BNG 331 – Cell-Tissue Material Interactions

An Introduction to and History of Biomaterials

Monday, April 1, 2013
Outline for today

Welcome to Spring 2013!

• Happy opening day!

• A bit about me

• Course and syllabus discussion

• Introduction: history of biomaterials and biocompatibility
A bit about me…

B.S. in Biomedical Engineering, Johns Hopkins University (May 2007)

Ph.D. in Bioengineering, University of Pennsylvania (August 2012)
Thesis: Engineering Hyaluronic Acid Hydrogel Degradation to Control Cellular Interactions and Adult Stem Cell Fate in 3D

Visiting Assistant Professor, Union College Bioengineering (September 2012 – present)

Max the pit-boxer dog (sometimes in my office)
Course overview

• MWF, 10:30am-11:35am, Bailey 100
• My contact information:
  – sudhir.khetan@gmail.com (email), 518-388-6261 (phone), Butterfield 109 (office)
  – Office hours (subject to change!): TW 2:00pm-4:00pm
    • However, if you want to see me other times, just walk by and see if I’m in or shoot me an e-mail to set up an appointment; I reply very promptly.
• www.orzo.union.edu/~khetans
• Let’s go over the syllabus...
An Introduction to Biomaterials

• What is a “biomaterial”?
  – One (of numerous) definitions: a biomaterial is “any material designed to interact in some fashion with a biological system”

• Some historical examples:

  - Canine metal implants 1829
  - Artificial heart 1881
  - Hip prostheses 1956
  - Silicone contact lens 2002
An Introduction to Biomaterials (cont.)

- Even earlier examples:
  - 3000 B.C.: earliest report of a surgical suture (in ancient Egypt)
  - 900 A.D.: estimated year (from carbon dating) of the first dental implant found in Europe, which was found to have properly integrated bone

- However, biomaterials do not have to be “fabricated devices”:

  Explants (e.g., arteries) from human cadavers
  porcine (i.e., from pig) heart valves
  Recombinant Erythropoietin (EPO)
Biological considerations for biomaterial implant success

- To understand the interactions of tissues/cells with implanted biomaterials or other devices, one must understand the wound healing response:

  ![Diagram of wound healing stages](image)

  - **Injury**
  - **Coagulation**
  - **Inflammation**
  - **Repair and Remodeling**

  Think of the successful avoidance/navigation of the process as a “pre-requisite” to the success of a biomaterial implant!

- In this course, we will examine each of these stages in-depth – how each can be disrupted, and the resulting effects on the ability of an implant to perform its intended function.

When did an appreciation for this mechanism first develop?
**Important dates in biomaterials history**

- **1829**: H.S. Levert studies canine responses to implanted metals
  - “*in vivo*” – in the living body of a plant or animal
- **1870**: British surgeon Joseph Lester introduces aseptic surgical techniques
  - “asceptic” – free from contamination by harmful bacteria, viruses or other microorganisms
- **1886**: German doctor H. Hansmann is the first surgeon to use metal plates for internal fixation
- **1931**: Boston surgeon Smith Peterson develops a metal cup for partial hip implants
- **1939 – 1945**: WWII spurs the development of many new materials and orthopaedic surgical techniques
  - Up until ~1950, mostly metals were used because very few plastics existed
- **1947**: first paper on polyethylene as a synthetic implant material
- **1949**: paper published about plastics “sweating out” additives, resulting in a strong (negative) biological reaction
  - Cellophane, Lucite and nylon

Was that last example enough of a “hint” that biological responses to materials should be studied mechanistically? **Unfortunately, not**
Post WWII – chaos reigns in the biomaterials world!

- After WWII, materials that had been rationed were now available and surgeons did not collaborate with scientists or engineers.
- **Surgeon hero** – dentists/doctors would invent “on the fly” when patients’ lives or functionality were at stake.
- Also, minimal government/regulatory activity was ongoing at this time:
  - Prior to 1938, Cosmetics and medical devices were overseen by the Post Office Department and Federal Trade Commission.
  - The FDA took over in 1938.
    - Dealt with increasing medical device “quackery” and the proliferation of medical technologies after WWII – case study: the Thalidomide tragedy (2:50)
    - Congress worked at passing a comparative device law in 1962 – the Kefauver-Harris Drug Amendments.
      - Almost 20 years of unmonitored work!
~1950 – present: a Biomaterials Revolution

• At the time of the 1962 Drug Amendments and Consumer Bill of Rights passages, the biomaterials of today did not exist; no companies were making them, nor was there a formal regulatory approval process
  – What is now the FDA medical device group

• The “quantum leap” in recent decades, enabled by increasingly better laboratory technologies (e.g., fluorescence microscopy), is the understanding of biocompatibility on a cellular and molecular level
  – Definitions vary, but biocompatibility can be described as the capacity of a material or device to not induce toxic or injurious effects on biological systems (i.e., to subvert the wound healing response mentioned earlier)
  – Before 1950, this lack of understanding translated to a very low implant success rate due to rejection by the immune system
Major focus areas for this course:

- Proteins
- Protein-surface interactions
- Coagulation
- Inflammation and infection
- The immune system
A look forward to recent technologies

- Biomaterials research in the *modern* era is marked by a high degree of **interdisciplinarity**:
  - Materials science
  - Chemistry and chemical engineering
  - Biology and bioengineering
  - Physics and biophysics
  - Biomechanics and mechanical engin.
  - Nanotechnology

- Example 1 – vascular stents
  - Boston Scientific’s “Epic” vascular stent system
    - Granted marketing approval by FDA in 2012
    - Made from nitinol (nickel titanium alloy)
  - [http://www.youtube.com/watch?v=llGxRd4yLE8](http://www.youtube.com/watch?v=llGxRd4yLE8)

How about a not-yet FDA approved, even newer example?
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- Example 2 – gold nanoshells
  - Gold nanoshells for “photothermal” anti-tumor applications
    - Have shown promise in in vitro studies
  
  [http://www.youtube.com/watch?v=VSObY7dlSaY](http://www.youtube.com/watch?v=VSObY7dlSaY)

These two examples are given to illustrate how far we have come!
However, not all new biomaterials technologies are highly invasive!!!
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- **Example 2 – AssureFit®**
  - Developed by Clemson undergrads in 2012
Please e-mail me your LBL groups (groups of 4) by Friday!!!