The concept of an immune system—the defense of the individual against infectious agents—is ubiquitous. Even bacteria have some protection (restriction enzymes in concert with modification systems) against parasites (plasmids) and pathogens (bacteriophages) that infect them. However, it is unlikely that such systems have a direct counterpart in higher organisms. As a consequence we will focus on the evolution of an immune system in multicellular organisms.

The evolution of the immune system can be studied by comparing the genes expressed by different species. The evolution of the immune system can be studied by comparing the genes expressed by different species.
Innate immunity has some of its origins in early eukaryotes such as the amoeba.

Amoebas behave like macrophages (move randomly unless exposed to a chemoattractant).

Early receptors for self or nonself (food).

Phagocytosis.

Antimicrobial peptides are likely to be the most ancient immune defenses. Antimicrobial defensins of a) plants, b) insects and c) mammals are structurally related and the progenitor gene may have been present in a common ancestor which lived approximately 2 to 3 billion years ago.

Toll-like receptors may represent the most ancient pathogen recognition system. Activation induces expression of antimicrobial peptides primarily acting on gram-positive bacteria and fungal pathogens.
Toll-like receptors genes have undergone extensive diversification in some invertebrate species

- humans 13 TLR (11-13 pseudogenes)
- mice 13 TLR (10 pseudogene)
- sea urchin 222 TLR (many pseudogenes but as other species a conserved signalling machinery)
- Drosophila 1 TLR

A second recognition system in Drosophila homologous to the mammalian TNF receptor pathway provides protection from gram negative bacteria.

Both Toll and Imd pathways activate gene transcription to eliminate infections.

The innate immune system is well developed in fruitflies, nematode worms and other invertebrate species.

These organisms have in common with vertebrates the genes that encode the intracellular signaling pathways leading from the cell surface to the activation of the transcription factor NFkB.

NFkB is the original and central signaling pathway of activation in innate immunity.
The complement system of echinoderms resembles the alternative pathway of complement activation in mammals.

The components of a primitive complement system in echinoderms:
- Factor B
- Factor C3
- Factor D
- Factor I
- T receptor
- Coelomocyte
- Bacterium

Most primitive function is opsonization (increasing the efficiency of pathogen uptake).

The lectin pathway of complement activation evolved in invertebrates.

The lectin pathway of complement activation is present in the invertebrate chordates:
- Ficolin
- MASP
- MBL-associated serine protease
- MBL = Mannose binding lectin

Chapter ? Evolution of the immune system

Tunicates; sea squirts

Chapter ? Evolution of the immune system

- The evolution of the immune system can be studied by comparing the genes expressed by different species
  - Evolution of the innate immune system
  - Evolution of the adaptive immune system(s)
Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes (a non-rearranging system)

Dscam Down syndrome adhesion molecule (opsonizes invading bacteria)

Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR (leucine rich repeat) domains

Adaptive immunity based on a diversified repertoire of Ig-like genes appeared abruptly in the cartilaginous fish
Overview of the evolution of the immune system in deuterostomes

- Nod-like receptor scavenger receptor
- Whole genome duplications

Different species generate immunoglobulin diversity in different ways

- MHC class I and II molecules are first found in the cartilaginous fish
- Both alpha/beta and gamma/delta T cell receptors are present in cartilaginous fish

Key events in adaptive immunity

- Agnatha have a rudimentary GALT system
- Teleosts (bony fish) possess thymus and spleen
- Amphibians show emergence of bone marrow
- Aves*/Reptilia/mammalia possess lymph nodes and germinal centers.

* Bursa of Fabricius a lymphoid organ in young chicks where B cells mature