

NAME: \_\_\_\_\_

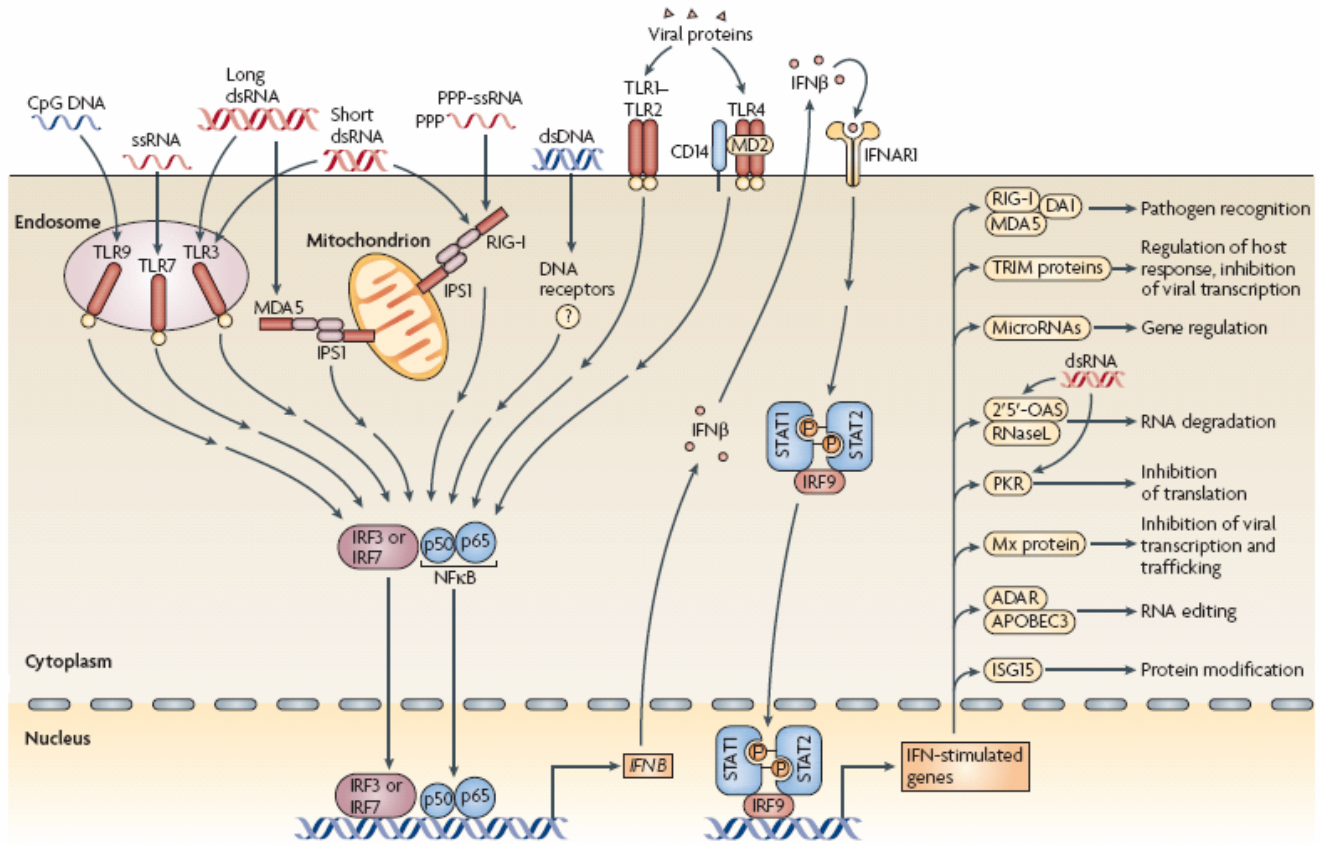
**INTD 5000 EXAM  
MICROBIOLOGY AND IMMUNOLOGY  
DECEMBER 17, 2007**

**PUT YOUR NAME ON ALL PAGES.**

**READ EACH QUESTION CAREFULLY AND FOLLOW THE SPECIFIC INSTRUCTIONS FOR EACH QUESTION.**

**\*WRITE CLEARLY. IF WE CAN'T READ IT, WE WILL NOT GIVE POINTS FOR IT. DO NOT EXCEED THE SPACES GIVEN FOR ANSWERS ON THE FRONT OF THE FOLLOWING PAGES.**

1) Vaccinia virus (a poxvirus) encodes multiple proteins to evade the host innate immune responses. Identify five molecules or pathways that are targeted by vaccinia virus proteins in the following diagram. You may simply draw arrows to indicate the molecules or pathways that are targeted. **(5 points)**



In addition, choose two molecules or pathways and describe how they are blocked by the vaccinia virus proteins. **(2 points)**

- 2) Explain how infection with a particular bacterial strain that carries a superantigen could cause sepsis syndrome. Begin your explanation with the mechanism by which the superantigen interacts with the host, followed by the sequence of steps that lead to pathology. Include cell types involved, surface structures on those cells that are engaged (a drawing would be good here), the cytokines produced, and the pathological effects of those cytokines. Remember that a picture is sometimes worth a thousand words. **(10 points)**
- 3) In a patient identified as carrying a genetic defect that results in the inability to produce  $\beta 2$  microglobulin, an immunodeficient state would be expected. In another patient, mutations in the TAP proteins could also result in an immunodeficiency leaving the patient susceptible to the same kind of infections as the first patient is susceptible. Briefly explain why both patients demonstrate dramatically increased susceptibility to the same class of infections. **(4 points)**

4) Indicate whether the following statements are TRUE (T) or FALSE (F). **(4 points)**

- a) \_\_\_\_\_ The host dectin-1 receptor only recognizes *Candida albicans* filamentous cells.
- b) \_\_\_\_\_ A significant number of AIDS patients have oral candidiasis infections as a result of low CD4<sup>+</sup> T cell counts.
- c) \_\_\_\_\_ The *Candida albicans* Hwp1 protein serves as a mammalian transglutaminase substrate mimic and forms a covalent linkage with host cells.
- d) \_\_\_\_\_ There are no known reservoirs for *Candida albicans* outside of mammalian hosts.

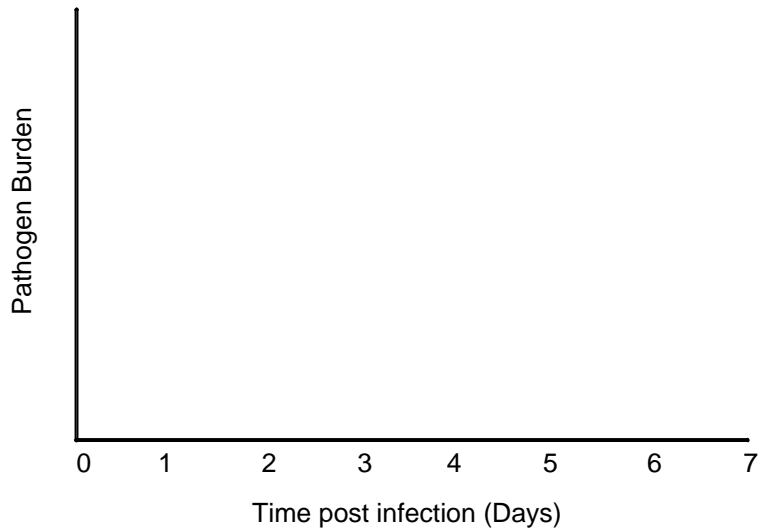
5) Describe three separate *Candida albicans* virulence properties. Briefly explain how each of these properties allows *C. albicans* to evade and/or attack the host immune system. **(3 points)**

a)

b)

c)

- 6) The innate and the adaptive immune system contribute to fighting and controlling infectious disease at different stages of the infection, relationships that can be described graphically. Therefore, graph the pathogen burden for a) a normal individual, b) a person lacking adaptive immunity, and c) a person lacking innate immunity. Clearly label the curves and indicate on the normal person's curve the point at which the adaptive immune response becomes dominant. **(7 points)**



- 7) Robert Koch provided the intellectual frame work to define the causative agents of infectious diseases (Koch's postulates). These postulates remain extremely useful even though today we now know that Koch's postulates have many technical limitations that were not appreciated at the time they were developed. Science has sufficiently advanced to the point that we can now overcome many of these problems. Please outline Koch's postulates and provide 2 examples of technical difficulties that would limit the use of the postulates. Make sure that your examples address limitations in separate postulates. Pick one of the limitations and design an experiment to get around that limitation. Do not propose infecting humans and do not exceed the space on the front of this page! **(7 points)**

- 8) As part of a CDC rapid response team you respond to a disease out-break in which people are getting infected with a unknown bacterial agent. This agent is highly aggressive and has 100% mortality in 3 days. The bacteria can be grown *in vitro*, will infect mice, and is amenable to genetics. As part of the follow up study you notice that infected mice don't produce IL-1, IL-6, and TNF- $\alpha$  all NF- $\kappa$ B responsive cytokines. Further studies indicate that the bacterium injects a cysteine protease into the host cell and this protease cleaves NF- $\kappa$ B inactivating it. A) In one sentence indicate at what stage of immunity this pathogen evades the immune response. B) Design a well controlled experiment to prove that the protease contributes to disease. (Do not exceed the front of this page!) **(7 points)**

- 9) TB is a major human health concern and we know that there are several factors that can significantly increase your odds of getting active disease. Most notably are AIDS, prolonged corticosteroid use, and heavy drug use. A) What is it about these co-morbidities that increases your risk of disease (no more than 1 sentence)? B) In one paragraph describe how TB is controlled in a healthy individual and how reactivation disease develops. (Do not exceed the front of this page) **(7 points)**

10) NS1 protein of influenza A virus is a potent antagonist of innate antiviral response. NS1 prevents production of antiviral factors by degrading cellular mRNAs. Describe the mechanism by which NS1 degrades cellular mRNAs and explain why influenza virus mRNAs are not degraded by NS1? **(4 points)**

And describe at least one mechanism by which NS1 prevents induction of antiviral response by type I interferon? **(3 points)**

11. What is a key advantage that B cells have compared to other professional antigen-presenting cells? Briefly explain. **(3 points)**

12. Using simple drawings, explain the concept of “linked recognition”. **(8 points)**

13. List 3 key features and/or functions of IgM. **(3 points)**

14) To control infection, mammalian hosts have evolved various humoral and cellular immune effector mechanisms that are shared during both innate and adaptive immunity. Name two major cellular effector mechanisms and briefly describe their roles in host defense against infection. **(4 points)**

15) When a bacterium infects the airway, the airway mucosal tissue can instantly launch defense mechanisms against the infection within days. This is because our airway epithelial cells can use receptors called PRR to directly detect the bacterial components defined as PAMP. Define PAMP **(1.5 point)** and PRR **(1.5 point)** and list 4 major PRRs **(0.5 point each)** so far identified.

True/False – worth 2 points each (**14 points total**)

For each of the statements below, note whether it is “true” (T) or “false” (F).

If the statement is “false”, correct it so that it will be “true”.

| Statement   | True or False? |
|---|----------------|
| Regulatory T cells (T <sub>REGS</sub> ) play an important role in peripheral tolerance as they enhance (increase) autoimmune responses to self proteins.  |                |
| Diagnosis of MG (myasthenia gravis) is complex and typically includes all of the following: testing for antibodies to AChR in the serum, testing functions of the peripheral and central nervous systems, and use of an acetylcholinesterase inhibitor.   |                |
| Immune regulation may change as we get older due to age-associated involution of the thymus. Since all B cells develop in the thymus, this would most likely result in <u>antibody</u> -mediated autoimmune disorders due to a loss of central tolerance. |                |
| Immune privilege means that the antigen is sequestered in a site in the body that is usually protected from cells of the immune system. Injury can release these antigens from their privileged site, potentially inducing an autoimmune response.        |                |
| Immune tolerance is defined as a <u>lack</u> of reactivity to “self” proteins. When tolerance is broken, autoimmune disorders may result.   |                |
| Many autoimmune disorders are characterized by genetic susceptibility (increased relative risk) that maps to the MHC (major histocompatibility complex). The linkage to MHC suggests a role for T cells in these disorders.                               |                |
| Although there is no cure for myasthenia gravis (MG), there are many treatments that may provide relief of symptoms. These include: acetylcholinesterase inhibitors, plasmapheresis, and immunosuppressive drugs.   |                |

**HAVE YOU CORRECTED ALL OF THE FALSE STATEMENTS?**