Biology 537, Immunobiology
Spring 2009
Final Take Home Exam

Name _____

If you want FULL CREDIT for each answer make sure that your answers are COMPLETE (☺)

1. Describe the cytokine interactions between $T_{helper}1$ and $T_{helper}2$ cells. Describe what each of these cytokines do and describe how these regulate humoral and cellular responses during antigenic stimulation. Finally describe how class switch is regulated. (10 points)

2. Describe the functions of the three types of interferon (3 points each)- what cells produce these interferons, how is each induced to be formed, and what are the functions of each.

3. Describe the process of complement activation and describe the actions of each component, both the "a" and "b" fragments. (10 points)

4. Describe the complement inhibition assay (5 points)

5. Find and describe **one** immune response to a specific cancer – **Pancreatic cancer**– (you can use the internet or any other source- **cite your sources**- the cancer can be genetic, environmental or due to any cause. Describe what pancreatic cancer is, the theoretical causes and then discuss the prognosis for treatment of the cancer– discuss the current treatment options and then discuss the FUTURE **IMMUNE** potential treatment options.(6 points)

6. Describe how you think that the study of immunology will affect life 20 years from now. Describe **three** advances within immunology that will occur during this time that will benefit health care. (5 points for each advance)

These next two "descriptions" are from excerpts from two of the Journal of Science articles that are on the Web Page. For each of these I would like you to interpret (IN YOUR OWN WORDS) what these excerpts are describing and how they are significant to Immunology today. There are some statements highlighted in "BOLD" and you should discuss the meaning and/or describe these sections in more detail while discussing how they differ from "accepted" text book views. ***(7.5 pts each)***

7. Although DCs can form peptide-MHCII complexes in lysosomes for delivery to the surface upon maturation, this may reflect the particular biology of DCs and not represent a general phenomenon. To solve these issues, we need better and more sensitive imaging and biochemical tools to identify when and where peptide-MHCII complexes form, combined with the use of genetics or conditional switches to disrupt predicted individual steps. Such tools must be applied not only to solve the problem in culture but also to investigate APCs in vivo.
Understanding the order of events remains a problem as well: **Textbooks often imply that internalized antigens are converted by proteolysis to peptides**, which bind at equilibrium to MHCII molecules. Yet, a variety of considerations **suggest that intact antigens can bind to MHCII before degradation**, with peptides being generated after exoproteolysis from both the N- and C-terminal ends [for review, see (11)]. Such a mechanism would be consistent with the observations that protein degradation in lysosomes does not produce even a transient accumulation of peptide intermediates and that professional APCs, such as DCs and B cells, exhibit greatly attenuated levels of lysosomal and endosomal proteases, conditions that would facilitate the sculpting of denatured antigens bound to MHCII. **How peptides are loaded onto MHCII molecules may be the most fundamental issue in the field**, but it still awaits direct proof by kinetic analysis and biochemical reconstitution.

8. The immune system is not an exception to this. **It harbors not only effector lymphocytes capable of attacking invading microbes but also an inhibitory population of T cells, called regulatory T (Treg) cells**. These lymphocytes are specialized in suppressing excessive or misguided immune responses that can be harmful to the host; for example, against normal selfconstituents in autoimmune disease, innocuous environmental substances in allergy, or commensal microbes in certain inflammatory diseases (1, 2). On the other hand, **overzealous Treg responses can impede host protective immunity in infectious disease and cancer**. Recent advances in our understanding of the molecular mechanisms that control Treg cell development have opened new avenues of investigation, but key questions concerning the antigen specificity of Treg cells, their homeostasis, and mechanism of action remain. Here we discuss our current understanding of the biology and function of Treg cells and how they might be **clinically exploited to control physiological and pathological immune responses to self and nonself-antigens**. Naturally occurring CD4+ Treg cells, which constitute approximately 10% of peripheral CD4+ T cells in normal individuals, characteristically express CD25 [the interleukin-2 (IL-2) receptor a chain, which is a component of the high-affinity IL-2 receptor] (1, 2). CD4+CD25+ Treg cells play a nonredundant role in maintaining immunological selftolerance and immune homeostasis. Their importance is made evident by the fact that the depletion of this population from normal rodents produces a variety of autoimmune inflammatory diseases, whereas reconstitution with CD4+ CD25+ T cells can inhibit disease development (1, 2). They are produced by the normal thymus as a functionally distinct and mature population, although there is evidence that T cells with similar immune suppressive activity can be generated from naïve T cells in the periphery. The identification of the transcription factor forkhead box p3 (Foxp3) as being specifically expressed by Treg cells and crucial for their function has provided a molecular framework for dissecting Treg function (3–5) (Fig. 1). **Mutations in the gene encoding Foxp3 in humans and mice result in impaired development and function of CD4+CD25+ natural Treg cells and lead to autoimmune inflammatory pathology.**