

Unit 2 - Evolution of immune system

Evolution of immune system

Innate immune mechanisms can be found in species at almost every level of the evolutionary tree of life.

When life evolved the primitive organisms like of bacteria, archaea and eukaryotes brought change in environment, also increased the concentration of atmospheric oxygen, this facilitated the evolution of multicellular organisms (metazoans) around 600 million years ago. Evolution in multicellular organisms provided new host opportunities for microbial pathogens so these multicellular organisms developed new mechanisms of defence to protect themselves from pathogens, thus the origin of defence mechanisms begin and evolved along with the life.

The most primitive metazoans like sponges and coelenterates possess an epithelial layer of cells within an intermediate mesogleal layer which performs the role of digestive cells and defensive cells that engulf foreign organisms. These phagocytic cells lead the way for the development of vertebrate macrophage. This innate immunity uses germline encoded pattern recognition receptors for pathogens to distinguish between self and foreign.

Second layer of complex immune defences called adaptive immunity evolved in vertebrates around 500 million years ago. The adaptive immunity have not evolved overnight but it took several years. The unique feature of an adaptive immune system is the development of lymphocytes, where each lymphocyte possess an antigen recognition receptor that can be used to trigger specific defence mechanism. This lymphocytes are the key cells in evolution of specific immune system. Lymphoid cells found first in pre-vertebrate named Deuterostomes. Later these lymphocytes evolved along with the life and the development of the diverse lymphocyte receptor allows vertebrates to recognize almost any potential pathogen or toxin and can generate antigen-specific responses to it. Antigen-activated lymphocytes differentiate into mature lymphocytes with cytotoxic and pro-inflammatory functions or into plasma cells that secrete antibodies and also provide protective memory of the antigen to fight the pathogen in future invasion.

Two types of adaptive immune system have evolved in vertebrates:

- Adaptive immune system in jawless vertebrates (hagfish and lamprey)
- Adaptive immune system of jawed vertebrates

Adaptive immune system in jawless vertebrates (hagfish and lamprey)

Lymphocytes present in jawless fish are indistinguishable from mammalian cells. But these Fish lymphocytes lack MHC (major histocompatibility complex) molecules, T-cell receptors and B-cell receptors. So jawless fishes use different types of antigen recognition receptor but use similar lymphocyte differentiation process to elicit specific immune response.

Adaptive immune system of jawed vertebrates

MHC (major histocompatibility complex) molecules, T-cell receptors and B-cell receptors based adaptive immune system is detected in cartilaginous fish but absent in lower chordates. For the evolution of adaptive immune system in jawed vertebrates it is believed that two

macroevolutionary events that had provided the platform for evolution of specific immune system are:-

- The invasion of *recombination-activating gene* transposon (RAG transposon)
- Whole-genome duplication (WGDs)

The invasion of *recombination-activating gene* transposon (RAG transposon)

The gene encoding an immunoglobulin superfamily (IgSF) exon was invaded by the recombination-activating gene transposon (RAG transposon) and invasion of this transposon helped in triggering B cell receptor and T cell receptor based immunity. RAG genes are present in all gnathostomes but not in jawless fish, and this suggests the reason for the absence of B cell receptor and T cell receptor in jawless fishes. RAG transposon activity is the major incident in the evolution of adaptive immunity, because the jawed vertebrates have advanced mechanisms and molecules that are involved in adaptive immunity when compared with jawless fish.

Whole-genome duplication (WGDs)

The vertebrate genome has undergone two rounds of Whole-genome duplication (WGD) after the emergence of urochordates and before the radiation of jawed vertebrates. The first round of WGD occurred in a common ancestor of jawed and jawless vertebrates, and the second round in a common ancestor of jawed vertebrates. These WGDs played a crucial role in the emergence of adaptive immune system in jawed vertebrates, in the form like many orthologues, that formed during WGDs, are now acting as essential components of the adaptive immune system in jawed vertebrates.

Immunoglobulins

The development of adaptive immune system led to the production of immunoglobulins where, among living animals immunoglobulins are first found in cartilaginous fish like sharks, skates and rays. These are generated by a somatic recombination mechanism. Among immunoglobulins, IgM is the most ancient antibody class and conserved the same function in all gnathostomes. In cartilaginous fish, IgM is abundantly secreted as monomer, but in bony fish it is secreted as tetramer. In addition to IgM and IgD other immunoglobulins are also found in higher vertebrates. IgG, which is involved in memory responses, Ig E, involved in inflammatory (and allergic) responses at epithelial surfaces. IgA involved in mucosal antibody. IgG and IgE are evolved from IgY, this IgY was found in amphibians and perform the function similar to IgG.