Standards in Scientific Communities II
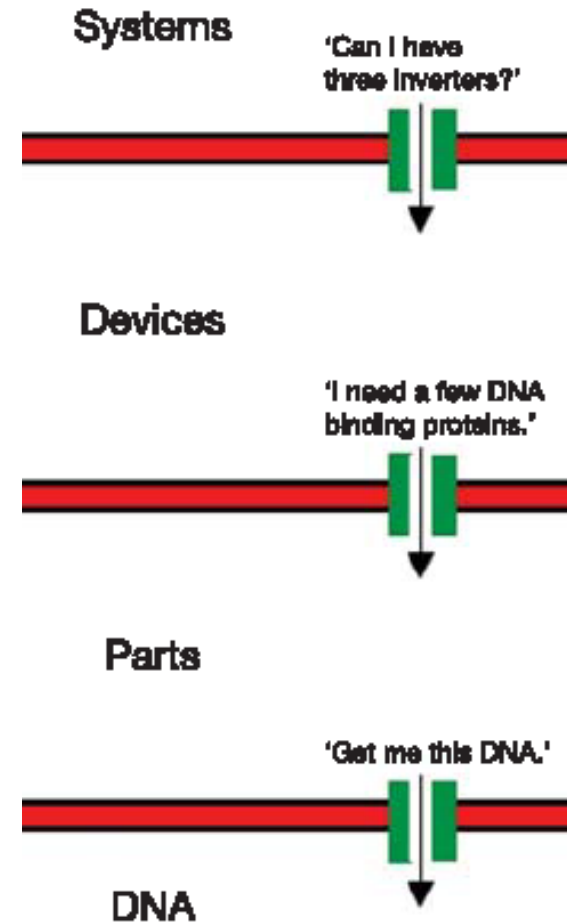
Module 3, Lecture 4

20.109 Spring 2013

Topics for Lecture 4

- Module 3 so far
- Standards in tissue engineering(+)
  - review and introduction
  - writing exercise
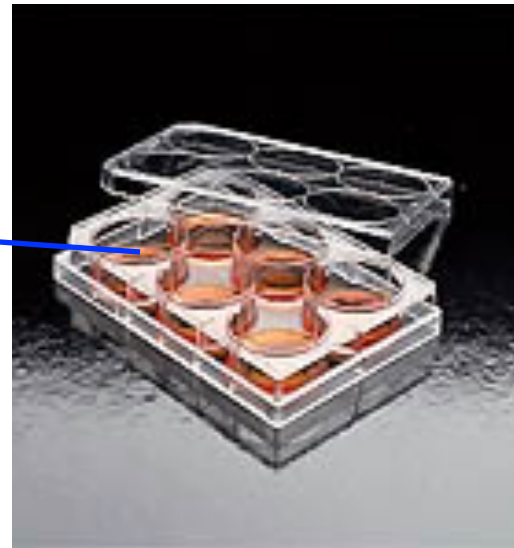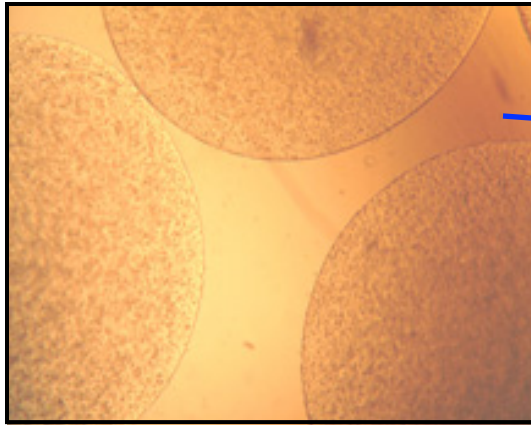 - discussion
  - modern context

Lecture 3 review

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

- And way back: What can you learn from a confidence interval? A t-test?

From D. Endy, *Nature* **438**:449

Module progress: week 1

- Day 1: culture design
  - What did/will you test?

- Day 2: culture initiation
  - Cells receiving fresh media every day
  - Half volume exchange due to soft beads

Module progress: week 2

- Day 3: viability/cytotoxicity testing
- Groups generally found
  - mostly live…
  - … but less than at 7d (S12-)
  - mostly round
  - not much clustering
- What conditions killed cells?
- Other interesting findings?
- How to explain the results?
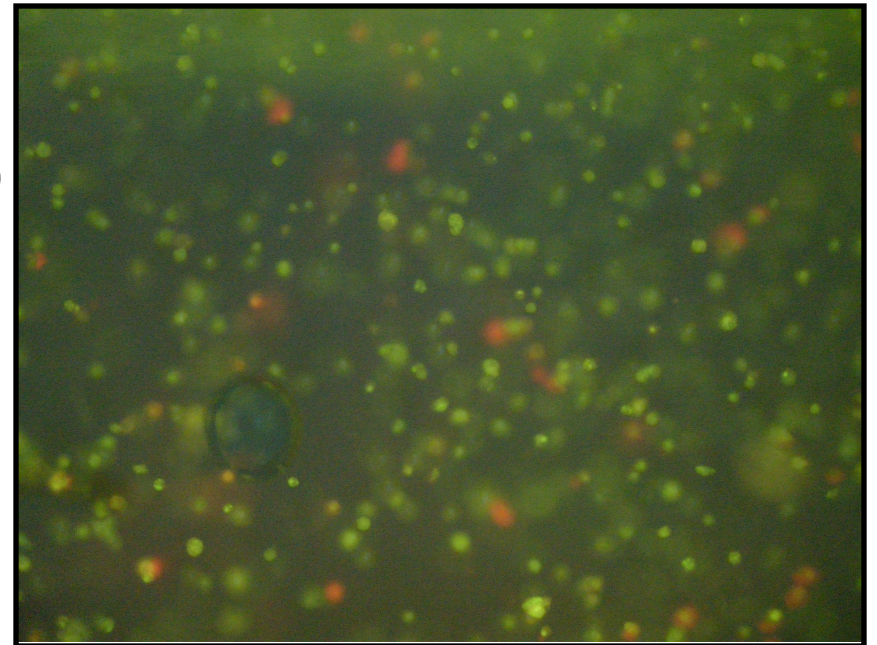- How to improve the assay?

Image from T/R Platinum

Assignment for report or addendum

- With your own data *or* a complete dataset to be announced and posted very soon…
- Get live cell count and/or live cell percent values for both culture conditions
- Calculate 95% CI for both means
- Plot means on bar graph with CI error bars
- Apply t-test to the means
  - For multiple comparisons, ANOVA is better
  - Comparing many means requires correction
  - Remember, $p = 0.05$ means 1 in 20 false positives!

Data standards: what and why?

- Brooksbank & Quackenbush, *OMICS*, **10**:94 (2006)

- High-throughput methods are data-rich

- Standards for **collection** and/or **sharing**

- Reasons
  - shared language (human and computer)
  - compare experiments across labs
  - avoid reinventing the wheel (save t, $)
  - integration of information across levels

- Examples
  - MIAME for microarrays
  - Gene Ontology (protein functions)

- Who drives standards?
  - scientists, funding agencies, journals, industry

www.geneontology.org

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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

  P.C. Johnson et al., *Tissue Eng* **13:**2827 (2007)

TABLE 6. NORMALIZED CONCEPT DOMINANCE
(I.E., TAKING PRESENT PROGRESS INTO CONSIDERATION)

|	O/P
Angiogenic control	3.3
Stem cell science	3.2
4. Cell sourcing/characterization.	
Clinical understanding/interaction	2.2
Immunologic understanding and control	2.0
Manufacturing/scale-up	1.1
Regulatory transparency	1.1
7 (tie). Standardized models.	
Multidisciplinary understanding/cooperation	0.8
Expectation management/communication	0.4
Pharmacoeconomic/commercial pathway	0.3
Multilevel funding	0.0
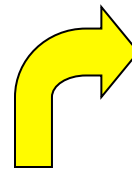
- 2007 US govt. strategic plan
  - standards listed as part of "implementation strategy"

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… ?
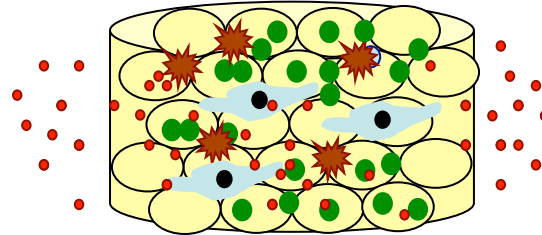
Can we standardize this TE construct?

Beyond TE standards: targeted support and improving communication

- P.C. Johnson et al., *Tissue Eng A* **17:**1+2 (2011)
- Survey of all interested parties in a TE society, from academia to early and established companies
- What are greatest hurdles to TE commercialization?

Academics

Obtaining sufficient
funds for research
Orienting research
to market needs

Startup companies

Obtaining adequate
operating capital
Recruiting experienced
management
Working with technology
transfer offices

Development-stage companies

Generating sufficient revenue
while staying financed
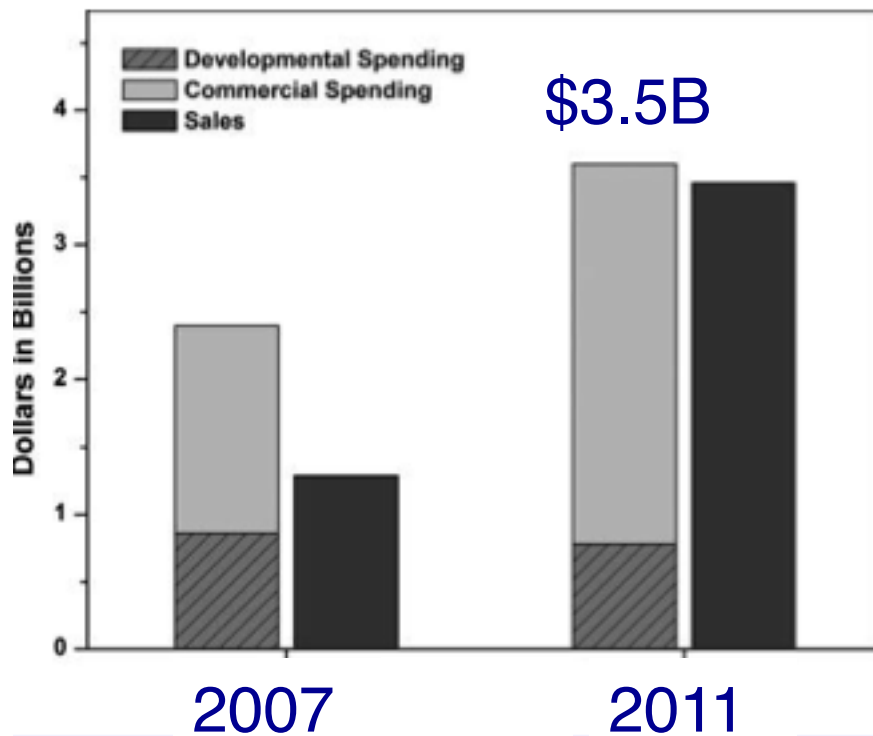Maintaining focus on
the evolving market

Established companies

Managing growth

Growing the intellectual
property base
Working with the FDA

Building a TE industry

Sales approaching spending*

$3.5B

2007   2011

* stem cell banking included

Bone/cartilage leads sales

| Commercial products (# of companies)	2011 Sales (in millions)
Orthopedic (19)	$1713
Wound healing (15)	$738
Multiple (16)	$554
Stem cell banking (18)	$312
Other (5)	$144
Total:	$3461

2-fold increase in jobs since 2007

Predict **5-10 years** for stem cell and cell/biomaterial combination products to really enter market

A. Jaklenec et al., *Tissue Eng B* **18:**3 (2012)

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Challenges in orthopedics and beyond

- C. H. Evans, *Tissue Eng B* **17:**6 (2011)
- Only three orthopedic products with clinical trials!
- Huge publication:product ratio
- Translational research doesn't advance careers (incentives)
- Perfect as the enemy of the good

At what point is it best to stop tweaking and move forward to the next phase of development?

InFUSE™ Bone Graft component

LT-CAGE™ Lumbar Tapered Fusion Device component
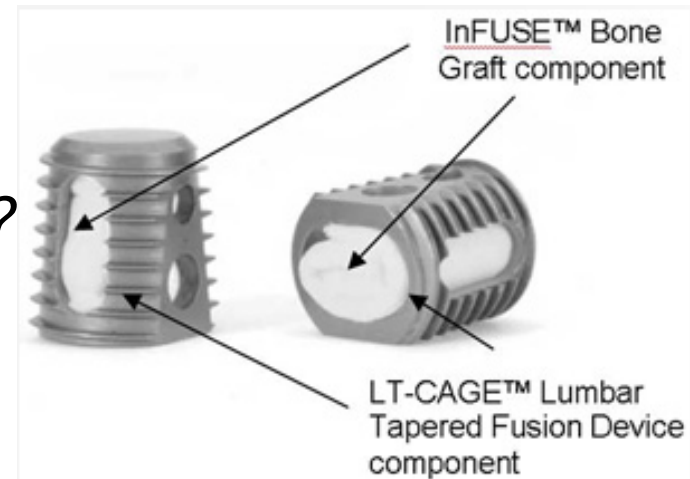
Lecture 4: conclusions

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

- TE has few products to market, but continues to grow. Challenges remain.

- Your thoughts here!

Medtronic Inc said it agreed to pay $85 million to settle a shareholder lawsuit accusing it of making misleading statements concerning Infuse, a genetically engineered bone graft used in spinal surgery.

(Reuters)

Next time: transcript and protein assays, imaging.