This exam is closed book, closed notes. There are 4 questions; please write your name on each page.

Good luck!

Grade:

#1 __________/ 25

#2 __________/ 25

#3 __________/ 25

#4 __________/ 25

Final Grade __________/ 100
Problem 1 – The Immune System

a. (6 points) Give three examples of elements of the innate immune response; in one sentence for each, explain why the element indicated is considered innate versus acquired:

<table>
<thead>
<tr>
<th>Element</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>skin</td>
<td>The skin serves as an anatomical barrier impermeable to most infections agents</td>
</tr>
<tr>
<td>enzymes in blood, stomach</td>
<td>Enzymes (and acids) “non-discriminately” kill and digest the particle/organisms</td>
</tr>
<tr>
<td>phagocytes</td>
<td>Same as above, except they engulf/metabolize the foreign objects</td>
</tr>
<tr>
<td>Natural killer cells (ok)</td>
<td>Typically function by destroying compromised host cells</td>
</tr>
</tbody>
</table>

b. (9 points) Briefly describe the steps in the clonal selection theory. They do not need to exactly match those from the lecture, but all of the theory’s important features should be included (hint: step 1 is differentiation of a hematopoietic stem cell into an immature lymphocyte). See Lecture 14, slide 5

i. every lymphocyte has specificity for one ligand (2)
ii. self-recognizing lymphocytes destroyed early in development (2)
iii. those that are activated produce copies of themselves (2)

c. (10 points; 1 point each) Label the components of the acquired immune response in the schematic below:

i. Blue border – the two sub-categories of the acquired immune response
ii. Green border – specific elements (cell types or otherwise) of the acquired immune response; the green lines point to the elements in question.
iii. Label the antigen presenting cell(s) that are shown (write “APC” directly on each)
Problem 2 – Wound Healing

a. The schematic below shows blank boxes representing the four phases of the wound healing response; please fill these in (one is done for you).

- Briefly (no more than 1-2 sentences for each event) describe two major events that occur in each of the phases (in other words, you should list eight events total). There are many choices for each phase; for example, one event in inflammation (please do not list this one!) is diapedesis of neutrophils into the tissue from the bloodstream, which allows them to migrate toward the site of injury.

For the events that occur in each phase above there are many choices, but here are some examples:

- **Coagulation**
  - Circulating platelets adhere to the sub-endothelial connective tissue
  - Additional platelets are recruited to form a platelet plug
  - A mature blood clot is formed via the addition of fibrin, with entrapped erythrocytes

- **Inflammation**
  - Circulating neutrophils and monocytes enter the tissue from the bloodstream via diapedesis
  - Macrophages in the tissue, either already residing there or having differentiated from monocytes, follow chemotactic gradients to the injury/infection site
  - The injury site is characterized by redness, heat, swelling and pain

- **Proliferative phase**
  - Growth factors released from platelets recruit neutrophils, macrophages, fibroblasts, and other cell types.
  - Fibroblasts dominate the wound site in this phase; they produce “low quality” collagen, or scar tissue
• Angiogenesis begins – budding of new blood vessels infiltrate into the scar tissue
• Maturation/remodeling
  • Disorganized collagen is re-organized to bear tension or compression along the appropriate axis for the tissue in question
  • The overall cell number present at the wound site decreases
  • Excess blood vessels that provided nutrients during the healing phases are disintegrated via apoptosis of constituent cells (namely, endothelial cells)
Problem 3 – Characterization of Biomaterial Surfaces

a. The images below are from LBL 5 paper “Different corrosive effects on hydroxyapatite nanocrystals and amine fluoride-based mouthwashes on dental titanium brackets: a comparative in vitro study”. Please indicate what surface testing method produced each image, and briefly describe each technique.

- For each method, your description should include the source of energy and what is detected by the detector.
  - **SEM** – A focused beam of high-energy electrons bombards the surface. Some electrons of the appropriate energy in the sample surface absorb the incident energy are ejected and these secondary electrons are detected and analyzed to provide information about the surface.
  - **AFM** – A cantilever/tip probe mechanically indents the surface. A laser reflects off the cantilever and is detected by the detector; depending on the amount of deflection of the tip upon the surface, the position of the laser on the detector provides information about the surface topography.

b. Of the surface characterization methods we discussed in class, list two that provide chemical composition information (as opposed to topographic information) about a surface.

- X-ray photoelectron spectroscopy (XPS), fourier-transform infrared spectroscopy (FTIR), secondary ion mass spectrometry (SIMS).
- Credit was also given for contact angle analysis, though this test is more limited (it indicates if the surface is hydrophilic or hydrophobic, but does not provide actual composition information).

c. Choose one of the techniques you listed in (b) above and briefly describe how it works.

- Please see the lecture posted online for this information.
Problem 4 – Biocompatibility and clinical testing

a. Provide a definition of biocompatibility (there are many possible correct answers!)
   - Please see the biocompatibility definitions provided in the lecture posted online

b. List (chronologically) and describe (in one or two sentences for each) the methods for testing and evaluating medical device materials.
   - in vitro testing
     - Provides information about cell toxicity and/or blood compatibility, usually done with constituent materials rather than the whole device
   - ex vivo testing
     - Uses viable human or animal tissues incubated outside the body; incubation of devices or constituent materials with these components can give a better view of biocompatibility (this test is not always used)
   - in vivo testing
     - Testing of the medical device or constituent materials (may be either) in small (mouse, rat) or large (sheep, pig) animal models. The main objectives are to test animal tolerance to the implant, implant function, and implant wear/durability (the latter usually assessed after explant following subject euthanasia)
   - Clinical trials
     - Prospective trials of the full device in humans for assessment of long-term biocompatibility and efficacy

c. Describe the rationale for following the chronological sequence of methods you listed in part (a) – why is doing so advantageous from cost/practicality/etc. perspectives?
   - The primary motivations for the following of this order of testing are both practical and moral. Practically, the more basic tests (starting with in vitro) are much less expensive and more rapid than tests involving whole organisms. Thus, these can serve as a proof-of-concept or a “first screen” to assess whether the constituent materials are biocompatible. These basic tests, in addition to animal trials, also minimize the danger to humans that receive the treatment during clinical trials.

d. List and briefly describe (in 1 – 2 sentences) 3 essential features of clinical trials.
   - These are given in the final slides of the Biocompatibility lecture posted online