Hamilton Institute

Stochastic Modelling of T Cell Repertoire Diversity

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Abstract:
T cells are specialised white blood cells that protect the body from infection and are also able to kill infected cells. T cells are characterised by the presence of a special receptor on their cell surface called T cell receptor (TCR). The specificity of the T cell, namely which pathogens it can recognise, is determined by the molecular structure of its TCR. T cells can be classified according to their TCRs. All T cells that have identical TCRs are said to belong to the same clonotype. There are two types of T cells: naive and memory. Naive T cells have not yet encountered pathogens and memory T cells have already encountered pathogen. In this talk, I will only consider the class of naive T cells. A diverse naive T cell pool is essential to protect against novel infections, as the immune system cannot predict which pathogens the organism will be exposed to during its life-time. A healthy adult human possesses approximately 10^(11) naive T cells, which belong to about 10^7-10^8 different clonotypes. The reliability of the immune response to pathogenic challenge depends critically on the size (how many cells) and diversity (how many different TCRs or clonotypes) of the naive T cell pool of the individual. Experimental evidence suggests that interactions between TCRs with self-peptides (self-peptide = a fragment of a household protein) displayed on the surface of specialised cells, called antigen presenting cells (APCs), are important in controlling naive T cell numbers. Naive T cells undergo one round of cell division after receiving a survival stimulus from these specialized APCs. Whether or not a particular naive T cell can receive a survival signal from an specialized APC depends both on the TCR it expresses and the array of self-peptides displayed on the surface of the APC. Competition amongst naive T cells for these interactions regulates the diversity of the naive T cell pool.

We have made use of a probabilistic (stochastic) model to describe this competition. In particular, we have modeled the time evolution of the number of T cells belonging to a particular clonotype. Our results indicate that competition maximizes TCR diversity by promoting the survival of T cell clonotypes that are most different from each other in terms of the self-peptides they are able to recognise.

Venue: Seminar Room, Hamilton Institute, Rye Hall, NUI Maynooth

Time: 2.00pm - 3.00pm (followed by tea/coffee)

Travel directions are available at www.hamilton.ie

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