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Under the Radar Screen: How Bugs Trick Our Immune Defenses

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Preparation: Details

- 2 papers per week, distributed the week before discussion. A brief overview of the topic will also be presented when papers are handed out.
 - How to read a paper ? What to think about ?
 - Title, does it make sense, does it reflect findings of the paper ?
 - Abstract, does it invite you to read the paper, does it say enough but not too much ?
 - Introduction, does it put the paper in context, does it inform on the content of the paper ?
 - Methods, are the techniques used appropriate, could they have used different techniques to get to the same results, are the techniques clearly described ?
 - Results, do results support claims made in the title/abstract, are the results well/clearly presented, are appropriate controls included, do results show what authors claim ?
 - Discussion, do they explain the results properly in the context of current literature and in view of other people's results, are they bringing forward relevant hypothesis, do they suggest relevant follow up ?
- 2-4 questions to prepare while reading the papers, also distributed the week before
 - These questions should guide your reading and help you think about different issues when reading the papers. You should prepare tentative answers for these questions.

The immune system

An overview

The purpose of the immune system is to seek out and destroy free pathogens as well as infected host cells.

Principal effectors of adaptive immunity: Cellular effectors = T cells

- Originate in the bone marrow
- Go through genetic rearrangement of their antigen receptor (T cell receptor or TCR) to create unique specificities
- Mature in the thymus gland where they are “educated/screened” to recognize normal self molecules from foreign ones.
- In the thymus, they also differentiate into CD4 and CD8 T cells. The expression of these co-receptors is associated with different functions:
 - CD8+ T cells: cytotoxic
 - CD4+ T cells: help B cells differentiate/mature

Principal effectors of adaptive immunity: Humoral effectors = B cells

- Originate in the bone marrow but do not mature in the thymus
- They also undergo genetic rearrangement of their antigen receptor, the B cell receptor (BCR)
- They need T cell help to mature and start secreting antibodies (soluble form of the BCR)
- Immature B cells express the BCR at the cell surface, mature B cells (aka plasma cells) secrete their BCR in the form of antibodies.

Antigen presentation

- Antigenes are presented to T cells through two kinds of molecules:
 - Major Histocompatibility Class I (MHC I)
 - Major Histocompatibility Class II (MHC II)
- Two different types of antigens need to be presented to T cells :
 - Intracellular antigens (synthesized inside the cell)
 - Extracellular antigens (present in the extracellular milieu and picked up by phagocytes)
- MHC I presents intracellular antigens
- MHC II presents extracellular antigens

Different classes of pathogens are handled differently by the immune system, a few examples

| Pathogen | Characteristic | Immune function |
|----------|---|---|
| Virus | Need host to replicate, intracellular protein synthesis | Antigen presentation through MHC class I/CD8 T cells NK cells |
| | May be found outside the cell | Endocytosis/phagocytosis (larger viruses) Antigen presentation through MHC class II/CD4 T cells Toll like receptors (non-specific receptors that recognize molecular patterns found on pathogens) |
| | May actively penetrate the cell | MHC class II and endocytic compartments |
| | Can be latent | |
| Bacteria | Can replicate outside the host | Antigen presentation through MHC class II/CD4 T cells Toll like receptors |
| | Are large and often found outside the cell | Humoral response (Antibodies) Phagocytosis |