EVOLUTION in immunity
EVOLUTION OF THE IMMUNE SYSTEM

Innate immunity
Toll like Receptor (TLR)

Phylogenetic tree showing the evolutionary relationships of different types of vertebrates, including Protostomes (Sea urchin and Tunicate), Echinoderms (Amphioxus), Urochordates (Lamprey and Hagfish), Cartilaginous fish (Shark), Bony fish (Zebrafish and Pufferfish), Amphibians (Xenopus laevis), Mammals (Mouse), Reptiles (Chick), and Birds (Chick).

TOLL LIKE RECEPTORS
TOLL LIKE RECEPTORS CAN RECOGNIZE PATTERNS

TLRs share a prototypical organization of N-terminal (N) extracellular leucine-rich repeat (LRR) motifs. TLRs are dimerized and the ectodomain forms a horseshoe-shaped solenoid.

François Leulier & Bruno Lemaitre
Nature Reviews Genetics 9, 165-178 (March 2008)
EVOLUTION OF THE IMMUNE SYSTEM

Adaptive immune system

Immunoglobulins (Abs and TCRs)
EVOLUTION OF THE IMMUNE SYSTEM

Protostomes

- Echinoderms
  - Sea urchin
- Urochordates
  - Tunicate
- Cephalochordates
  - Amphioxus
- Jawless fish
  - Lamprey, Hagfish
- Cartilaginous fish
  - Shark
- Bony fish
  - Zebrafish, Pufferfish
- Amphibians
  - *Xenopus laevis*
- Mammals
  - Mouse
- Reptiles
- Birds
  - Chick

No Immunoglobulins

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ADAPTIVE IMMUNITY?

Hagfish

Lamprey
ADAPTIVE IMMUNITY

• Capacity of transplantation rejection
• The responses to skin allografts is specific
• Accelerated second-set rejections indicates immunological memory.
CHALLENGE WITH BACTERIA

• Able to produce serum antibodies.

• Responses have been connected with cells that are morphologically similar to the lymphocytes from jawed vertebrates.
Somatic diversification of variable lymphocyte receptors in the agnathan sea lamprey

Zeev Pancer\textsuperscript{1,2}, Chris T. Amemiya\textsuperscript{6}, G\ötz R. A. Ehrhardt\textsuperscript{1,5}, Jill Ceitlin\textsuperscript{7}, G. Larry Gartland\textsuperscript{1,4} & Max D. Cooper\textsuperscript{1,2,3,4,5}

Nature 430, 174-180 (8 July 2004)
VLRs in lamprey lymphocytes are assembled by DNA rearrangement. Each VLR receptor, VLRs are generated in lymphocytes by DNA rearrangement. Each VLR comprises a set of highly diverse LRR modules capped by di- or tri-cysteine motifs.

To increase the combinatorial diversity of VLRs in lampreys, the lamprey genome contains numerous LRR genes. By shuffling domains through homologous recombination, a VLR of one to eight LRR modules is assembled.

This study provides the first description of monoclonal VLRs generated in transfected mammalian cells. Leukocyte-directed, small interfering (si)RNA against cyclin D1 shows that siRNAs with guts from flanking VLR genes can inhibit the cell cycle regulator, CyD1, a cell cycle regulator, is upregulated in mouse CD4+ and CD8+ T cells. Leukocyte-directed CyD1 siRNA inhibits the immune response.

Assembly of lamprey variable lymphocyte receptors (VLRs), compared with the V(D)J-rearrangement that gives rise to mammalian antibody genes, describes a more ancient parallel evolution involving LRR modules. The most ancient antigen receptors might soon take a central place in the biotech industry.

Like receptors and plant pathogen resistance, humoral antibodies has led to binding scaffolds that flank the gene encoding the germline antibody genes including bovine serum albumin and keyhole limpet hemocyanin. They failed to sequentially incorporated into the germ-line gene via gene conversion. Jawed vertebrate antibody genes are assembled via recombination activating gene (RAG)-mediated joining of immunoglobulin receptors, this study provides the first description of monoclonal VLRs generated in transfected mammalian cells.

Zeev Pancer & Roy A Mariuzza

NATURE BIOTECHNOLOGY VOLUME 26 NUMBER 4 APRIL 2008
TOLL LIKE RECEPTORS CAN RECOGNIZE PATTERNS

TLRs share a prototypical organization of N-terminal (N) extracellular leucine-rich repeat (LRR) motifs.

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GENOME DUPPLICATIONS

![Genome Duplication Tree Diagram]

**Protostomes**
- **Echinoderms**
  - Sea urchin
- **Urochordates**
  - Tunicate
- **Cephalochordates**
  - Amphioxus
- **Jawless fish**
  - Lamprey, Hagfish
- **Cartilaginous fish**
  - Shark
- **Bony fish**
  - Zebrafish, Pufferfish
- **Amphibians**
  - *Xenopus laevis*
- **Mammals**
  - Mouse
- **Reptiles**
- **Birds**
  - Chick

The diagram illustrates the evolutionary relationships among different animal groups, with time measured in million years ago. The timing of genome duplication events is indicated by the numbers on the branches.

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GENOME DUPLICATIONS

![Phylogenetic tree of vertebrates](image)

- **Protostomes**
  - Echinoderms
    - Sea urchin
  - Urochordates
    - Tunicate
  - Cephalochordates
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    - *Xenopus laevis*
  - Mammals
    - Mouse
  - Reptiles
  - Birds
    - Chick

**Timeline:**
- 800 MYA (Million years ago)
- 600 MYA
- 400 MYA
- 200 MYA
- 0 MYA

*Current Opinion in Genetics & Development* (1996)
It has recently been demonstrated that this organism contains histocompatibility-relevant genes and lymphocyte immune signaling-relevant genes, i.e., components that may be recruited by adaptive immune processes.

*Fish & Shellfish Immunology, Volume 26, Issue 6, June 2009, Pages 843-849*
Zhenhui Liu, Lei Li, Hongyan Li, Shicui Zhang, Guangdong Ji and Yanling Sun