Standards in Scientific Communities II; Cell Viability

Module 3, Lecture 4

20.109 Spring 2011
Lecture 3 review

- What can you learn from a confidence interval? A t-test?

- What are three general engineering principles that might help make biology more “engineerable”?

Topics for Lecture 4

• Standards in tissue engineering
  – introduction
  – writing exercise
  – discussion

• Cell viability
  – your data
  – relation to diffusion
How valued are TE standards?

- 2007 strategic plan for TE clinical success by 2021
  - 24 int’l leaders in TE listed high-priority areas
  - 1/3 named standards
- Analysis
  - concept dominance
  - progress so far
  - standards 7th of 14


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<tr>
<th>Concept Dominance</th>
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<td>Angiogenic control</td>
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<td>Stem cell science</td>
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<td>Immunologic understanding and control</td>
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*7 (tie). Standardized models.*

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<td>Expectation management/communication</td>
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<td>Pharmacoeconomic-commercial pathway</td>
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<td>Multilevel funding</td>
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- 2007 US govt. strategic plan
  - standards listed as part of “implementation strategy”
How useful are TE standards?

• See 2005 editorial by A. Russell
  – proposes need for standards
  – in data collection and sharing
• Choose and respond to a student excerpt (~10’)
• Pros/cons/etc… ?

Can we standardize this TE construct?
Module progress: week 2

- **Day 3: viability/cytotoxicity testing**
- Groups generally found
  - mostly live
  - mostly round
  - not much clustering
- How can we improve the assay?
- What conditions killed cells?
- Other interesting findings?
- How do we explain the results?

Image from W/F Orange
Factors affecting cell viability

• Cell-related
  – density
  – interactions

• Cytokine-related
  – proliferative
  – apoptotic

• Materials-related
  – bulk permeability
  – macro-porosity
  – toxicity
Diffusion in 3D constructs

- Nutrients, $O_2$
- Affected by:
  - construct size $R$
  - cell density $\rho$
  - diffusivity $D$
  - conc. in medium $[O_2]_{\text{bulk}}$
- Concentration profile:
  - can be solved (DE)
  - $[O_2]$ $\downarrow$ toward center
  - steepness $= f(D, \rho, ...)$
Significance of diffusion in TE

- Characteristic limit $\sim 100 \, \mu m$
- Diffusion and viability profiles correlated
- How can we make thick tissues?
  - *in vitro*: dynamic/perfusion culture
  - *in vivo*: promote rapid angiogenesis
Modeling cell viability in TE constructs

- Porous PLGA scaffolds
- Seeded cells as in (A) or (B)
- Observed after 10 days
- Model includes
  - Diffusion
  - $\text{O}_2$ use
  - Cell growth
- Model assumes
  - $[\text{O}_2]_{\text{bulk}}$ is constant
  - Quasi-steady state

Dunn et al. results for cell viability

• A more uniform than B
• Cell growth matches O₂ tension
• Claim of predictive capability
Lecture 4: conclusions

- Strategies besides standardization may take precedence in some BE fields.

- Cell viability in TE constructs is affected by cell, material, and soluble factors.

- Modeling can elucidate nutrient diffusion and cell viability profiles.

Next time: transcript and protein assays, imaging.