Written Exam in MOL 8002 (01. June 2012)
Molecular mechanisms of host defence

1.) a) Briefly outline the different mechanisms employed by cells to ensure that the genome is copied with high fidelity.
b) What is the approximate accumulated error frequency at each base pair for each cell generation?

2.) Mention major types of mutagenic DNA base damage that can result from
   a. γ-irradiation
   b. UV-irradiation
   c. Methyl chloride

3.) Nucleotide excision repair (NER) is a major mechanism of DNA repair. Which type of DNA damage, in principle, is repaired by NER and name the most common source of mutagen inflicting this type of damage.

4.) Briefly explain why lack of geminim may lead to genomic instability.

5.) Homologous recombination (HR) and non-homologous end joining (NHEJ) are the main pathways for repair of double-strand breaks (DSBs). Briefly describe the main steps in the canonical HR.

6.) Scientists have to date described 4 inflammasomes.
   a. Name the inflammasomes
   b. Name the major proteins inflammasomes are composed of
   c. Give an example of an agens that may function as an activator for each of the inflammasomes.
   d. What are the major effector mechanisms of inflammasomes?

7.) What is the mechanistic explanation for the significant success of Anakinra-treatment (IL-1 receptor antagonist) in Muckle-Wells patients?

8.) Antigen-specific T cells are potent effector cells of the adaptive immune system. Naïve CD4+ and CD8+ T cells can be activated, when their T cell receptors recognize antigenic peptides presented in the context with MHC molecules on professional antigen-presenting cells (APCs).
   a. Into which main effector T cell subsets can naïve CD4+ and CD8+ T differentiate upon activation?
   b. How can antigen-specificity of T cells be demonstrated experimentally?

9.) Antigen-specific T cells recognize foreign antigen as well as in some cases altered/overexpressed self-antigens and thus contribute to host defence against infections as well as tumours.
   a. Name possible health problems that can arise if T cell responses are misdirected (recognition of "non-pathogenic" antigens)?
   b. Name possible health problems that can arise from a status with reduced adaptive immune / T cell function (such as in HIV infection, immunosuppressive therapy)?
   c. Auto-immune T cells are present also in healthy individuals. Name two mechanisms that normally prevent development or control activation of auto-reactive T cells?

10.) Development of new and more effective vaccines (e.g. against HIV, malaria, tuberculosis) is an urgent need. What immunological properties are desirable for newly developed vaccines?

11.) What are the key regulatory factors for osteoclast activation?

12.) Describe how hepatocyte growth factor (HGF) or Dickkopf-1 (DKK-1) may be involved in the bone destruction associated with rheumatoid arthritis and multiple myeloma.

13.) Pre-eclampsia is a pregnancy disorder characterized by harmful placental and systemic inflammation. How may a) pathogens/PAMPs and b) endogenous danger signals/DAMPs contribute to this disease?

Pre-eclampsia = svangerskapsforgiftning. Placenta = morkake.

14.) Fetal cells are "foreign" to the maternal immune system since their MHC expression is derived from a combination of maternal and paternal genes. How is this potential problem overcome in pregnancy

MHC = Major Histocompatibility Complex. Fetal = foster.