Standards in Scientific Communities

Module 3, Lecture 3

20.109 Spring 2008

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Topics for Lecture 3

- Review of Module 3 so far
- Neal Lerner on Module 3 essay
- Standards in scientific communities
  - general engineering principles
  - standards in synthetic biology
  - standards in data sharing
  - standards in tissue engineering

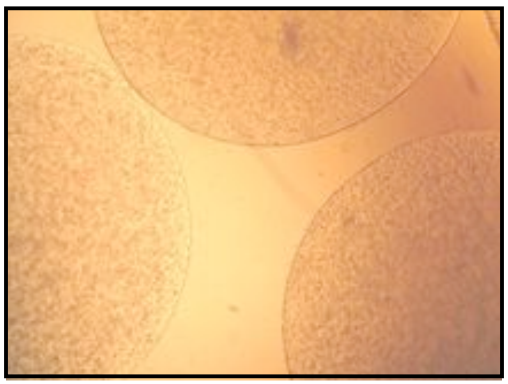
Module 2, Part 2 assessment

- Right idea overall! Average was ~B+
- Some confusion and *incompleteness*
  - example: lack of comparing -IPTG to +IPTG samples, or expected vs. observed MW on PAGE
- Interpret each piece of data thoroughly
- Make connections between different pieces of data - is it consistent?
  - simple example: cell growth (OD values) vs. purified protein recovered
- Optional HW: summary of revisions
  - bonus ~5 pts. to homework grade
  - due by Module 3, Day 7

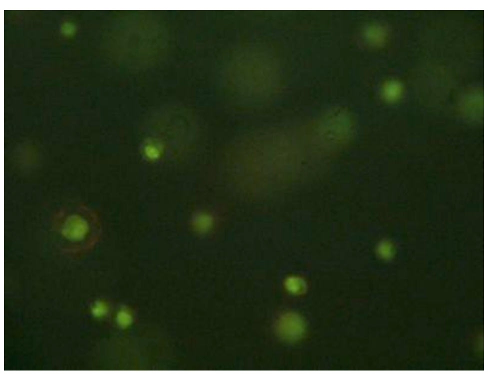
Module overview: lab

Day 1: design

Day 2: seed cultures



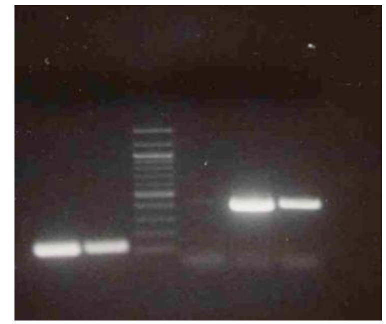
Day 3: viability assay



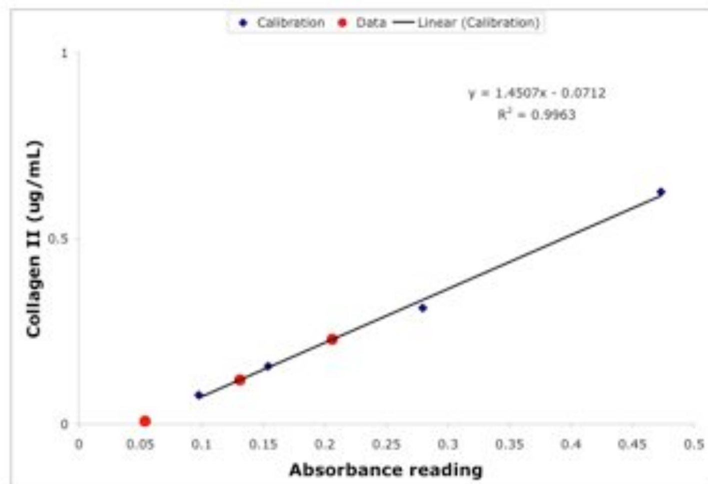
Day 4: prep RNA+cDNA

Day 5: transcript assay

Day 6: protein assay

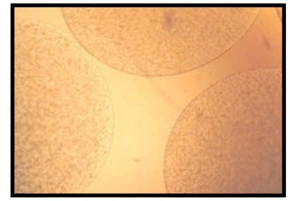


Day 7: remaining analysis



Day 8: your research ideas!

Module progress: week 1

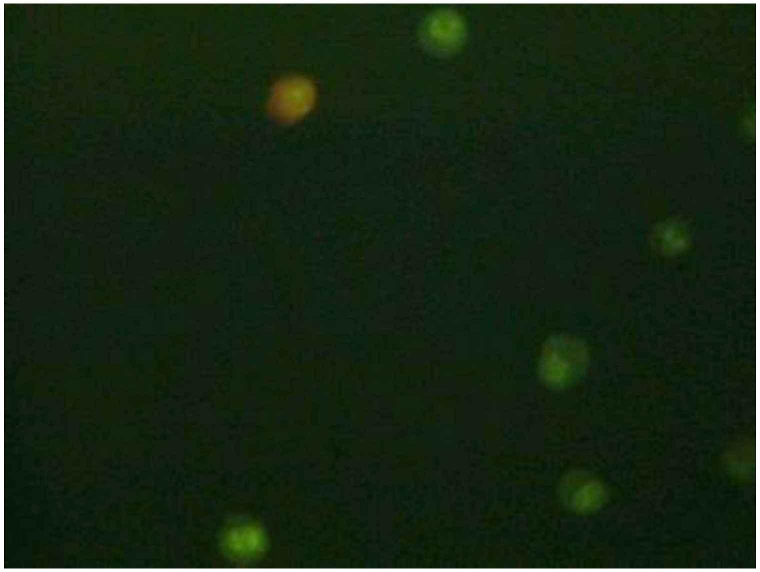


- Day 1: culture design
- Parameters being varied:
  - brand of alginate, weight percent alginate
  - cell density
  - concentration of calcium cross-linker
  - application of compressive stress
  - additives: collagen II, inhibitor of actin
- Day 2: culture initiation
  - low cell recovery on W/F (10-15M) vs. T/R (60-70M)
  - cells receiving fresh media every 2-3 days

- Recall purpose of the experiment:
  - affecting chondrocyte de-differentation to fibroblasts
  - why is this useful information for tissue engineering?

Module overview: week 2

Day 3: test cell viability/cytotoxicity in three culture conditions



Green stain: SYTO10 = viability
Red stain: ethidium = cytotoxicity

Assay readout: fluorescence

Working principle? **Relative cell-permeability**

Preparation for Day 3 viability assay

- 2D culture preparation
  - enzymatic removal of cells: trypsin/EDTA
  - treat cell suspension with fluorescent dyes
- 3D culture preparation, option 1:
  - create single-cell suspension, as for 2D
  - how? depolymerize alginate with calcium chelator, namely EDTA in a citrate buffer
- 3D culture preparation, option 2:
  - cut bead in half with spatula
  - treat whole construct with fluorescent dyes
  - what extra information does this option provide?

Module 3 essay

- Essay on standards in TE
  - draft due D4, final due D6
  - learning goals: engage in a modern discussion on a meta-scientific issue

- Presentation by N. Lerner

Data Set: Annual Deaths in the United States from Substance Abuse, 1988

Tobacco	346,000
Alcohol	125,000
Alcohol & Drugs	4,000
Heroin/Morphine	4,000
Cocaine	2,000
Marijuana	75

Task: Draw three conclusions from these data.

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N. Lerner

N. Lerner

Essential Moves for the Tissue Engineering Essay

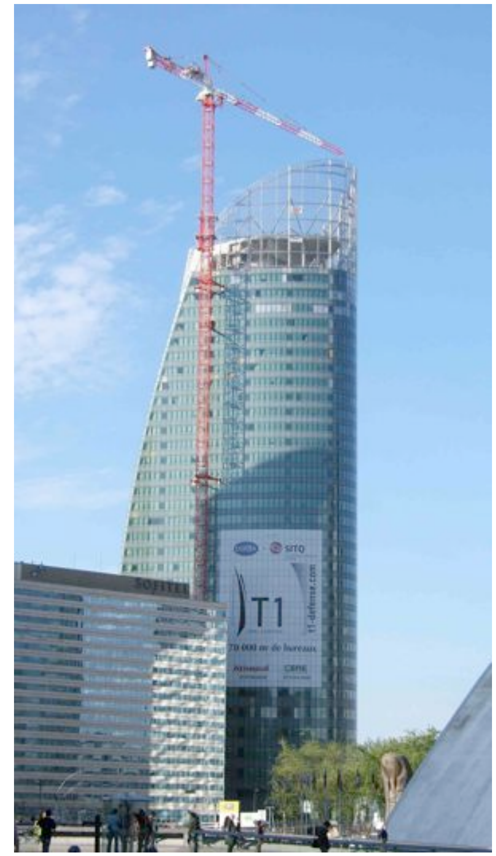
1. Establish the importance of the field--what is the potential for tissue engineering?
2. Establish the barriers to realizing that potential (i.e., the “problem”):
   - Lack of standardization
   - Other barriers?
3. Offer a method or approach to overcome those barriers/that problem.

Essential Moves for the Tissue Engineering Essay (cont.)

4. Support your approach with evidence:
   - Analogy to other fields who have overcome similar barriers
   - Specific examples of your proposed approach in action
5. Reiterate the importance of solving the “problem” you have described. What are the potential benefits of doing it and the negative consequences of not doing it?

Engineering principles, after D. Endy

- D. Endy, *Nature* **438**:449 (2005)
- Is biology too complex to engineer, or does it simply require key “foundational technologies”?
- Standardization
  - analogy: screw threads, train tracks
  - standardize: “biological functions, experimental measurements, and system operation”
- Decoupling
  - analogy: architecture vs. construction
  - general statement: design vs. fabrication
- Abstraction
  - analogy: writing
  - can work at level of improving word choice, sentence construction, paragraphs, or flow/coherence of entire piece
  - copy-editor vs. editor



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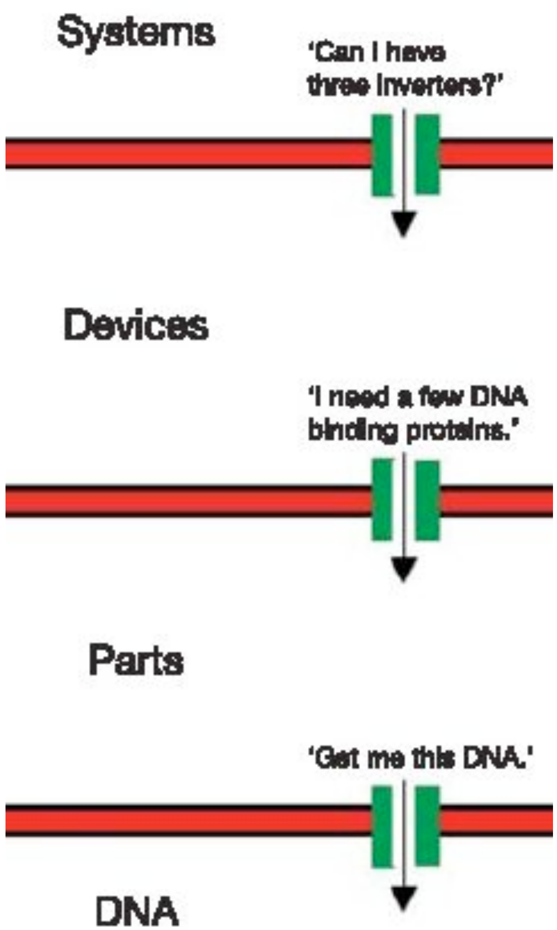
Application to synthetic biology

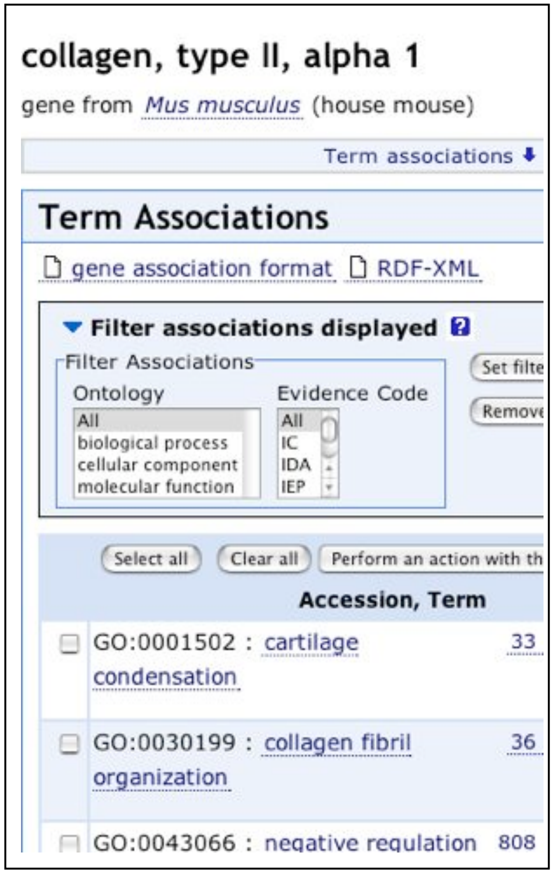
- D. Endy, *Nature* **438**:449 (2005)
- Synthetic biology, in brief: programming DNA to perform a desired task
  - e.g., chemical synthesis by bacteria
  - e.g., genetic circuits (signal transduction)
- Standardization (analogy: screw threads)
  - Registry of Standard Biological Parts
  - standard junctions, off-the-shelf RBS, etc.
- Decoupling (analogy: buildings)
  - DNA design vs. fabrication: requires rapid, large-scale synthesis of DNA
- Abstraction (analogy: writing)
  - DNA vs. parts vs. devices vs. systems
  - common manipulations that avoid secondary structure formation (analogy: processing)
- Rewards *and* risks to consider



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

Data standards: what and why?

- C. Brooksbank & J. Quackenbush, *OMICS*, **10**:94 (2006)
- High throughput methods yield much data
  - e.g. from Module 2 orals: structural genomics
- Standards for both **collection** and **sharing** may be desired
  - Ability to compare experiments across labs
  - A shared language (human and computer)
  - Avoid reinventing the wheel
  - Integration of information across levels
- Examples:
  - MIAME for microarrays
  - Gene Ontology (protein functions)
- Who drives standards: community of scientists, funding agencies, journals, companies (e.g., microarray manufacturers).



www.geneontology.org

How valued are TE standards?

- 2007 strategic plan for TE clinical success by 2021
- Use of Hoshin process for prioritizing strategies
- Standards suggested by 8 of 24 leaders in TE
- Taking into account both need and progress so far, standards 7th of 14 areas

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

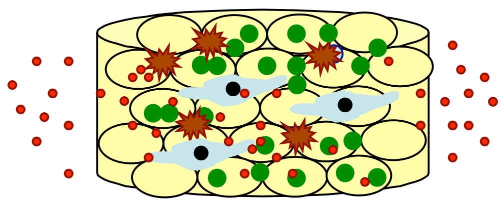
	O/P
Angiogenic control	3.3
Stem cell science	3.2
Molecular biology/systems biology	2.8
Cell sourcing and cell/tissue characterization	2.7
Clinical understanding/interaction	2.2
Immunologic understanding and control	2.0
Manufacturing/scale-up	1.1
Regulatory transparency	1.1
Standardized models	1.1
Enhanced biomaterial functionality	0.8
Multidisciplinary understanding/cooperation	0.8
Expectation management/communication	0.4
Pharmacoeconomic/commercial pathway	0.3
Multilevel funding	0.0

- 2007 strategic plan by MATES IWG agency
  - standards listed as part of “implementation strategy,” though not as one of eight “strategic priorities”

See *References* section in essay assignment, Johnson et al.

How useful are TE standards?

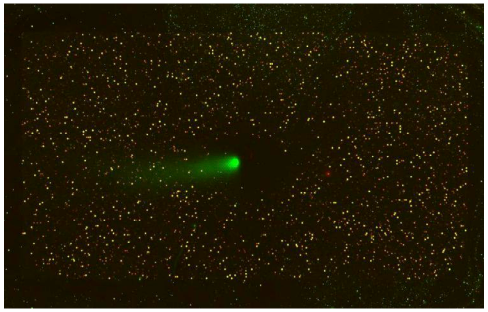
- See *References* section in essay assignment, A. Russell
- 2005 editorial proposes need for standards in data collection and sharing for TE experiments
- Pros
  - compare data across labs
  - discuss:
  - protocol optimization
  - improve publication rates and/or quality
  - market entry could be easier
  - help or hurt strategic prioritization
- Cons
  - stifle innovation
  - discuss:
  - reduces competition
  - loss of information
  - new great models brushed aside
  - company monopolies



Is this TE construct standardizable?

Lecture 3: conclusions

- Standardization of data collection and data sharing is of interest in several BE disciplines.
- Other general engineering principles or specific strategies may take precedence over standardization in a particular field.



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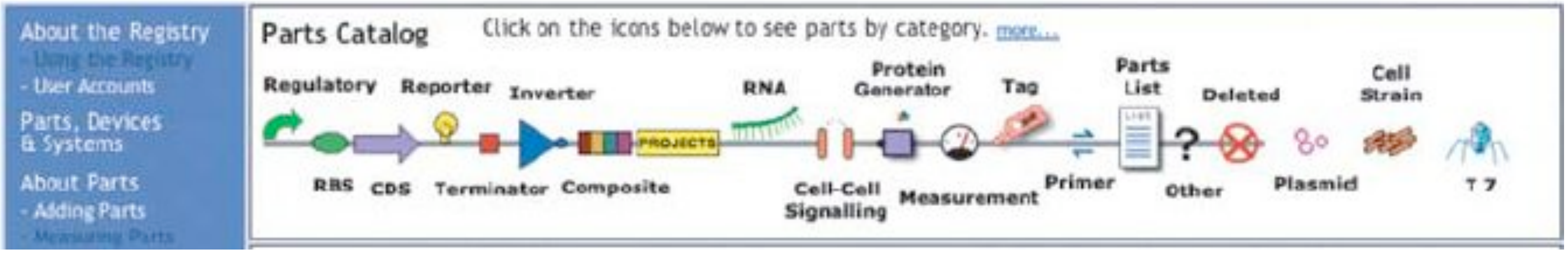
Microarray data
(standard analyses)



From D. Endy, *Nature* **438**:449 (standardization of biological "parts")

Next time: factors affecting cell viability (and your data!), a closer look at cartilage.