ImmunoBiology 2018

• Coordinator: Can Keşmir ([c.kesmir@uu.nl](mailto:c.kesmir@uu.nl)) Kruyt, Z509
• Web Page: tbb.bio.uu.nl/immbio (check regularly for updates)
• Book: The Immune System by Peter Parham, 4th edition
• Teachers: Bontrop, de Boer, van Bergen en Henegouwen, Borghans, and Kesmir, together with a number of quest lecturers.
• Schedule: via a Google calendar, see Web page. Self study is indicated in this schedule.

Form of the course

• Lectures
• Article discussions and debate (16 groups in total, groups of 5-6)
• Experimental work (Practica, in groups of 5-6 further separation in groups A and B)
• 6 Werkcolleges/Computer Exercises
• Groups are to be found in BlackBoard.

Assessment

• Two Exams: 20% & 40% (you need a minimum of 5,5 on average)
• One written reports:
  ✓ 25%: About one of the computer exercise/werkcollege (there are 6 all together)
• Article presentations and discussions or debate (15%)
• It is obligatory to keep a lab-book during computer exercises/werkcollege and deliver this at the latest 1st of July

Bonus point for the exam:

• Enroll in rocketmix system of Garland Science Press.
• Make the modules 1-20
• This gives you a bonus point on your exam grade.
Evaluations of last year: points to improve

1. Rstudio kwam over voor de mensen die geen systeembiologie hebben gedaan, vooral voor MLS is dat erg handig, zodat ze weten dat ze het goed hebben gedaan en niet het eerste COO aan het prutsen zijn.

This year I have booked a half day COO to prepare you better for R exercises. This will be prior to all COOs, and hopefully will help you to work easier with R.

2. Het eerste tentamen was makkelijker dan verwacht op basis van de te leren stof, met name omdat het alleen maar meerkeuzevragen waren.

The first exam will be digital and including open questions. It is scheduled for May 17th.

3. Ik vond het tweede deel van de cursus vrij veel. Er was 1 tentamen en 3 verslagen die in moeten worden geleverd. We hebben helemaal geen bijpassende experimentele rapporten getekend, zodat niet alle informatie wat meer tijd nogmaals lassen.

We canceled the experimental report, the material you learn during the experimental part will be tested during the exam.
Chapter 1 & 3:

Elements of the Immune System and their Roles in Defense

Immunology is the study of physiological mechanisms that humans and other animals use to defend their bodies from invasion by other organisms. The hosts invest heavily in cells dedicated to defense, which collectively form the immune system.

Survival for Immunity: The Price of Immune System Activation for Bumblebee Workers

Yannick Moret* and Paul Schmid-Hempel

Parasites do not always harm their hosts because the immune system keeps an infection at bay. Instead, the cost of using immune defenses could itself reduce host fitness. This indirect cost of parasitism is often not visible because of compensatory resource intake. Here, workers of the bumblebee Bombus terrestris were challenged with lipopolysaccharides and microbe-tainted beads to induce their immune system under starvation (i.e., not allowing compensatory intake). Compared with controls, survival of induced workers was significantly reduced by 10 to 70%.

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Three main lines of defense
Immune cells

Adaptive immune responses in Jawless vertebrates

Not all the species have adaptive immune responses
Innate and adaptive immunity are complimentary

How do innate immune cells recognize their target: movie

What do the innate immune cells recognize on the pathogens?
A Pathogen Associated Molecular Pattern (PAMP) is any molecule that is common among large groups of microorganisms. PAMPs are only found on pathogens, not on human cells.

Innate immune cells have several receptors to recognize PAMPs

- Lectins: Recognize microbial carbohydrates. e.g. Mannose receptors. Are primarily expressed on macrophages.
- NOD-like receptors: Cytoplasmic receptors that recognize bacterial cell wall components.
- Scavenger receptors: Bind to negatively charged lipids found on microbes as well as damaged molecules of self lipoproteins.
- Toll-like receptors (TLRs): Recognize a variety of PAMPs and are expressed by almost all cells of the immune system.
**Movie Janeway 1.1**

**Innate recognition of the pathogens**

Toll-like receptors sense the presence of infection.

**TLRs are polymorphic and diversity increases with the complexity of the ligand**

Sensing via TLR4 starts synthesis of inflammatory cytokines.
**Different receptors cause production of different cytokines**

- TLR4 detects bacterial or fungal PAMPs, initiates a MyD88-dependent signaling cascade that results in the production of the pro-inflammatory cytokines TNF-α, IL-1, and IL-6. These proinflammatory cytokines initiate an inflammatory cascade that ultimately recruits leukocytes and other immune mediators.

- TLR3 detects viral PAMPs, initiates signaling that leads to the production of type I interferons, IFN-α and IFN-β. These type I interferons help activate NK cells and induce the ‘interferon response’ in neighboring cells.

**Innate immune system causes inflammation at the site of infection**

- Healthy skin is not inflamed
- Surface wound introduces bacteria, which activate resident effector cells to secrete cytokines
- Vasodilation and increased vascular permeability allow fluid, protein, and inflammatory cells to leave blood and enter tissue
- The infected tissue becomes inflamed, causing redness, heat, swelling, and pain
Inflammation attracts NK cells to the side of infection

Next step is the activation of the adaptive immune system

Cytotoxic T cells

Innate immune system

Adaptive immune system

Figure 1.23 The Immune System, 4th ed. (© Garland Science 2015)

Cartoon courtesy of Eric Riets

Antigen recognition by T cells

- The epitopes recognized by T-cell receptors are often buried
- The antigen must first be broken down into peptide fragments
- The epitope peptide binds to a self molecule, an MHC molecule
- The T-cell receptor binds to a complex of MHC molecule and epitope peptide

Antigen recognition by B cells

- B cells produce antibodies
- Specific antibody
- Neutralisation
- Spontaneous
- Complement
- Agglutination
- Inhibition
- Antigen destruction by phagocytes

Resting B cell
- Membrane-bound Ig

Encounter with antigen
- B cell
- B cell

Stimulated B cell gives rise to antibody-secreting plasma cells
- Plasma cells
- Secreted antibody
Hallmark of the adaptive immune system: diversity

Adaptive immune responses generally give rise to long-lived immunological memory and protective immunity

Clonal selection of lymphocytes by a pathogen

Lymphocyte recirculation
Chapter 1  Elements of the Immune System and their Roles in Defense

Most lymphocytes are present in specialized lymphoid tissues

Circulating lymphocytes meet lymph borne pathogens in draining lymph nodes.

Chapter 1  Elements of the Immune System and their Roles in Defense

Spleen provides adaptive immunity to blood infections

Chapter 1  Elements of the Immune System and their Roles in Defense

Most lymphoid tissue is associated with the gut
Innate Immunity: Chapter 2

• Complement System:
  Lecture by Piet Gros, 30th of April.

Mucosal Gut Immunity
  Nature movie: