Exam KEY

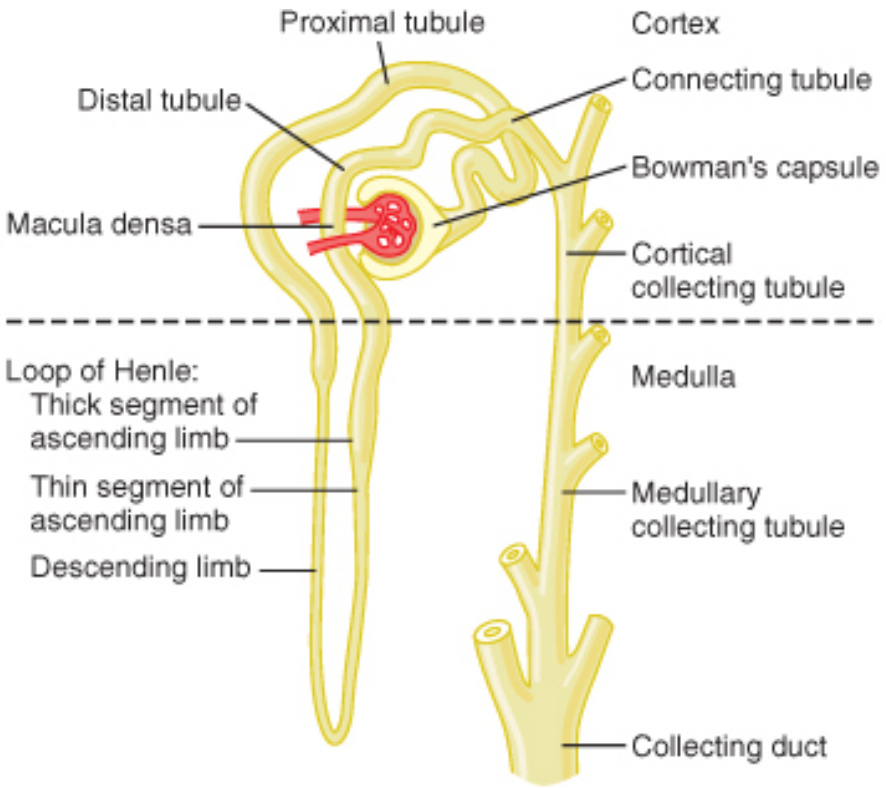
NROSCI/BIOSC 1070 and MSNBIO 2070
Exam # 3
December 2, 2016

Total POINTS: 100 20% of grade in class

1) a) Assuming the typical 'normal' values of plasma glucose of 100 mg/100 ml and a renal transport maximum for glucose of 375 mg/min (along with a normal glomerular flow rate and renal plasma flow rate), draw a schematic of a nephron, labeling the parts for the nephron, and indicate the glucose concentration in each part of the nephron. **(5 pts for the schematic, 5 points for the glucose concentrations).**

Key parts to draw and label: Proximal Tubule (1), Descending Limb (1), Ascending Limb (1), Distal tubule (1), Collecting Duct (1).

Key point for glucose transport: 100% reabsorption in proximal tubule (concentration is 100 mg/100 ml at Bowman's capsule and 0 mg/ml at the end of the proximal tubule).



b) Describe the nature and location of the key transporters involved in the reabsorption of glucose. **(5 points).**

Need to include secondary active transport on apical membrane of the proximal tubule (2 pts), facilitated diffusion of glucose on the basolateral membrane (1.5 pts), and the Na-K-ATPase on the basolateral membrane (1.5 pts).

c) Describe what would happen if plasma glucose levels increased 5-fold (i.e., to 500 mg/100 ml). **(5 points).**

This would exceed the transport maximum for glucose. Normal filtration rate is near 125 ml/min, and this would mean that 125 ml/min * 5 mg/ml or 625 mg/min are being filtered. The essential point is that 375 mg/ml glucose is being absorbed in the proximal tubule, and the rest is excreted in urine.

2) Antagonists of vasopressin V2 receptors and of aldosterone receptors would each produced diuresis.

a) Why would each produce diuresis? **(5 points).**

Antagonists of vasopressin retard the insertion of aquaporin into the collecting duct (2.5 pts)

Aldosterone upregulates the basolateral Na+/K+ pumps (1 pt) and Aldosterone upregulates epithelial sodium channels (ENaCs) in the collecting duct (1.5 pts).

b) What would the major problem be with using either clinically as a diuretic drug? **(5 points).**

Major problem with vasopressin antagonist would be high plasma osmolarity (2.5 pts) and major problem with Aldosterone antagonist would be high plasma K+ (hyperkalemia)(2.5 pts).

3) The arterial pressure perfusing the kidneys and intestine are very similar. However, an ultrafiltrate of plasma is pushed into the lumen of the nephron but not the lumen of the intestine. Why? ***(10 points).***

In both, regulation of Kf is the key (balance of hydrostatic and oncotic pressures inside and outside the capillaries). Glomerular hydrostatic pressure (hydrostatic pressure in the renal capillaries) is much higher than the hydrostatic pressure in the GI capillaries (5 pts). This is regulated by the relative resistances of the afferent and efferent arterioles, with afferent arteriole dilation increasing glomerular hydrostatic pressure and efferent arteriole dilation decreasing glomerular hydrostatic pressure (2.5 pts). Autoregulation plays a much higher role in the kidney than in the GI arterioles, and this autoregulation is dependent on myogenic control and tubuloglomelular feedback (2.5 pts).

4) Consider an elderly female patient weighing approximately 100 lbs who has a creatinine clearance of 200 ml/min and a PAH clearance of 600 ml/min.

a) Describe the most likely renal abnormality in this patient. **(7 points).**

The patient has a high GFR with a normal renal plasma flow. The most likely abnormality causing this is a breakdown of the filtration barriers.

b) What might be measured in the urine to readily confirm your diagnosis **(3 points)**.

Protein would be present in the urine.

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5) Define or describe the terms below in 1-3 sentences. **(3 points each).**

a) Opsonization: Antibodies tagging of antigen for destruction by phagocytic cells.

b) Anergy: State of lymphocyte non-responsiveness to antigen; results from antigen recognition in the absence of co-stimulation.

c) Perforin: One of the main ways in which T cells and NK cells destroy other cells is to transport and secrete these cytolytic proteins. Perforin self assembles to create a channel through the membrane, allowing loss of cytoplasm and allowing other cytolytic proteins to enter the cell and trigger destruction of the target cell.

d) Killer inhibitory receptor: KIRs are expressed by natural killer (NK) cells and regulate the killing function of these cells by interacting with major histocompatibility (MHC) class I molecules.

e) NETosis: A form of neutrophil cell death that involves the release of DNA (chromatin) and granular contents to the extracellular space to form an extracellular trap formation that acts to immobilize microbes and prevent their dispersal in the host. NETs also serve for attachment of bactericidal enzymes including myeloperoxidase and leukocyte proteases.

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6) Indicate the cytokine with the following properties: **(2 points each).**

a) Produced by Th2 cells and Treg; inhibits T cell responses; limits the stimulatory capacity of antigen producing cells; a deficit results in autoimmunity.

IL-10

b) Produced by Th1 cells and CTLs; inhibits Th2 responses; drives CTL and Th1 responses; induces IgG2a synthesis by B cells; a deficit results in infections with intracellular microbes and poor tumor clearance.

Interferon-γ (IFN γ)

7) While innate receptors have limited specificity, adaptive immune cells possess incredible diversity in the number of antigens they can recognize. This diversity results from the generation of adaptive immune cell receptors via somatic gene rearrangement.

a) What two enzymes are instrumental for generating the variable regions of adaptive immune cell receptor found on T cells? **(2 points each; 4 points total).**

Recombination-activating genes (RAG)
Terminal deoxynucleotide transferase (TdT)

b) Explain in two or three sentences what these two enzymes do during the generation of the variable regions of the T cell receptor? **(3 points each; 6 points total).**

RAG proteins recognize and bind to recombination signal sequence (RSS) that flanks antigen receptor gene segments and introduce double strand breaks between the gene segments and the RSSs. The RAG proteins then cooperate with DNA repair factors to rejoin the DNA ends.

Terminal deoxynucleotidyl transferase (TdT) generates more diversity; some gene segments are inverted and gene segment ends typically undergo non-template nucleotide addition by the enzyme.

8) Neutrophils are the first immune cells on the scene after tissue damage. Your friend wants you to invest in their biotech start up that will focus on finding natural supplements that are able to support the development of neutrophil memory responses to antibiotic resistant bacteria. What is wrong with their business model? **(5 points).**

Unlike the adaptive immune system, innate cells do not have memory. The neutrophil response to the bacteria will be of the same speed and magnitude every time, regardless of the supplements your friend tries.

9) The generation of autologous induced pluripotent stem cells from adult cells remains a costly, time consuming and highly variable process. Those currently attempting to implement stem cell correction of nerve, heart, or muscle damage most typically use allogeneic sources for stem cells. Given your understanding of transplant immunology, explain why you would need to provide immunosuppression to a person receiving allogeneic, but not autologous, stem cells injected into their damaged heart after a myocardial infarction. **(5 points).**

You would need to provide immunosuppression to patients receiving allogeneic stem cells because their T cells, and potentially B cells, will recognize non-self HLA (major histocompatibility complex; MHC) expressed on the stem cells. Even if the stem cells are HLA (MHC)-matched with the recipient, their T cells will recognize peptides not encoded in their own cells on self-HLA (minor histocompatibility antigens). Autologous stem cells would express only self HLA (MHC) and all recipient T and B cells recognizing self HLA or self-derived peptides would have already been removed during education in the primary lymphoid organs.

10) There are several factors that can direct isotype switching in B cell. Name or describe two of these factors. **(4 points).**

Any two of the following is acceptable (2 points each):

a. The number of times a B cell has productively encountered its cognate antigen. With repeated exposure the isotype express by that B cell will move from IgD and IgM to other isotypes.
b. The presence of cytokines
c. CD4+ T cell help/co-stimulation

11) Rate from least to worst with regards to impact the listed immune deficiencies on immune responses to viral pathogens. **(4 points).**

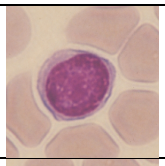
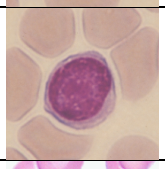
a) Loss of CD3
b) Eosinophil deficiency for major basic protein
c) Loss of CD8
d) Loss of IL-4 receptor on B cells

Least	b) Eosinophil deficiency for major basic protein
	d) Loss of IL-4 receptor on B cells
	c) Loss of CD8
Worst	a) Loss of CD3

Exam KEY

12) You are in charge of characterizing PBMCs using a new flow cytometer that also takes a picture of a representative cell from each identified population. You obtain a grant from the World Health Organization (WHO) to take this new medical equipment in Africa to characterize individuals that are resistant to Schistosomiasis, or "snail fever". Snail fever is a parasitic disease spread by water contamination by people and snails infected with *Schistosoma* worms. The WHO has provided you a standard panels of antibodies that recognize CD markers (CD3, CD4, CD8, CD20, CD56) and IgD. The cytometer and antibodies have arrived safely and you are ready to start characterizing subject blood samples.

Identify the population of immune cells represented in each panel by their CD markers, size, granularity and digital image. **(1 point each; 3 points total).**

Small agranular cells, CD3+, CD4+, CD8-, CD20-, CD56-, IgD- CD4+ T cells or T helper cells	
Small agranular cells, CD3-, CD4-, CD8-, CD20+, CD56-, IgD+ B cells	
Large, very granular cells with CD3-, CD20-, CD56-, CD8-, CD20-, CD56-, IgD- Eosinophils