L3 – What to Attack?

The immune system must distinguish pathogenic infectious agents from commensals, self-antigens and environmental antigens. Pattern recognition receptors (PRR) recognise pathogen-associated molecular patterns (PAMP) and damage/danger-associated molecular patterns (DAMP).

- PAMPs are particular molecular patterns that are typically associated with infectious agents. They can be anything from carbohydrates not normally expressed in vertebrates, proteins only found in bacteria such as flagellin, double-stranded RNA typical of RNA viruses and other things. PAMPs are not found in the host.
- DAMPs are endogenous danger signals; they are structures inside our body and are molecules our cells begin to express in response to an infection or tissue damage; they are not foreign. DAMPs play a role in sterile injury, where an immune response occurs in the absence of any infectious agent (for example, bruising).

Recognition of antigen by the immune system

- PRRs – there are a few 100 PRRs and separate genes, which do not vary very much from one individual to another, encode each one. Polymorphism describes the variation in genes from one individual to another and PRRs show very low polymorphism. Many PRRs are lectin-like in that they recognise exposed microbial sugars. They can be subdivided into at least 5 distinct families on the basis of their structure (Toll-like receptors, nod-like receptors, C-type lectin receptors, RIG-like helicase receptors and scavengers).
- Major Histocompatibility complex (MHC) – first discovered by Peter Medawar. MHCs can be responsible for the rejection of tissue transplants between genetically different individuals. MHCs, produced in the endoplasmic reticulum, are cell surface molecules. There are a lot of different variants of MHCs and each variant can bind many different peptide sequences. The average length of peptide that MHC class II presents to a helper T cell is 15 amino acids, whilst it is 8-10 for MHC class I. There are about 12 MHCs that are expressed, these are what we call the classical MHCs. Non-classical MHCs are MHC-like, but not exactly MHCs. MHC class I and II are classical MHCs. 3 sub-groups of MHC class I: in humans they are called HLA-A, B and C. 3 sub-groups of MHC class I: HLA-DP, DQ and DR. These genes vary enormously; they are highly polymorphic.
- T-cell receptor (TCR) – found on surface of T lymphocytes and are highly specific. Genetic recombination of TCR genes creates huge diversity.
- Antibody/B-cell receptor (BCR) – found on the surface of B-lymphocytes as well as in soluble forms and is highly specific. The B cell receptor on the surface of the B-cell is a transmembrane version of the antibody, which was first found in its soluble, secreted form. Genetic recombination of BCR genes creates huge diversity.