On Modelling the Immune System as a Complex System

Summary of the article
On Modelling The Immune System as a Complex System
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Complex Systems

- Multiple interacting elements.
- Collective behavior cannot be simply inferred from the behavior of its elements.

Immune System (IS)

- A complex network of cells and chemicals.
  - Many different kinds of cells
  - Hundreds of different chemicals.
- The cells in the IS have the ability to recognize objects as either damaging or non-damaging.

Immune System Components

- Master glands, principally the thymus and the bone marrow.
- Various sites that temporarily harbor immune cells
- Different classes of "soldier" cells, which carry out specialized functions, including cells that:
  - alert,
  - activate,
  - engulf,
  - kill,
  - clean up, and
  - cells and molecules that facilitate,
- Many immune cells also synthesize and secrete special molecules that act as messengers, regulators, helpers or suppressors in the process of defending against invaders.

Immune System Processing

- The IS performs pattern recognition tasks.
- It learns and retains a memory of the antigens that it has fought.
- The IS contains more than 100 000 000 000 different clones of cells that communicate via cell-cell contact and the secretion of molecules.
- Performing complex tasks such as learning and memory involves cooperation among large numbers of components of the IS.

Immune Network

- The main components of IS are the innate and the adaptive ones.
- The innate component contains (among others) the complement system, macrophage, dendrite cells, and natural killers.
- The adaptive component contains the B-cells, Th-cells and Tc-cells.
- Both components are interconnected by a large number of cytokines that cause activation and/or inhibition.

Emergent Properties

- The ability to distinguish any substance (typically called antigen Ag) and determine whether it is self or non-self.
- If Ag is non-self, then IS determines whether to tolerate it or to respond to it.
- If it decides to respond to it then IS determines whether to eradicate or to contain it.
- The ability to memorize most previously encountered Ag, which enables it to mount a more effective reaction in any future encounters.

Immune Network Interactions

- When a bacteria invades the body, dendrite cells (and other Ag presenting cells (APC)) identify it, process it and present it to the Thcells together with a second signal to stimulate the Th-cells.
- Without this second signal the Th-cells go into a state of anergy (become paralyzed).
- Once activated, the Th-cells activate (through cytokines) B-cells and macrophages.
- B-cells secrete antibodies (Ab), which together with the complement system and macrophage eliminate the Ag.
- While this process is going on, some B-cells become memory B-cells.
- Such cells are long lived and can mount a faster and stronger effect against that Ag in future encounters.

Immune Network Interactions

- A similar scenario occurs for viruses but in this case Th activates Tc, natural killers and macrophage to attack infected cells and eradicate the virus.
- While this process is going on, some T-cells become memory T-cells

Adaptability

- The antibodies which enter our bodies are very diverse.
- Mechanisms have to exist to produce immune effectors with constantly changing random specificity to be able to recognize these Ag.
- Wide diversity of IS contains the danger of autoimmunity.
- Hene, mechanisms that limit autoimmunity should exist.

Properties of Immune System

1. Decentralized system.
2. Functions in the presence of noise.
3. Effectors are multi-function, i.e. most of them have more than one function to perform (e.g. macrophage both engulf Ag and present Ag to activate mature Thcells). Almost every function of IS is done by more than one effector (IS is multipathways).
4. Multi-objectives: Has to maximize harmful Ag elimination and at the same time minimize harm to self. All this should be done with limited resources.