Standards in Scientific Communities II

Module 3, Lecture 4

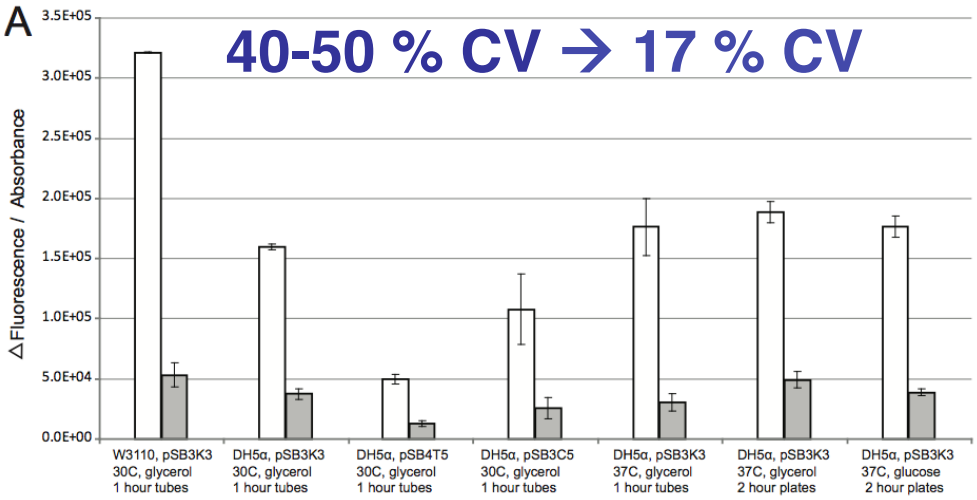
20.109 Spring 2014

Topics for Lecture 4

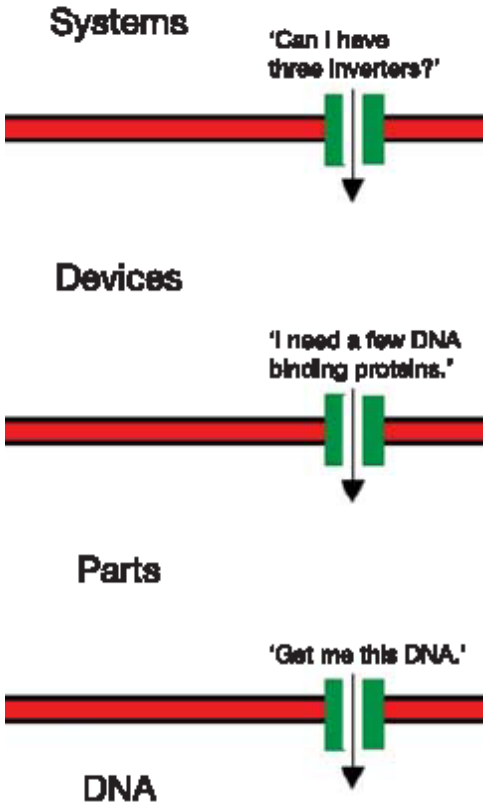
- Module 3 so far
- Standards in tissue engineering(+)
  - review and introduction
  - writing exercise
  - discussion
  - modern context

Lecture 3 review

- How does the M3D3 viability assay work?
- What are three general engineering principles that might help make biology more “engineerable”?



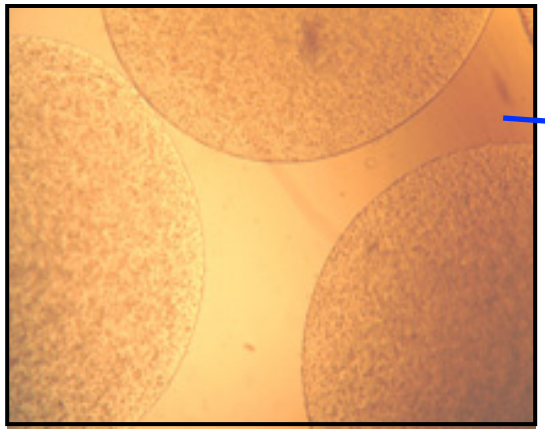
J.R Kelly et al., *J Biol Eng* **3**:4 (2009)



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

Module progress: week 1

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



- Day 2: culture initiation
  - Cells receiving fresh media every day
  - Half of volume exchanged, half kept

Module progress: week 2

- Day 3: viability/cytotoxicity testing
- Groups generally found
  - many live cells
  - MSCs fared more poorly(?)
  - mostly round
  - not much clustering
  - some beads fell apart
- What conditions killed cells?
- Other interesting findings?
- How could we improve the assay?

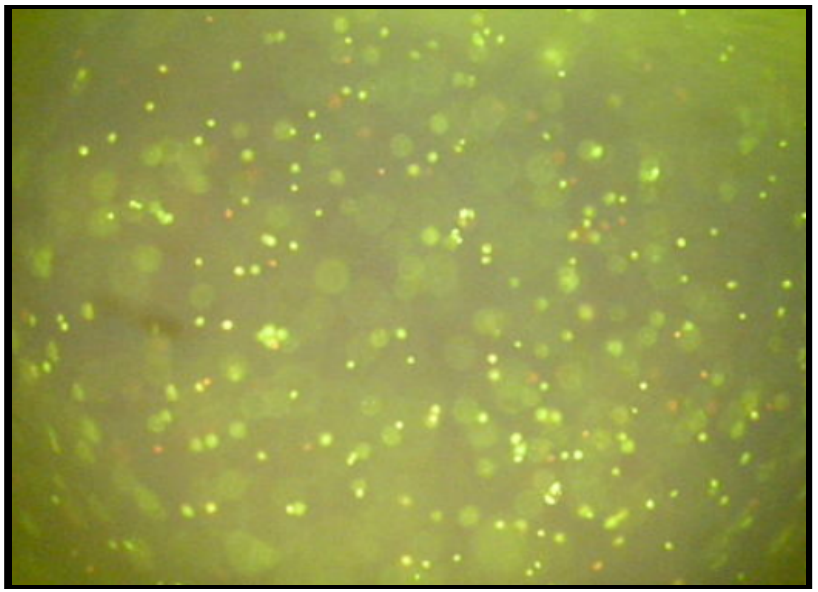
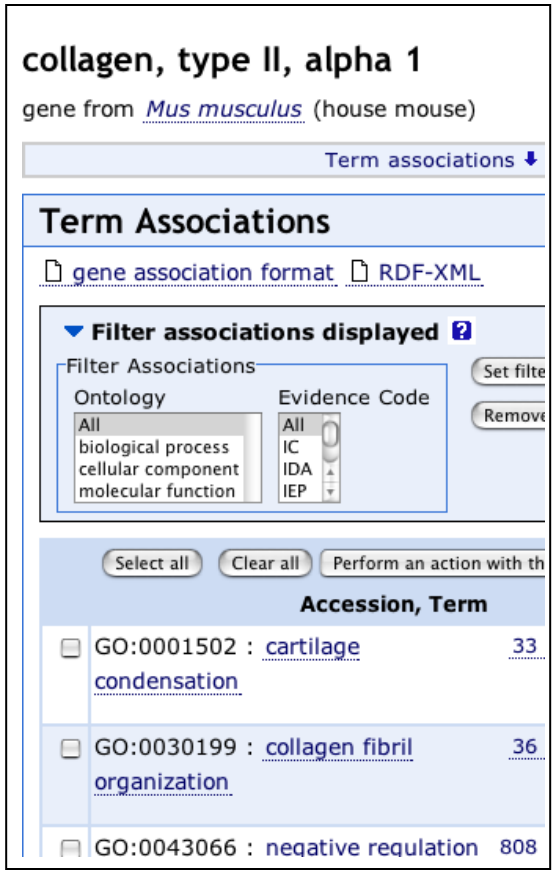


Image from T/R Org/Red

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
  - ask questions about others' data
  - avoid reinventing the wheel (save t, $)
  - integrate information across levels
- Examples
  - MIAME for microarrays
  - Gene Ontology (protein functions)
- Who drives standards?
  - scientists, funding agencies, journals, industry



www.geneontology.org

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
  - progress so far
  - concept dominance
  - 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
[illegible]	[illegible]
Immunologic understanding and control	2.0
Manufacturing/scale-up	1.1
[illegible]	[illegible]
Multidisciplinary understanding/cooperation	0.8
Expectation management/communication	0.4
Pharmacoeconomic/commercial pathway	0.3
Multilevel funding	0.0

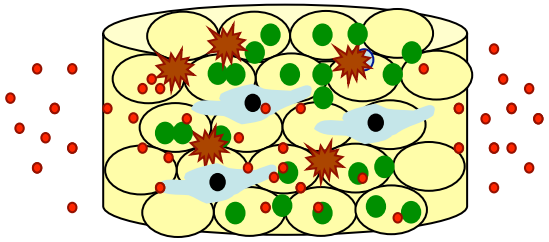
4. Cell sourcing/characterization.

7 (tie). Standardized models.

- 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

Development-stage companies

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

Startup companies

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

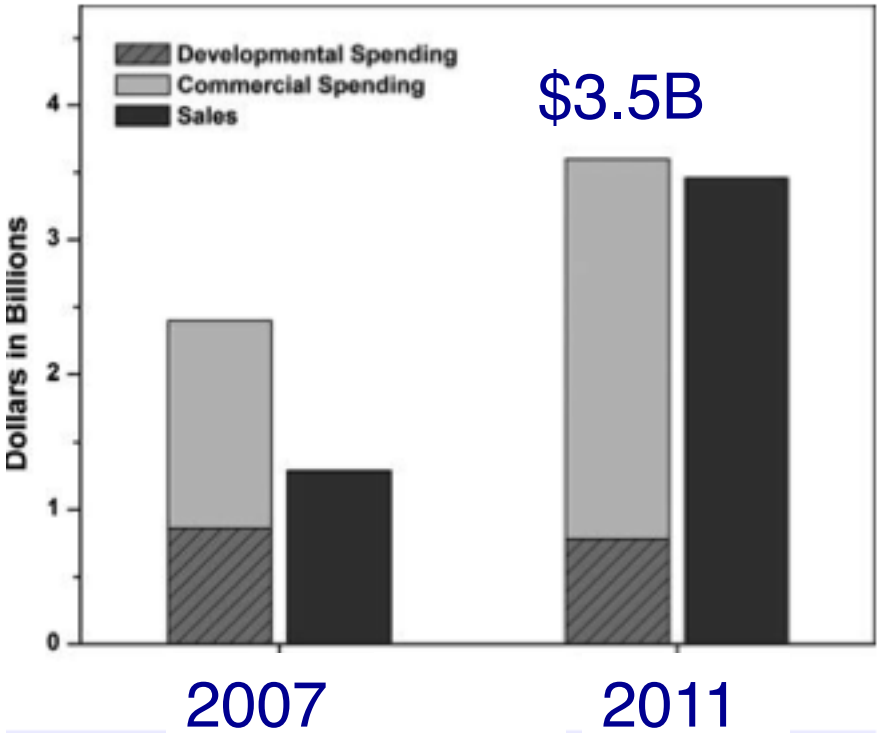
Established companies

Managing growth
Growing the intellectual property base
Working with the FDA

Broadest view/ awareness

Building a TE industry

Sales approaching spending*



* 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)

Existing TE products (mostly US+EU)

Table 1 TE products currently available on the medical market

Intended use	Product name (Company)	Cell type used	Scaffold/material used
Skin	Dermagraft® (Shire regenerative medicine, st Helier, Jersey)	Allogenic fibroblasts	Bioabsorbable polyglactin mesh
	Apligraf (Organogenesis Inc., Canton, MA, USA)	Allogenic fibroblasts and keratinocytes	Type I bovine collagen matrix
	MySkin (Altrika Ltd, Sheffield, UK)	Autologous keratinocytes	Silicone coated with a chemically controlled plasma polymer film
	OrCell (Forticell Bioscience, Englewood Cliffs, NJ, USA)	Allogenic fibroblasts and layer of keratinocytes	Type I bovine collagen sponge
	PolyActive (HC Implants BV, leiden, Netherlands)	Autologous cultured fibroblasts and keratinocytes	A compound of polyethyleneoxide terephthalate and polybutylene terephthalate
Cartilage	Hyalograft 3D (Fidia Farmaceutici s.p.a.)	Autologous chondrocytes	Hyaluronic acid
	Bioseed-C (BioTissue Technologies, GmbH, Freiburg, Germany)	Autologous chondrocytes	A polyglycolic/polylactic acid and polydioxane based material
	CaReS® (Arthro-Kinetics, Germany)	Autologous chondrocytes	Rat collagen type I
	J-tec, Japan Tissue Engineering Co	Autologous chondrocytes	Atelocollagen gel
	Novocart Inject Novocart 3D (Melsungen, Germany)	Autologous chondrocytes	Polymerizable hydrogel Collagen type I
Bone	FormaGraft (NuVasive, San Diego, CA, USA)	Autologous bone marrow aspirate[a]	Hydroxyapatite, beta-tricalcium phosphate and bovine collagen granules
	Healos® (DePuy Synthes, Warsaw, IN, USA)	Autologous bone marrow aspirate	Type I bovine collagen fibers coated with hydroxyapatite
	Vitoss® Foam (Orthovita/Stryker, Malvern, PA, USA)	Autologous bone marrow aspirate[a]	B-TCP, Collagen, bioactive glass
	Grafton (Biohorizons, Birmingham, AL, USA	Autologous bone marrow aspirate[a]	DBM
	CopiOs (Zimmer, Warsaw, IN, USA)	Autologous bone marrow aspirate	Autologous bone marrow aspirate

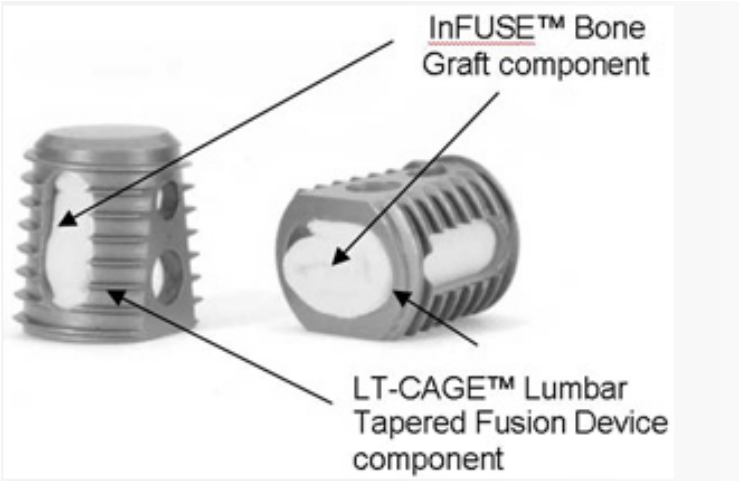
Most scaffolds *not* (yet?) synthetic

M. Lewandowska-Szumiel & I. Kalaszczynska, *J Mater Sci: Mater Med* **24**(2013)

Challenges in orthopedics and beyond

- C. H. Evans, *Tissue Eng B* **17:**6 (2011)
- Only three orthopedic technologies 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?"



OTOH: Medtronic Inc said it agreed to pay **$85 million** to settle… [accused] of making misleading statements concerning Infuse (Reuters)

Lecture 4: The state of TE*

- 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!

(* not our last word on this topic)

Home > Products > NOVOCART® Inject

What is NOVOCART® Inject?

Note: Being sold but also still in trials.

Next time: transcript + protein assays, imaging.