Institute for Biomedical Research, University of Birmingham

Introduction and Overview

The thymus is the unique site of production of T-cells, an essential arm of the adaptive immune system which is targeted by vaccinations as a defense against infectious diseases. In generating a potent cohort of pathogen-clearing T-cells, small numbers of cells capable of attacking tissues within the body are also produced. Under normal conditions these are kept in check by "regulatory" cells, however if the balance of "auto-immune" and regulatory cells is altered, it has the potential to trigger auto-immune diseases, such as rheumatoid arthritis and diabetes.

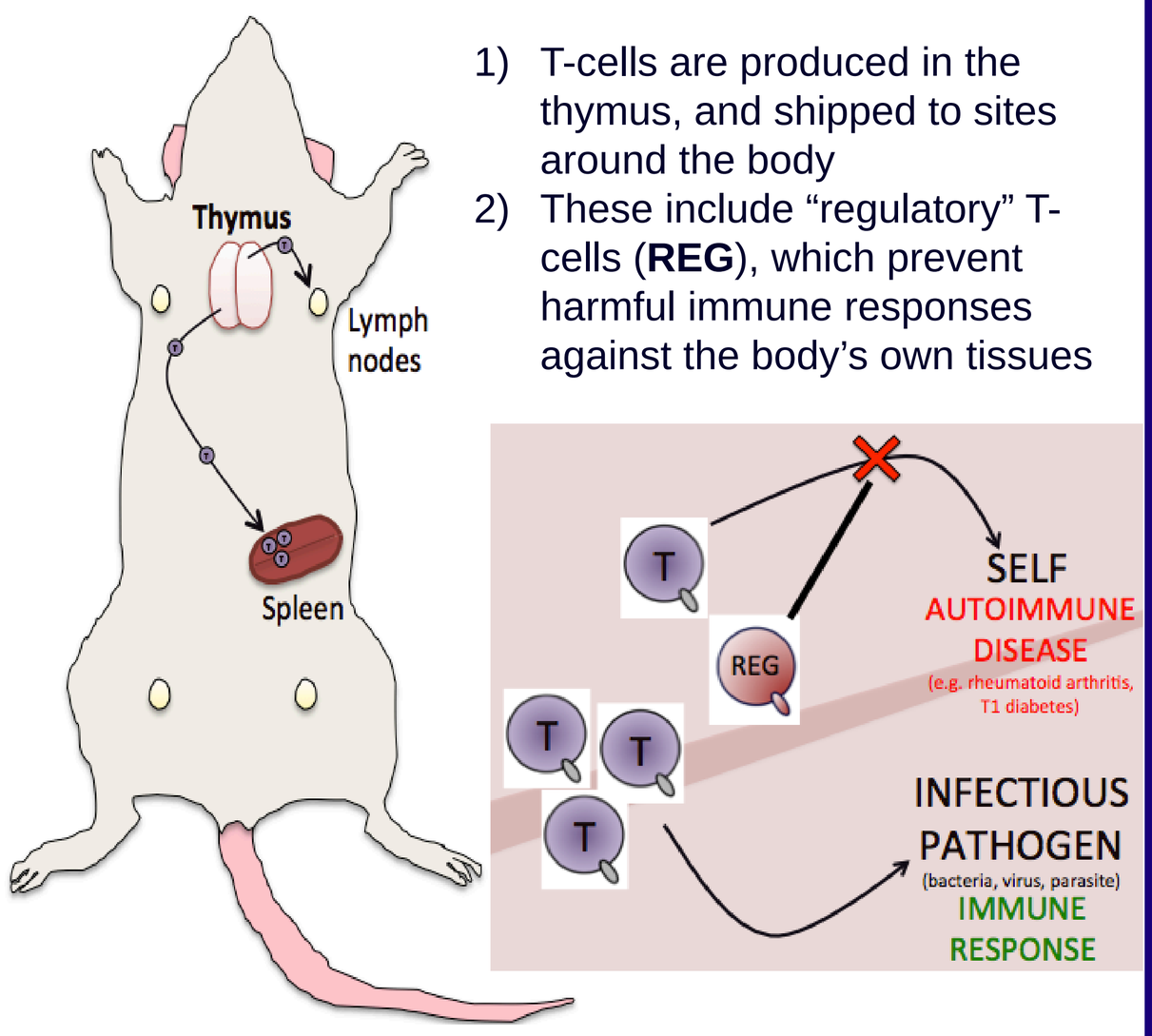
Using mouse models, we aim to investigate the potential to manipulate thymic production of anti-inflammatory T-cells to aid treatment of auto-immune disease.

The adaptive immune system consists of B-cells and T-cells



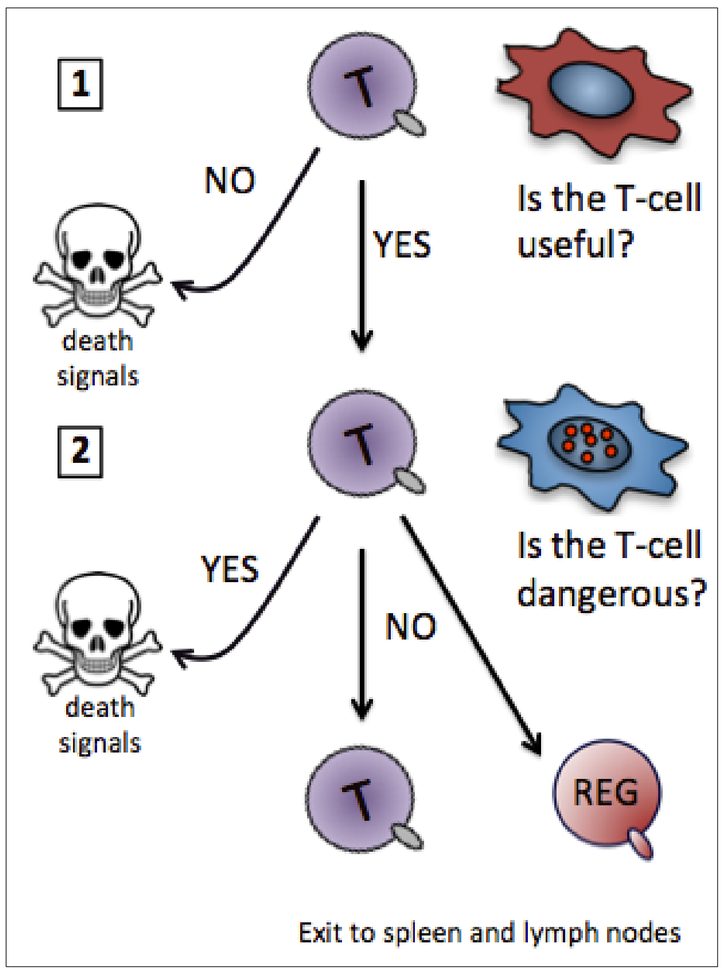
1) B-cells produce antibody to both detect and destroy bacteria
2) T-cells detect bacteria indirectly via a "T-cell receptor", which identifies bacterial proteins on the outside of infected cells
3) T-cells attack by releasing other soluble proteins ("cytokines")

T-cells with multiple protective functions are produced in the thymus



1) T-cells are produced in the thymus, and shipped to sites around the body
2) These include "regulatory" T-cells (**REG**), which prevent harmful immune responses against the body's own tissues

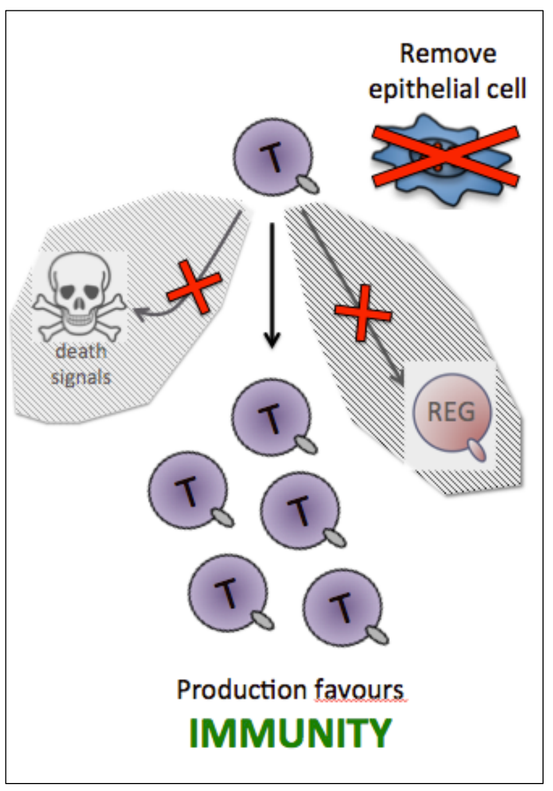
Epithelial cells in the thymus filter out non-functional, and potentially harmful T-cells



- The thymus is divided into two regions, cortex and medulla
- Each region is home to specialized epithelial cells; **cortical** cells (**red**), and **medullary** cells (**blue**)

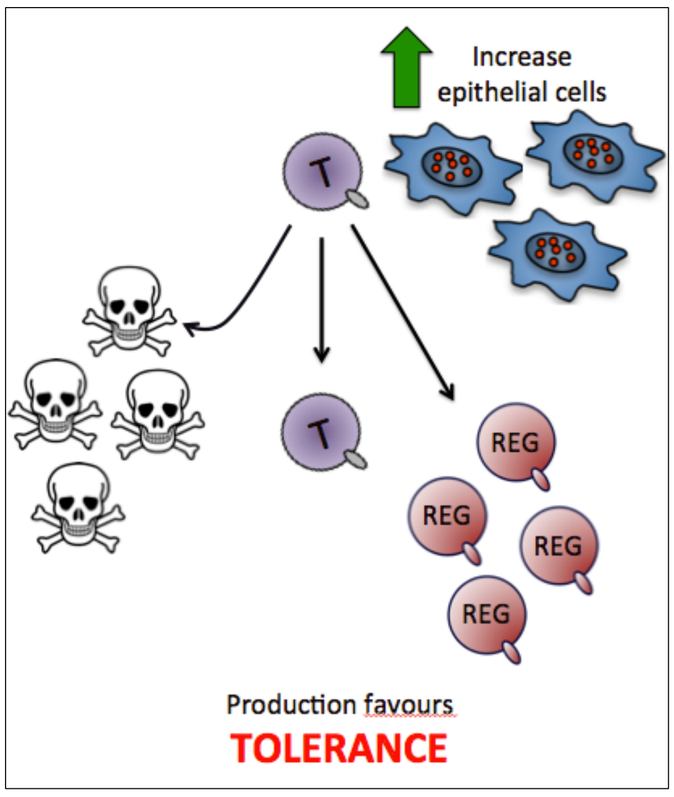
1) Non-functioning T-cells receive death signals from **cortical** cells
2) Potentially autoimmune cells receive death signals from **medullary** cells

Thymic epithelial cells may be a useful treatment target in cancer and autoimmunity



1) If we **remove** medullary epithelial cells, we increase the production of T-cells which protect against **cancer** and **infection**

1) What happens if we **increase** the number of medullary epithelial cells?



- Can we increase the production of regulatory cells?
- This could be used to treat **auto-immune diseases**