Harnessing Nano for Drug Delivery

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3/17/15
What is Drug Delivery?
What is Drug Delivery?
Why is drug delivery useful?

Patient friendly
- Easy to use
- Reduced pain
- Reduced frequency

Improved adherence

Improved pharmacokinetics

= Improved Patient Outcomes
Opportunities Incorporating Existing Drugs

**Generic Drug**
- TIME, CAPITAL, RISK
- VALUE

**Drug Delivery Product**
- 3-6 years, $10-50M
- 66% Phase 3 Success Rate*

**New Drug**
- 10-15 years, $1-2B
- 41% Phase 3 Success Rate*

*Data for comparable products presented by Teva Pharmaceuticals at PODD conference 2014
Different Systems, Different Hurdles

- **Mucosal** (Oral, gastrointestinal, buccal, ocular, vaginal, alveolar, bronchial)
  - Thick coating of slow-flowing mucus
  - Often active immune response
- **Dermal**
  - Thick and hydrophobic
  - Exposed externally
- **Parenteral** (Intravenous, intramuscular, subcutaneous, cranial)
  - Needles/invasive
- **General**
  - Bioavailability (eg: hepatic first pass clearance)
What’s going on in the body at the nano level?

- Transportation
- Internalization (eg: vesicles)
- Migration (eg: cilia)
- Reorganization (eg: microvilli)
- Actuation
- DNA replication
- Communication
- Receptor binding
Why Micro/Nano?

• Unique properties
  – Surface area to volume ratio
  – Integration with electronics
  – Scalable manufacturing via semiconductor techniques
  – Novel material properties (color, electrical properties, etc)

• Biological scale
  – Cell membrane interactions
  – Cell signaling interactions
  – Close in size to macromolecules
Opportunities for Nano-Enabled Drug Delivery

Free floating
- Nanoparticles

Coatings/integral
- Nanowires
- Nanopores/Nanotubes

http://phys.org/news104677694.html

Cell-Nanowire Interface

Nanowires and microvilli are similar in scale

Nanoscale features allow interdigitation with microvilli, leading to increased van der Waals force.

Nanocoatings

https://pharm.ucsf.edu/desai/research/vascular-stents

Diffusion from Nanoporous Silicon Membranes

Fine et al., Lab on a Chip, 2010

Martin et al., 2005, Journal of Controlled Release

Lopez et al., 2006, Biomaterials
Inorganic Nanoporous Devices

- Titania nanotubular membranes
- Silicon nanochannels
- Alumina nanoporous capsules

Scale bar – 500 nm
Management Team

Original Founding Team

Adam Mendelsohn, PhD
Chief Executive Officer
Director

Kayte Fischer, PhD
Chief Technology Officer

Lily Peng, MD, PhD
Consulting VP of Clinical Development

Non-Founding Management

Tomoyuki Yoshie, PhD
VP of Device Research

Wouter Roorda, PhD
VP of Pharmaceutical Product Development

Adam Monkowski, PhD
VP of Device Technology Development
Benefits of NanoPortal Device

- Constant Rate Delivery
- Large Payload in a Small Device
- No New Materials
- Adherence Assured

![Graph showing Serum Activity and Time with side effects depicted]

![Image of a NanoPortal device]

![Image of titanium oxide]

![Image of a doctor and a child giving thumbs up]
NanoPortal™ Membrane

Titania Nanotube Layer (grown from titanium surface)

Pure Titanium

whole membrane

window to nanotubes

open nanotubes
As-Fabricated Titania Nanotubes

Tube bottoms, as fabricated
Diameters can be modified

Side view
~60 microns
Most lengths can be achieved

Nanotube tops
Diameters can be modified
Nanoscale Constrained Release

**NanoPortal™ Technology**

- **Fickian**, diminishing release-rate over time
- **Non-Fickian**, constant release-rate over time

Drug release curves over time.
NanoPortal™ Exhibits Size-Dependent Constant-Rate Delivery
(data produced from prior-generation membranes)

Polyethylene glycol, 40 kDa, Fickian release

FITC-Fab₂, 110 kDa, Constant-rate release

Similar membranes used for both molecules
Controllable Nanotube Diameters

0 nm pore size

17 nm pore size

33 nm pore size

Scale bars are 200 nm

Decreasing nanotube diameter
Devices Function in Rats

**In Vitro Running**
- Total mass (mg PEG MW=40 kDa)

- Delivery is complete around 80-85% of loaded mass

**In Vivo**
- Plasma concentration (ng/ml PEG MW=40 kDa)

- Delivery Complete at Day 14

- Identical devices tested in parallel *in vitro* (top) and *in vivo* (bottom); n=5

- Decays as expected after delivery is complete
NanoPortal™ as a Platform Technology

- Minimized Implant Design
- Extendable Implant Duration
- Tunable Delivery Rate
- Tunable Pore Size
## Classes of Ideal Drug Candidates

### Selection Criteria

1. Chronic treatments
2. Constant-rate delivery is desirable

<table>
<thead>
<tr>
<th>Molecule Type</th>
<th>Example</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Molecules with Compliance Issues</td>
<td>Anti-psychotics (Risperidone)</td>
<td>Schizophrenia, Bipolar Disorder</td>
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<tr>
<td>Small Peptides / Hormones</td>
<td>GLP-1 Agonist (Exenatide)</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Enzyme Replacements</td>
<td>Glucocerebrosidase (Cerezyme)</td>
<td>Gaucher, Fabry</td>
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<tr>
<td>Antibodies</td>
<td>Natalizumab (Tysabri)</td>
<td>Multiple Sclerosis</td>
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<tr>
<td>siRNA</td>
<td>Miravirsen</td>
<td>HCV</td>
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**Top Pipeline Opportunities:** Exenatide, Teduglutide, Octreotide
The Original Idea and Team
Getting Started (2007-2010)

- Business plan competitions – 2007-2009
- Grant funding – 2009
- Incorporation – 2009

3 Co-founders

- IP negotiations – 2010

2 Co-founders + 1 Employee
The Bay

Management of Technology

Haas Healthcare Association

University of California Berkeley
Haas School of Business

Lester Center for entrepreneurship and innovation
entrepreneurship @Berkeley

Innovation Accelerator
UC San Francisco

qb3 ucb.ucsf.ucsf

The Venture Innovation Program in Life Sciences

nанобионизион medical

Center for BioEntrepreneurship

CBE

Center for Entrepreneurship & Technology

BAYBIO

East Bay Biomedical Manufacturing Network
Initial Incubator (2010-2011)

• Moved into incubator lab at UC Berkeley

2 Co-founders + 1 Employee
The East Bay Innovation Center (2011-2013)

• 2 offices!
• 5 lab benches!
• Lots of shared facilities, for better or worse

2 Co-founders + 1 -> 5 Employees = 7
Facility Upgrade! (2013-present)

2 Co-founders +
5 -> 10 Employees + 1-2 Interns = 13-14!

< 500 sq ft
to > 6000 sq ft
slightly larger than a grain of rice

LEARN MORE ABOUT NANOPORTAL™ TECHNOLOGY >

Thank you for your attention!

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