Basic immunology in 20 minutes

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4 November 2004

What is the immune system?

• Biological mechanism for identifying and destroying pathogens within a larger organism.
  – *Pathogens*: agents that cause disease
    • Bacteria, viruses, fungi, worms, etc.
Why would a computer scientist study the human immune system?

- Massively parallel information processing mechanism – with 6.5B users!
- Incredibly effective example of a distributed system built from diverse components which are constantly being renewed.
- May inspire better computer security systems (stay tuned for next week), as it's
  - adaptive – can train self to react to new threats
  - error-tolerant – small mistakes are not fatal
  - self-protecting – protects itself

Review slide – this is all in the paper.
Roadmap

• Many introductions present IS as a giant parts list.

• We'll briefly consider it as a set of barriers, from a pathogen's perspective.

• Disadvantage: lots and lots and lots of supporting details omitted. Ask questions.

• Advantages: fast, tailored to hobby-horse concepts of immunologically-inspired security.
  
  – Namely negative selection, costimulation, combinatorial & junctional diversity, and somatic hypermutation. *(Don't ask questions about this line. We'll get to this.)*
First line of defense is the *innate* immune system.

(This wasn't in Hofmeyr.)
Innate immunity

Pathogens (ubiquitous) vs Skin (think firewall)

Skin repels nearly everything

Macrophage ingests & destroys most pathogens

Hard-coded detectors for common pathogenic signatures.

Very few penetrate skin

Very, very few evade innate immunity

Not to scale.
Rarely, nasty germs can evade the innate immune system. Enter *adaptive* immunity.
Adaptive immunity

**T cells** destroy infected cells to eradicate intracellular pathogens. (Some bacteria, all viruses)

**B cells** secrete antibodies to attack extracellular pathogens. (Most bacteria)

The colors of the receptors indicate specificity: each can bind to one specific antigen. Adaptive immunity can only attack targets that it has prepared for.
Suppose you're a pathogen.

You've avoided the innate immune system.

Should the adaptive immune system give you pause?

Why would one of these receptors be able to bind to you?

Suppose you're new. As-yet-unseen.

Impossible, right?
T cell development, briefly outlined

Prototype cell, moves from bone marrow to thymus gland

Creates T cell receptor by sloppy gene rearrangement. (next slide)

Self-targeted T cells are deleted (2 slides from now)

Useful, non-self-reactive T cells are released from the thymus
T cell receptor (TCR) creation

(1) TCR = V segment + D segment + J segment. Genome contains several different copies of each. Pick one from each set. *(Combinatorial diversity.)*

(2) Join the copies together using a sloppy technique that introduces randomness into the junctions. *(Junctional diversity.)*

(3) If you get an in-frame protein, continue.

*From a few dozen (to several dozen) segments for each category (V,D,&J) the human immune system creates over $10^{11}$ different antibody receptors.*
T cell refinement

Candidate T cells are exposed to most of the proteins in the human body. For presentation, proteins are chopped into fragments and displayed on specialized presentation molecules.

T cells that do not bind to any presentation molecules are allowed to die.

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T cells with moderate binding strength are retained.

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Strongly autoreactive T cells are killed (negative selection).

T cells from the green zone are approved.
Summary of the last three slides

Your immune system has a repertoire of T cells capable of binding and destroying cells that exhibit almost any foreign protein.
Suppose you're a pathogen.

You've avoided the innate immune system.

Should the adaptive immune system give you pause?

Why would one of these receptors be able to bind to you?

Suppose you're new. As-yet-unseen.

Impossible, right? **Wrong!**
It is unlikely that any intracellular-pathogen-infected cell will escape binding by a T cell.

The first binding will lead to replication of the bound T cell and (if all goes well) eventual clearance of the infection.
OK, so I'm toast. But what happens if a T cell binds a human cell? (They're moderately autoreactive, right?) Will the human cell be lysed?
Answer: **Costimulation**

To be activated, a T cell needs to see both its first signal (the target antigen) and a second “**DANGER**” signal.

The “**DANGER**” signal is provided by antigen presenting cells when they detect signs of infection (cell lysates, certain cytokines, etc.)

T cells cannot be activated without a “**DANGER**” signal. If a T cell receives its first signal without the second, it may become tolerized to its target.

If you haven't noticed, *bold italic* means important!
I'm an *extracellular* pathogen. What should I expect?

Most pathogens are not self-aware.
B cells improve themselves via *somatic hypermutation*

Activation via B/T collaboration

*Clonal expansion*

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Somatic hypermutation (random mutation of BCR)

Advantageous mutations increase secreted antibody binding affinity

Deleterious mutations