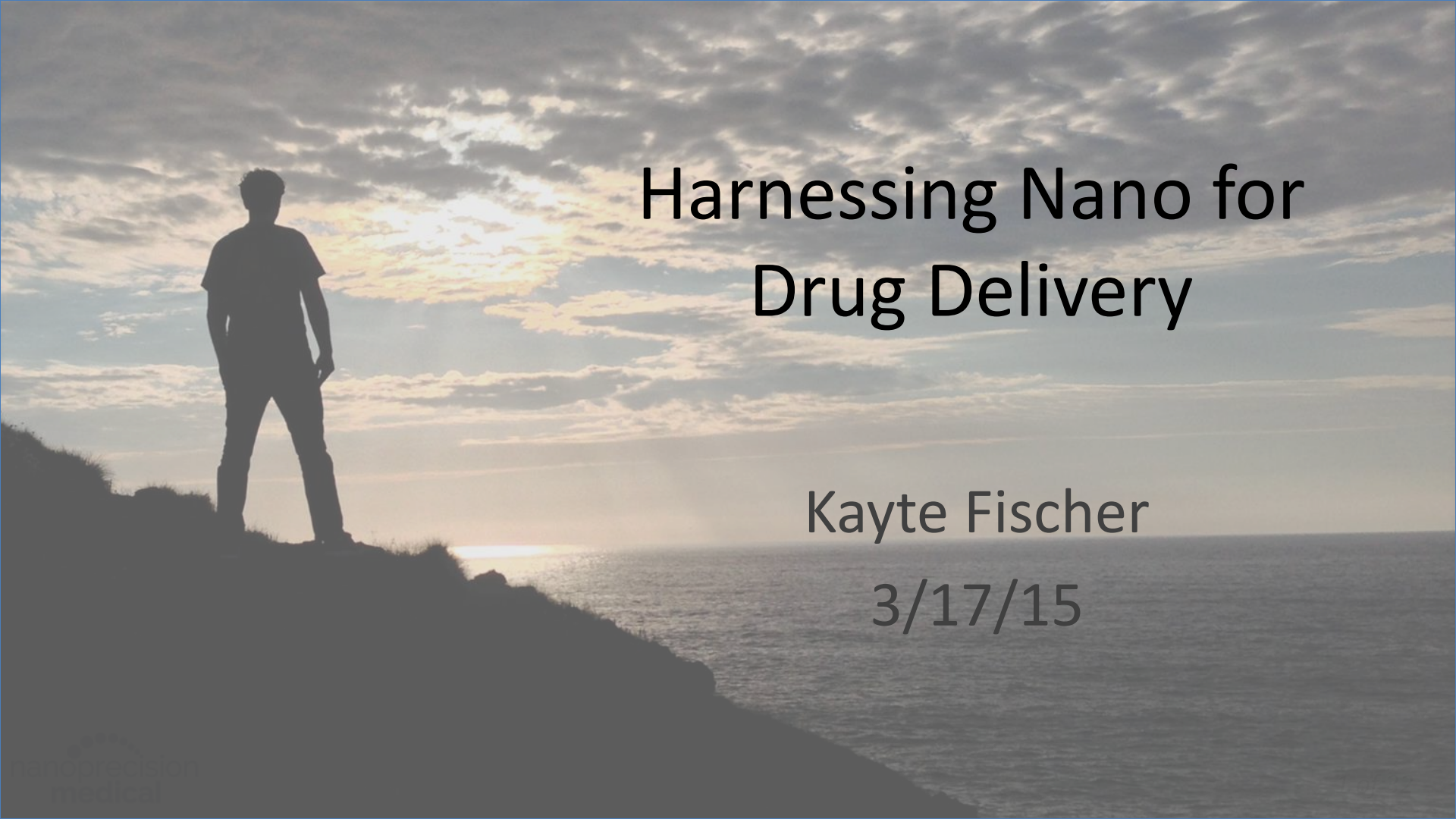
Harnessing Nano for
Drug Delivery
Kayte Fischer
3/17/15
nanoprecision
medical

What is Drug Delivery?

34° Precipitous

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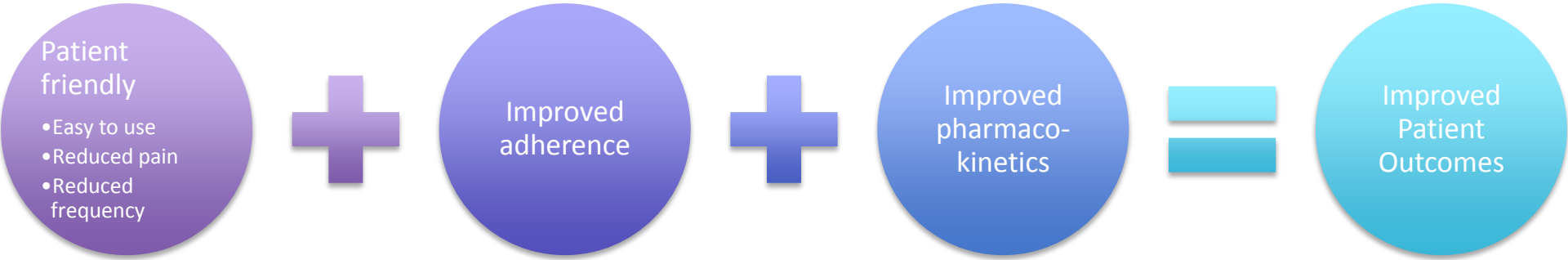
What is Drug Delivery?

Why is drug delivery useful?



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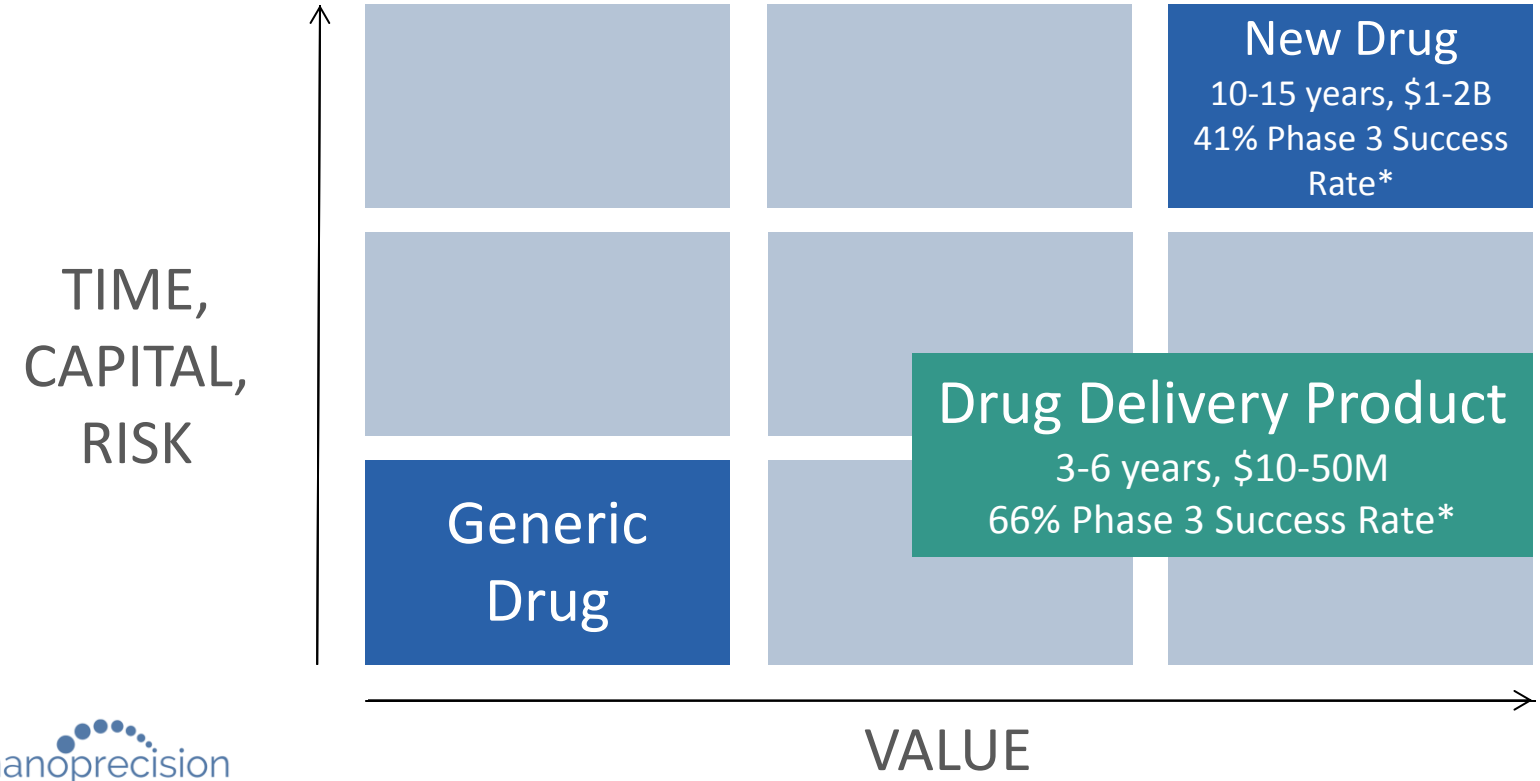
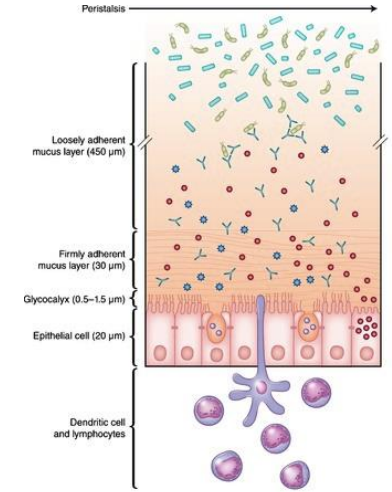
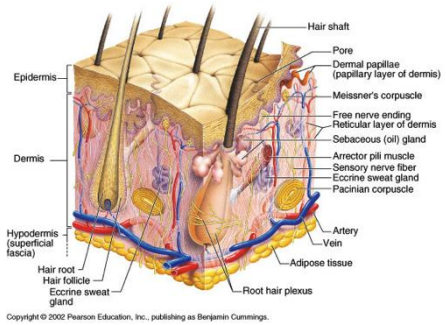
Opportunities Incorporating Existing Drugs



*Data for comparable products presented by Teva Pharmaceuticals at PODD conference 2014

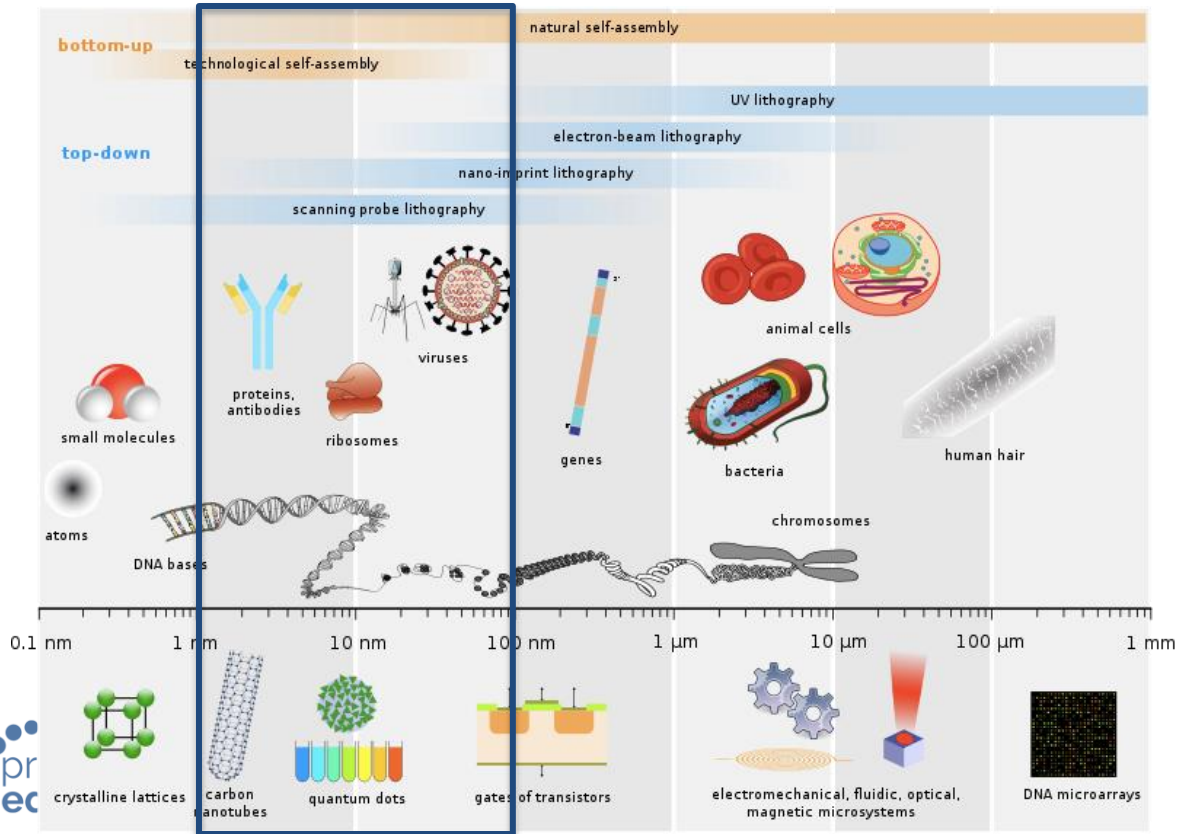
Different Systems, Different Hurdles





- 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)

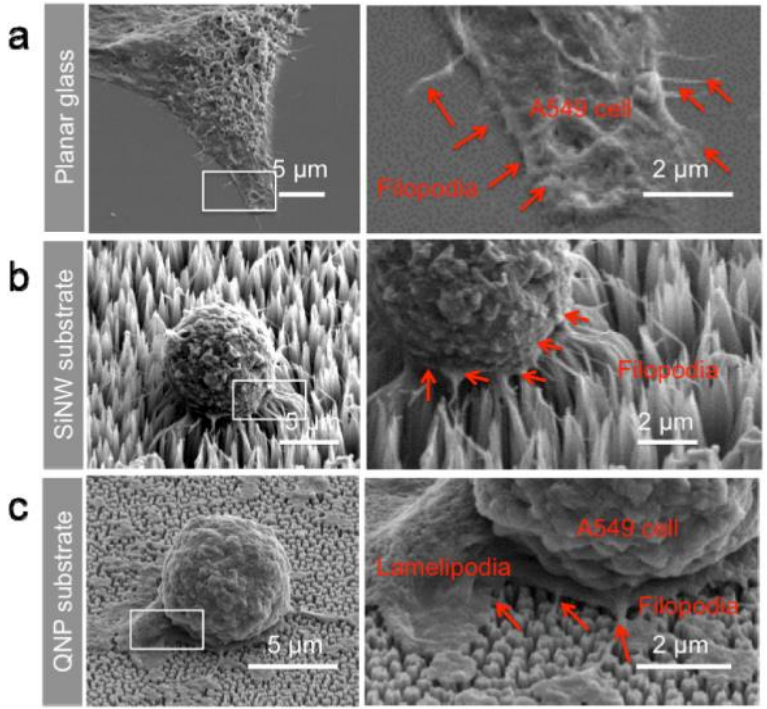
What's going on in the body at the nano level?



- 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



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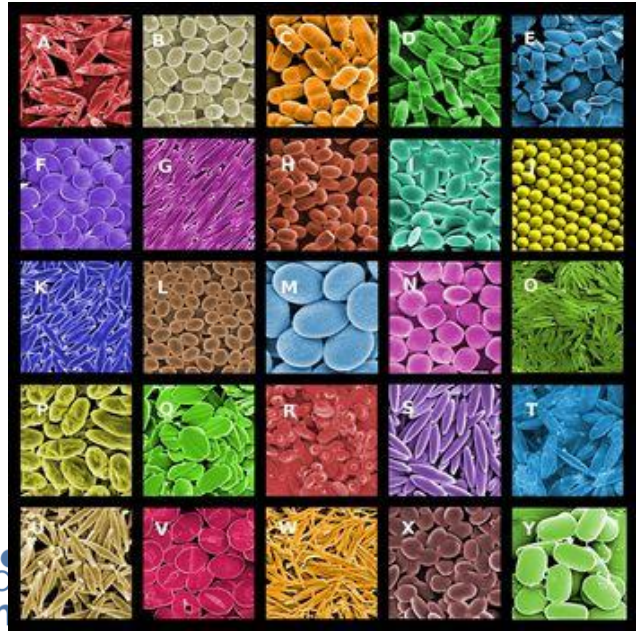
Dong-Joo Kim *et al* 2012 *Nanotechnology* **23**

Opportunities for Nano-Enabled Drug Delivery

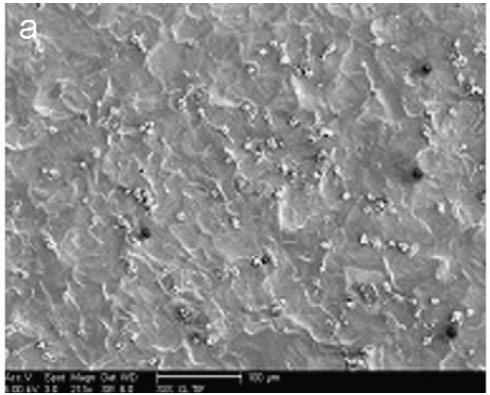
Free floating

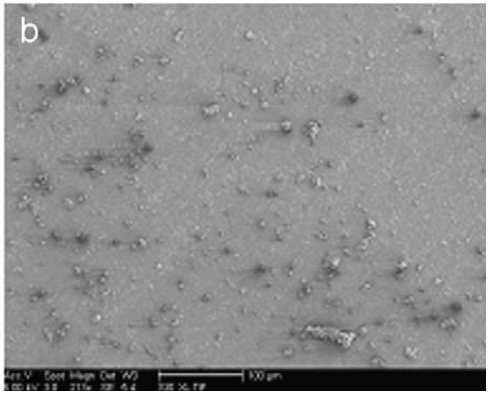
- Nanoparticles



Coatings/integral

- Nanowires
- Nanopores/Nanotubes

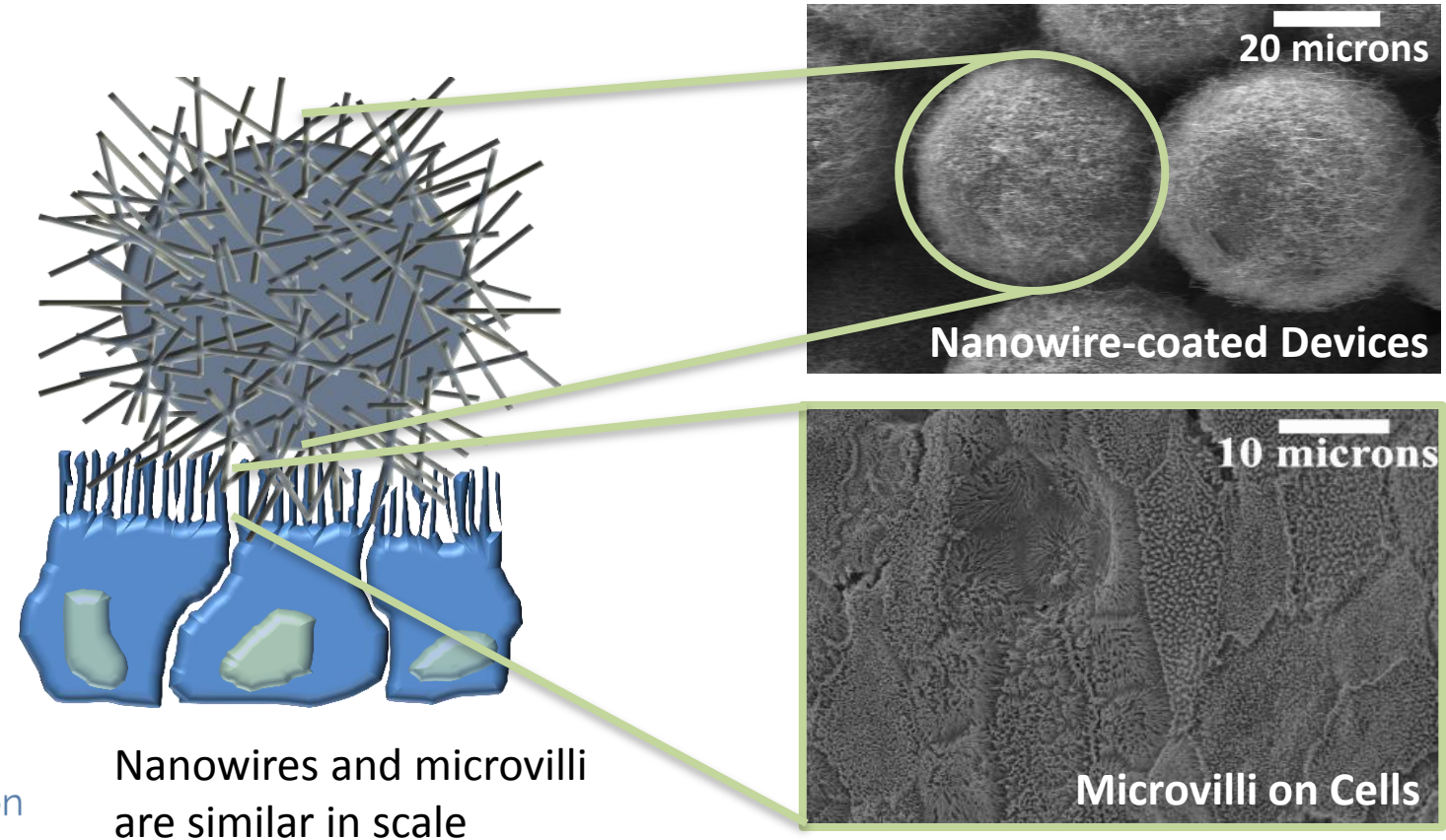




Popat, et al. Biomaterials 28 (2007).

http://phys.org/news104677694.html

Cell-Nanowire Interface



Nanowires and microvilli are similar in scale

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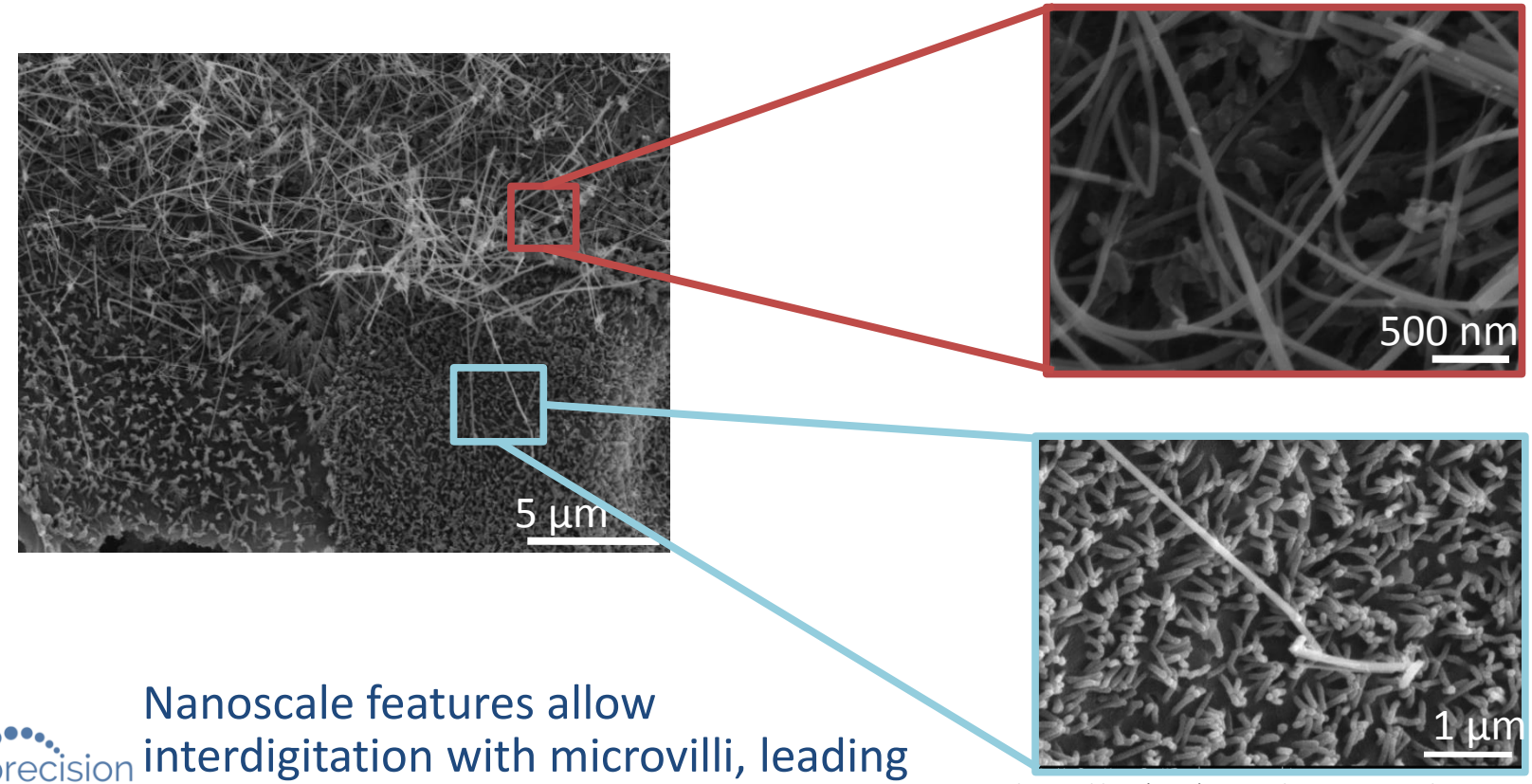
Fischer, Kathleen (2010) Doctoral Dissertation. Silicon Nanowires for Bioadhesion and Drug Delivery.

Cell-Nanowire Interface



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

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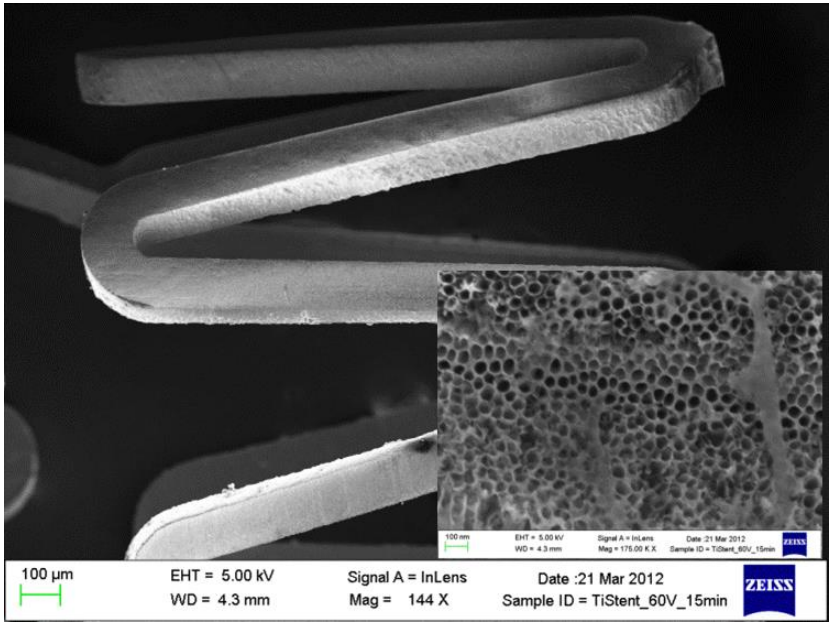
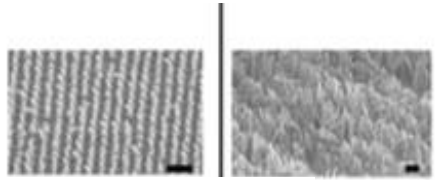
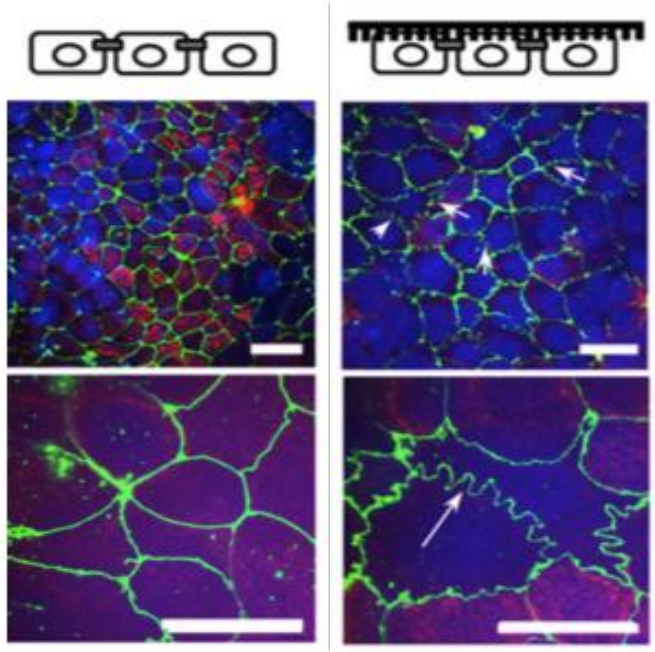
Fischer, Kathleen (2010) Doctoral Dissertation. Silicon Nanowires for Bioadhesion and Drug Delivery.

Nanocoatings



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





Kam, et al. Nano Letters, 2013.

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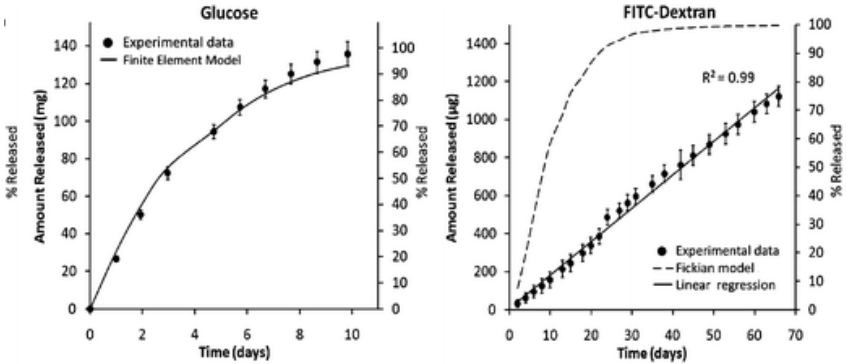
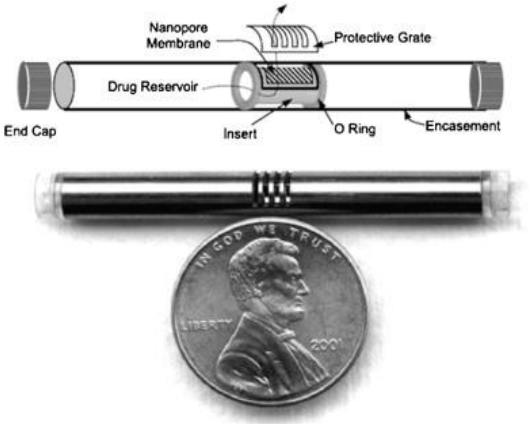
Diffusion from Nanoporous Silicon Membranes



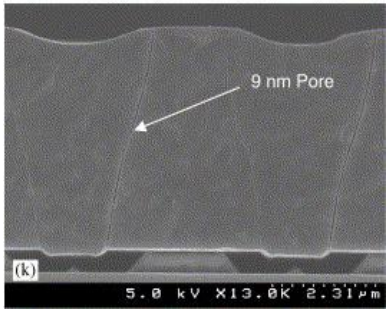
Experimental Details

Molecule	nCH (nm)	Solution Conc. (mg/mL)	Release Rate (µg/day)
DF-1 Fullerene	5	2	20
DF-1 Fullerene	13	2	exp.
Glucose	5	495.44	exp.
FITC-Dextran	22	5	17
BSA	22	20	30
BSA	22	40	30
INFα-2b	13	1	6

Fine et al., Lab on a Chip, 2010



Martin et al., 2005, Journal of Controlled Release



Lopez et al., 2006, Biomaterials

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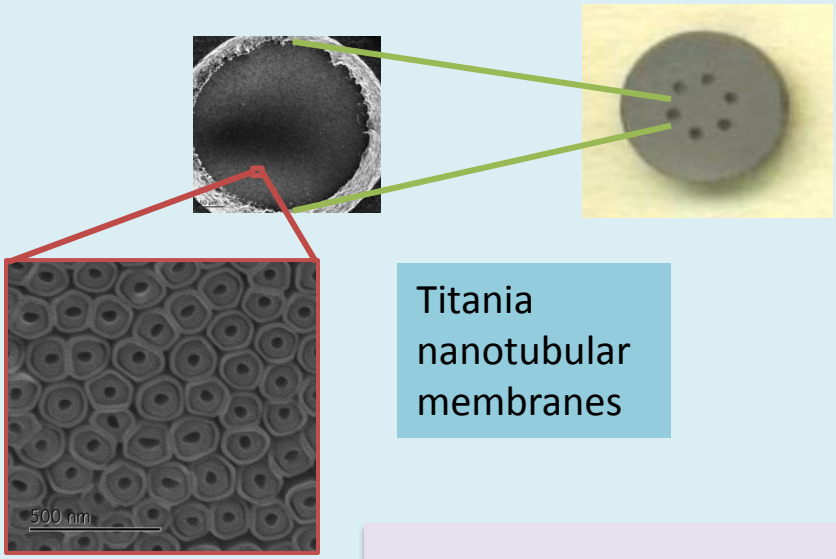
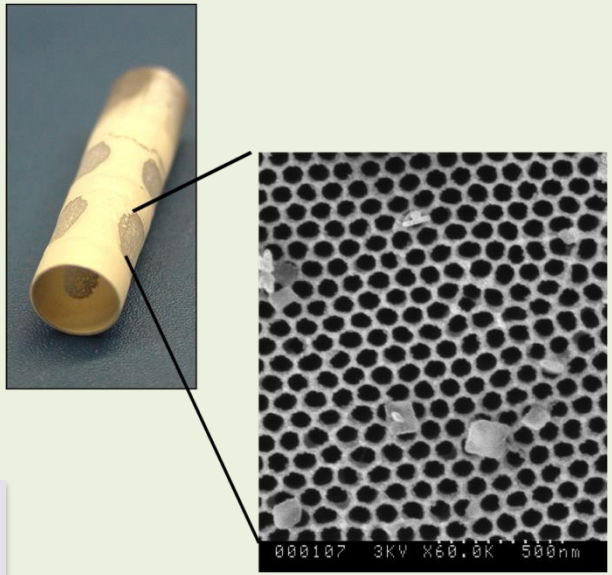
Inorganic Nanoporous Devices

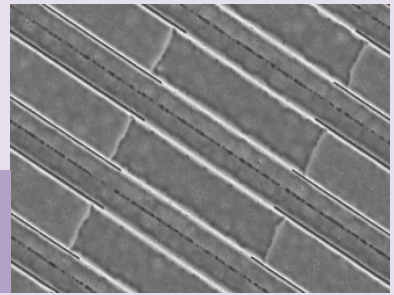


Titania nanotubular membranes

Scale bar – 500 nm



Alumina nanoporous capsules



Silicon nanochannels

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Nano Precision Medical

www.nanoprecisionmedical.com

Management Team

Original Founding Team

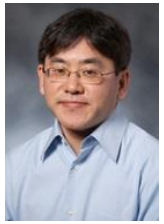
Adam Mendelsohn, PhD
Chief Executive Officer
Director

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

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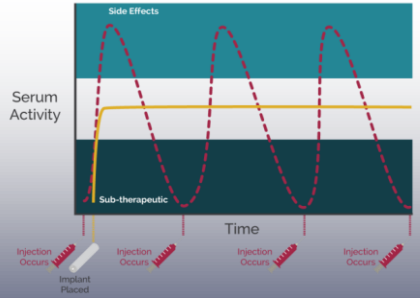
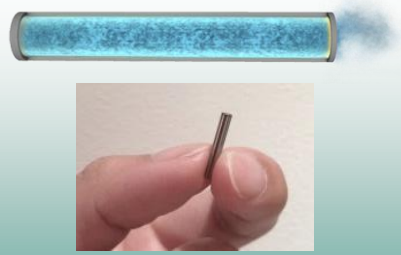
Benefits of NanoPortal Device



Constant Rate Delivery



Large Payload in a Small Device

No New Materials

Adherence Assured

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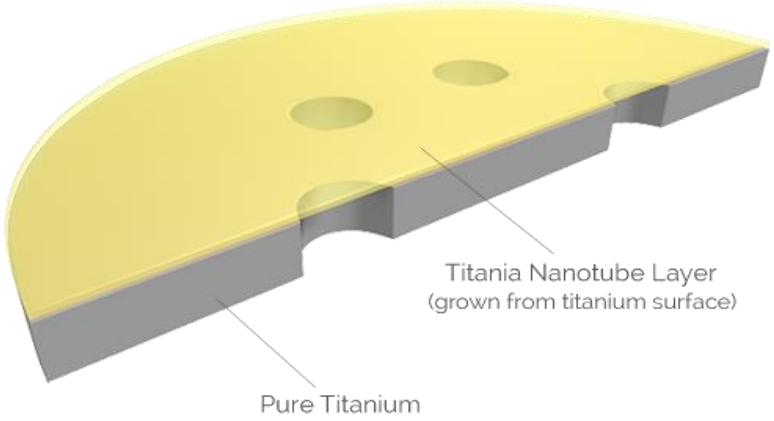
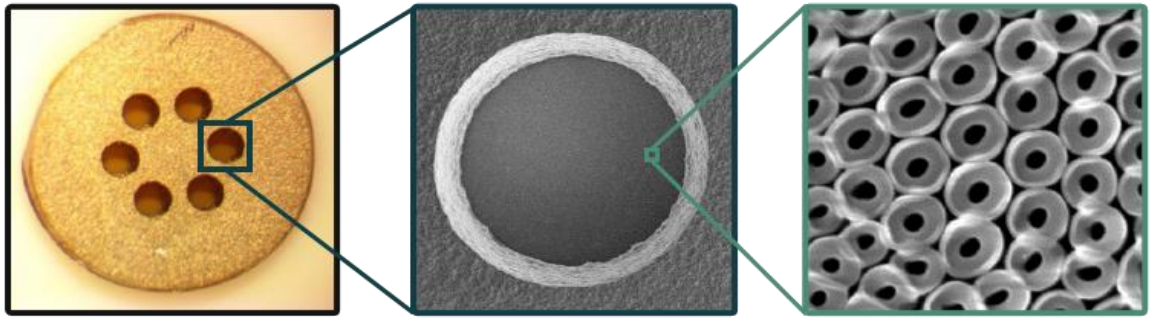
Nano**Portal**™ Membrane





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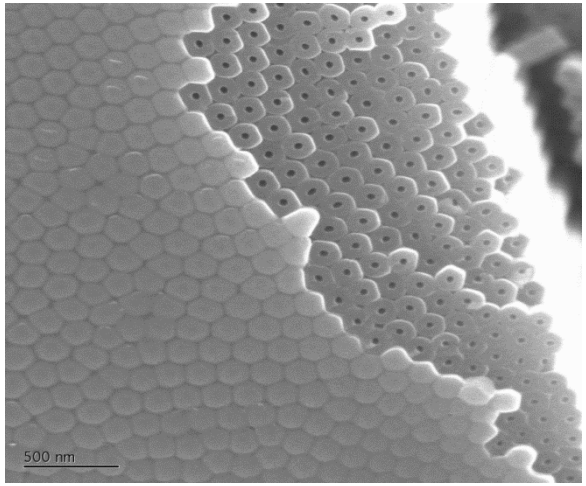
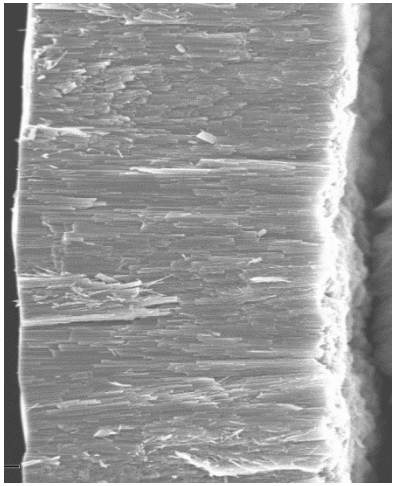
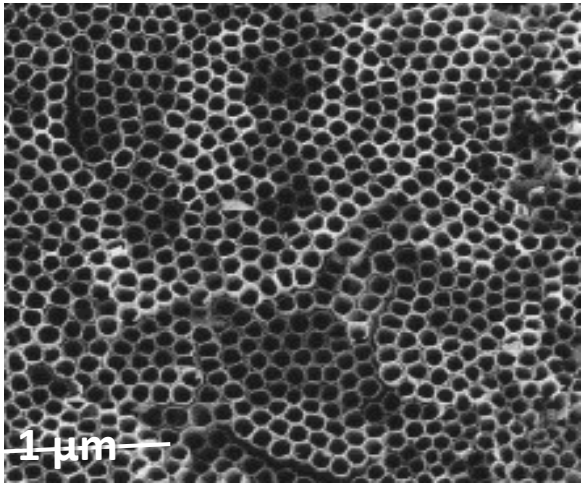
As-Fabricated Titania Nanotubes



Tube bottoms, as fabricated
Diameters can be modified



Side view
~60 microns
Most lengths can be achieved



Nanotube tops
Diameters can be modified

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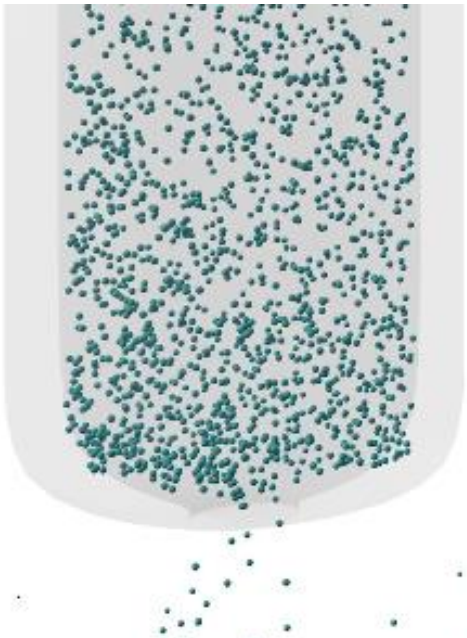
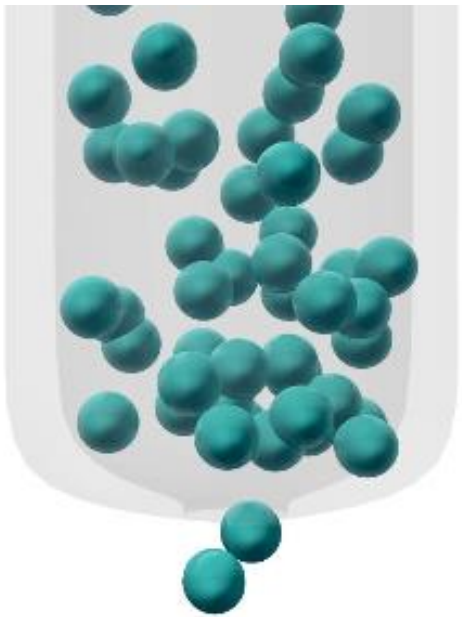
Nanoscale Constrained Release

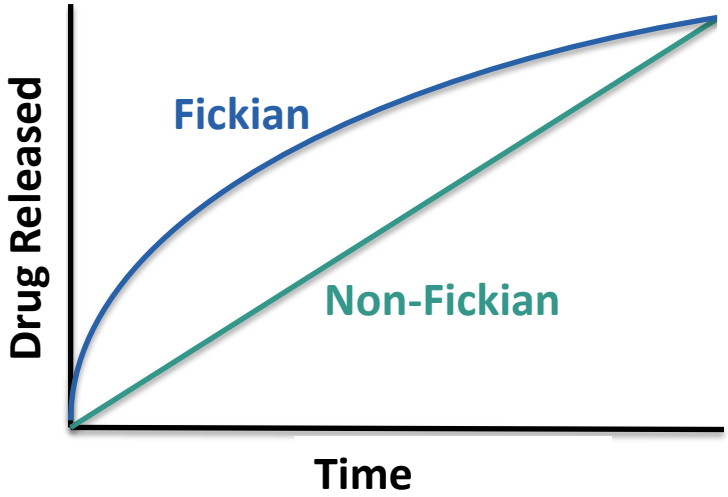
NanoPortal™ Technology



Fickian, diminishing release-rate over time



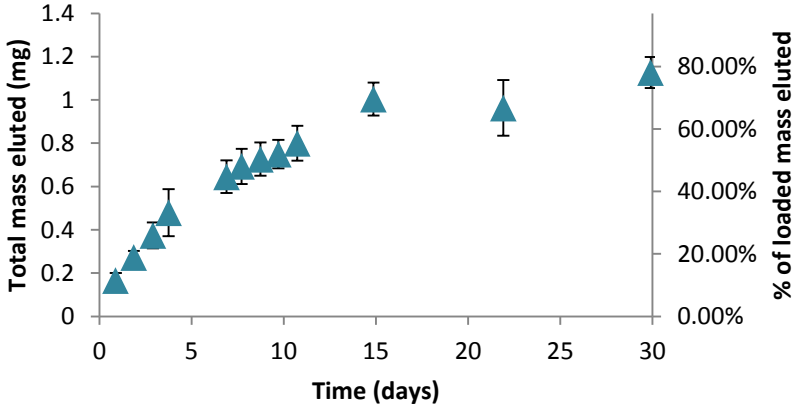
Non-Fickian, constant release-rate over time

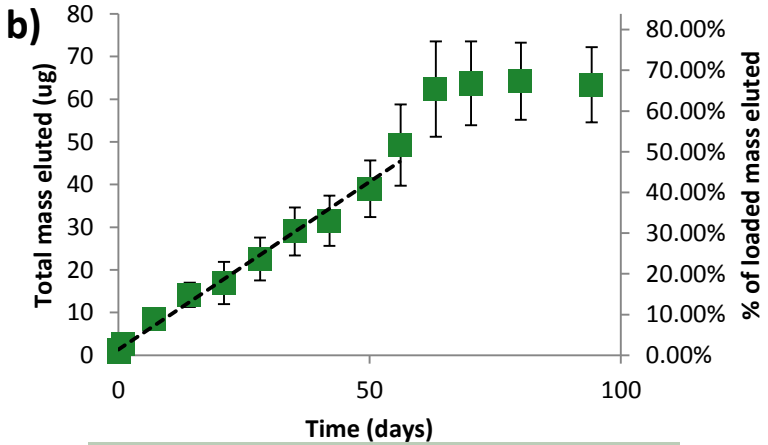


Drug release curves over time

NanoPortal™ Exhibits Size-Dependent Constant-Rate Delivery

(data produced from prior-generation membranes)



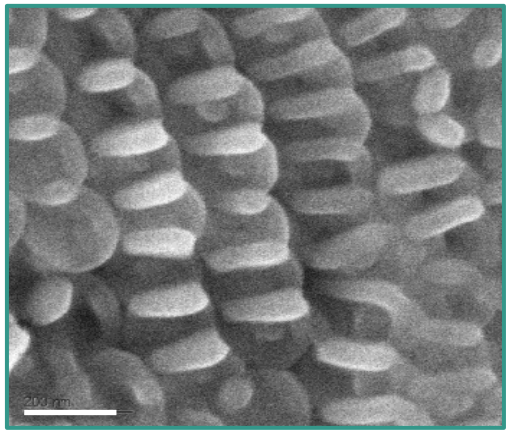


Polyethylene glycol, 40 kDa, Fickian release

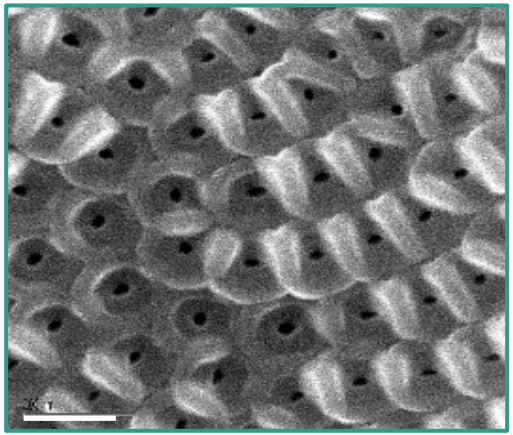
FITC-Fab$_2$, 110 kDa, Constant-rate release

Similar membranes used for both molecules

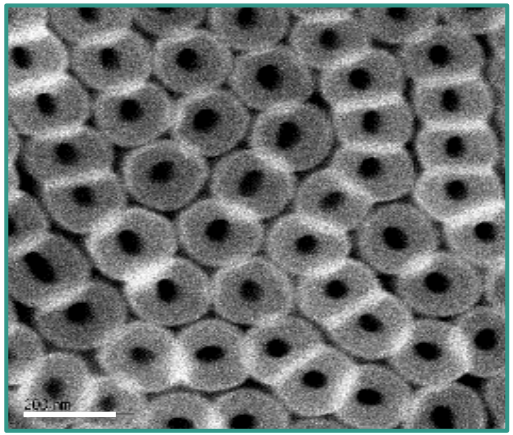
Controllable Nanotube Diameters



0 nm pore size



17 nm pore size



33 nm pore size

Decreasing nanotube diameter

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Scale bars are 200 nm

Devices Function in Rats

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

Decays as expected after delivery is complete

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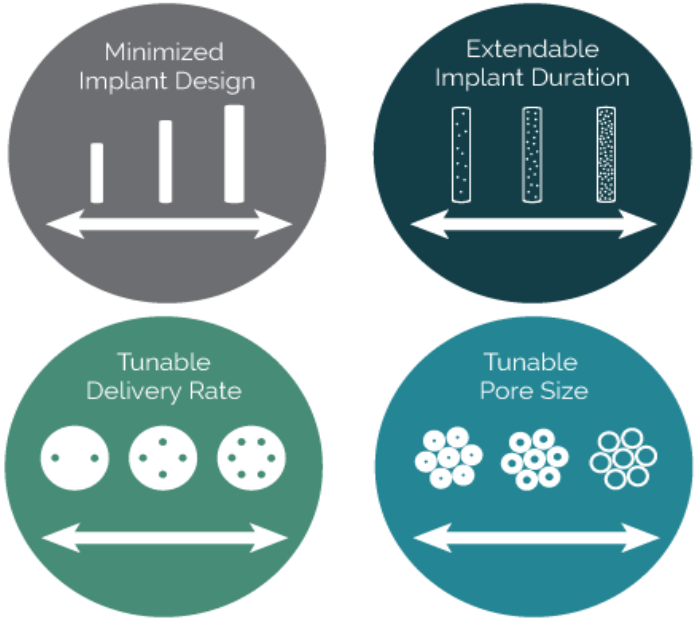
Nano**Portal**™ as a Platform Technology



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Classes of Ideal Drug Candidates

Selection Criteria

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

Molecule Type	Example	Indication
Small Molecules with Compliance Issues	Anti-psychotics (Risperidone)	Schizophrenia, Bipolar Disorder
Small Peptides / Hormones	GLP-1 Agonist (Exenatide)	Diabetes
Enzyme Replacements	Glucocerebrosidase (Cerezyme)	Gaucher, Fabry
Antibodies	Natalizumab (Tysabri)	Multiple Sclerosis
siRNA	Miravirsen	HCV

Top Pipeline Opportunities:
Exenatide,
Teduglutide,
Octreotide

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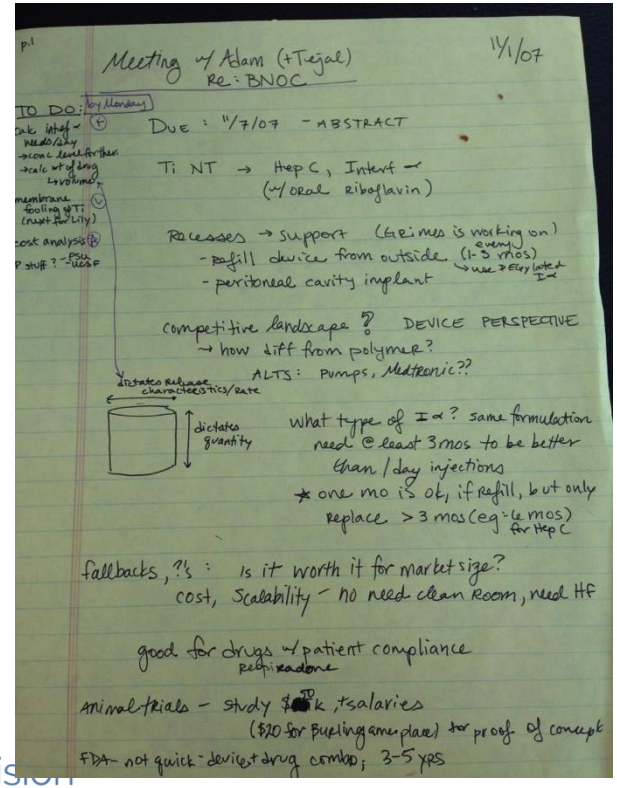
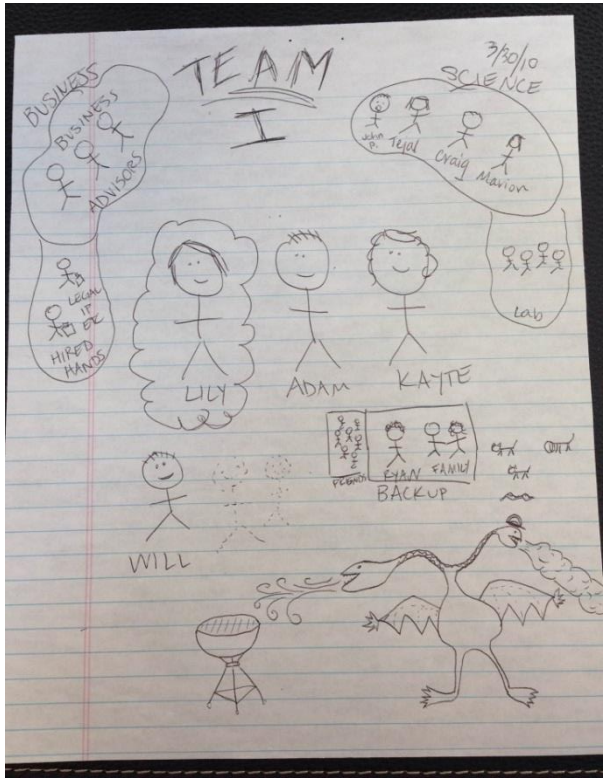
The Original Idea and Team





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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

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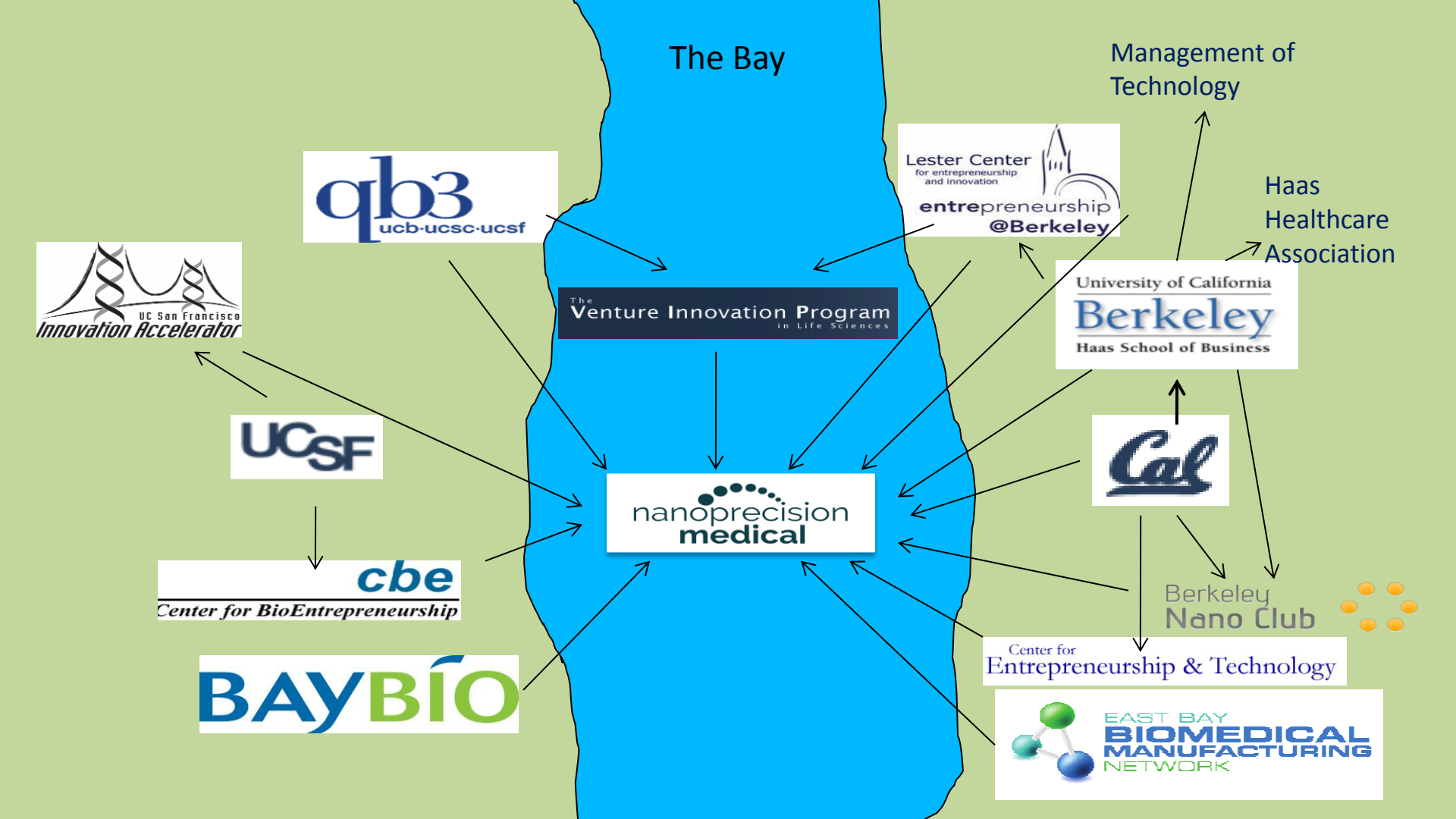
The Bay
Management of Technology
Lester Center for entrepreneurship and innovation
entrepreneurship @Berkeley
qb3 ucb·ucsc·ucsf
Haas Healthcare Association
UC San Francisco Innovation Accelerator
The Venture Innovation Program in Life Sciences
University of California Berkeley Haas School of Business
UCSF
Cal
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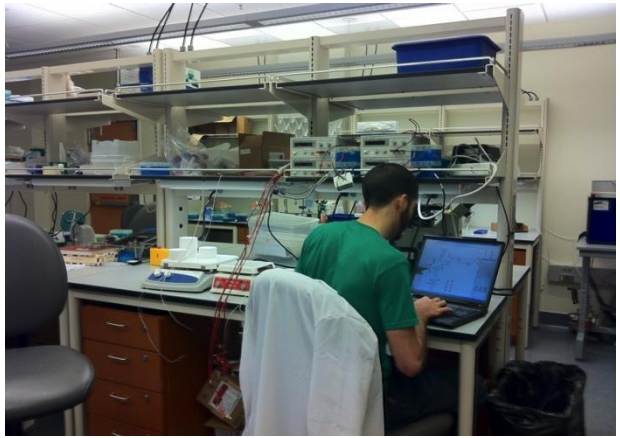
cbe Center for BioEntrepreneurship
Berkeley Nano Club
Center for Entrepreneurship & Technology
BAYBIO
EAST BAY BIOMEDICAL MANUFACTURING NETWORK

Initial Incubator (2010-2011)



- Moved into incubator lab at UC Berkeley

2 Co-founders + 1 Employee

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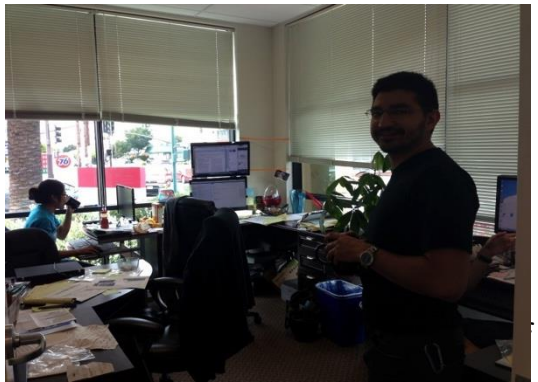
The East Bay Innovation Center (2011-2013)

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

2 Co-founders +
1 -> 5 Employees = 7



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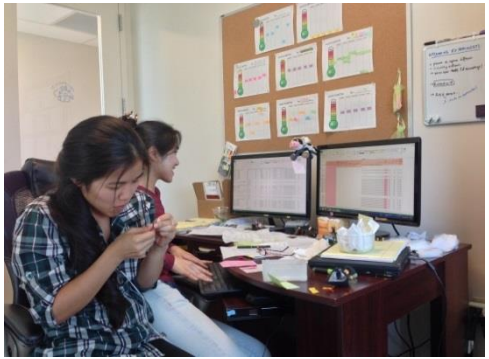
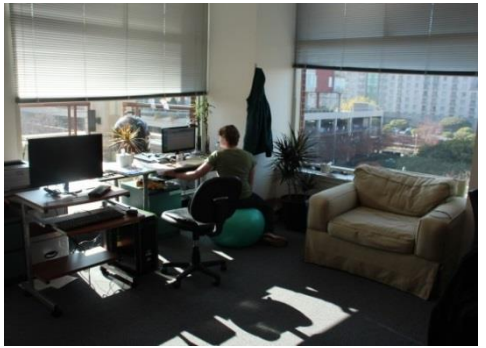
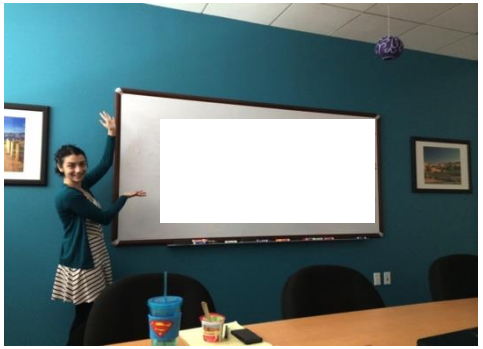
Facility Upgrade! (2013-present)

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



< 500 sq ft
to > 6000 sq
ft





Thank you for your attention!

Contact: Kayte Fischer
kayte@nanoprecisionmedical.com
www.nanoprecisionmedical.com

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