

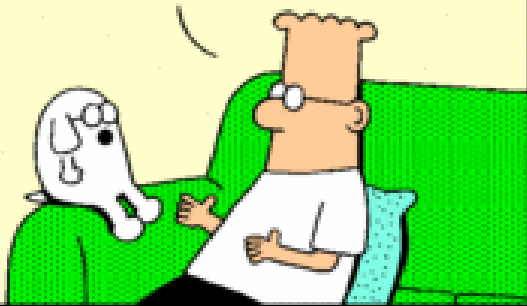
Pulmonary Delivery of PRINT Nanoparticles for Novel Vaccine Strategies

**Cathy Fromen
CCR 2014 Annual Meeting
May 20, 2014**

**Department of Chemical and Biomolecular Engineering
North Carolina State University
University of North Carolina at Chapel Hill**

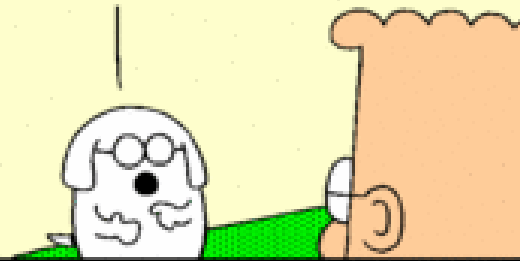
Is "Nanomedicine" Just Another Buzz Word?

MY BOSS WANTS ME TO INVENT NANOTECHNOLOGY STEM CELLS BECAUSE IT SOUNDS GOOD.



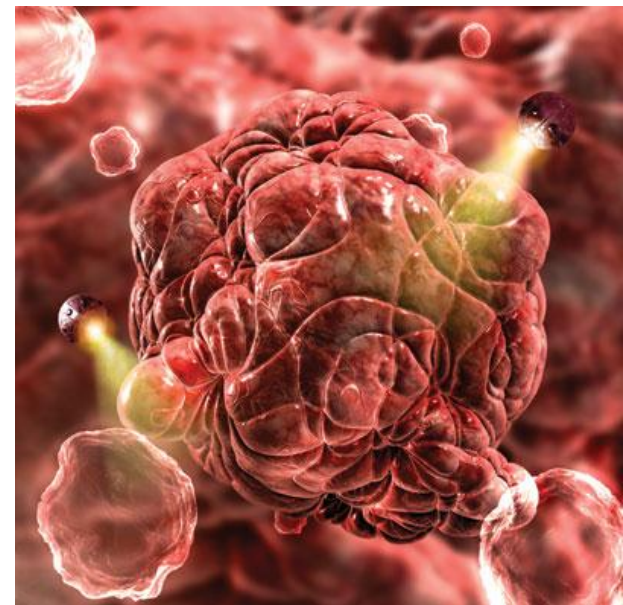
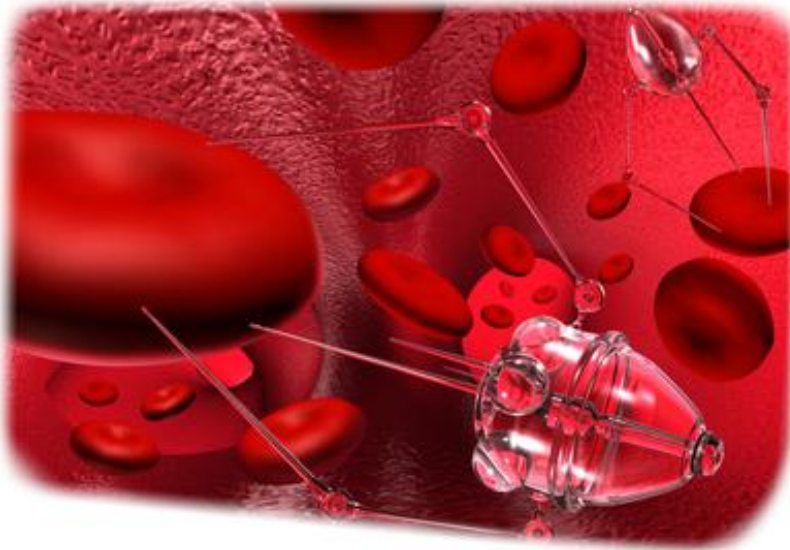
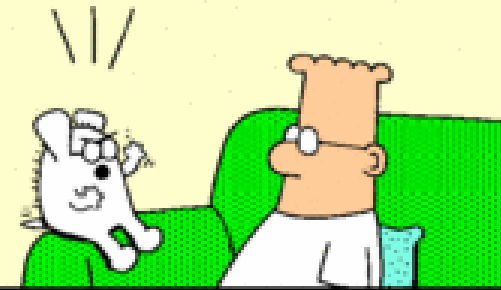
www.dilbert.com scottadams@aol.com

TRY POINTING TO YOUR EMPTY HAND AND SAYING, "YOU CAN'T SEE THEM BUT THEY'RE ALMOST DONE!"

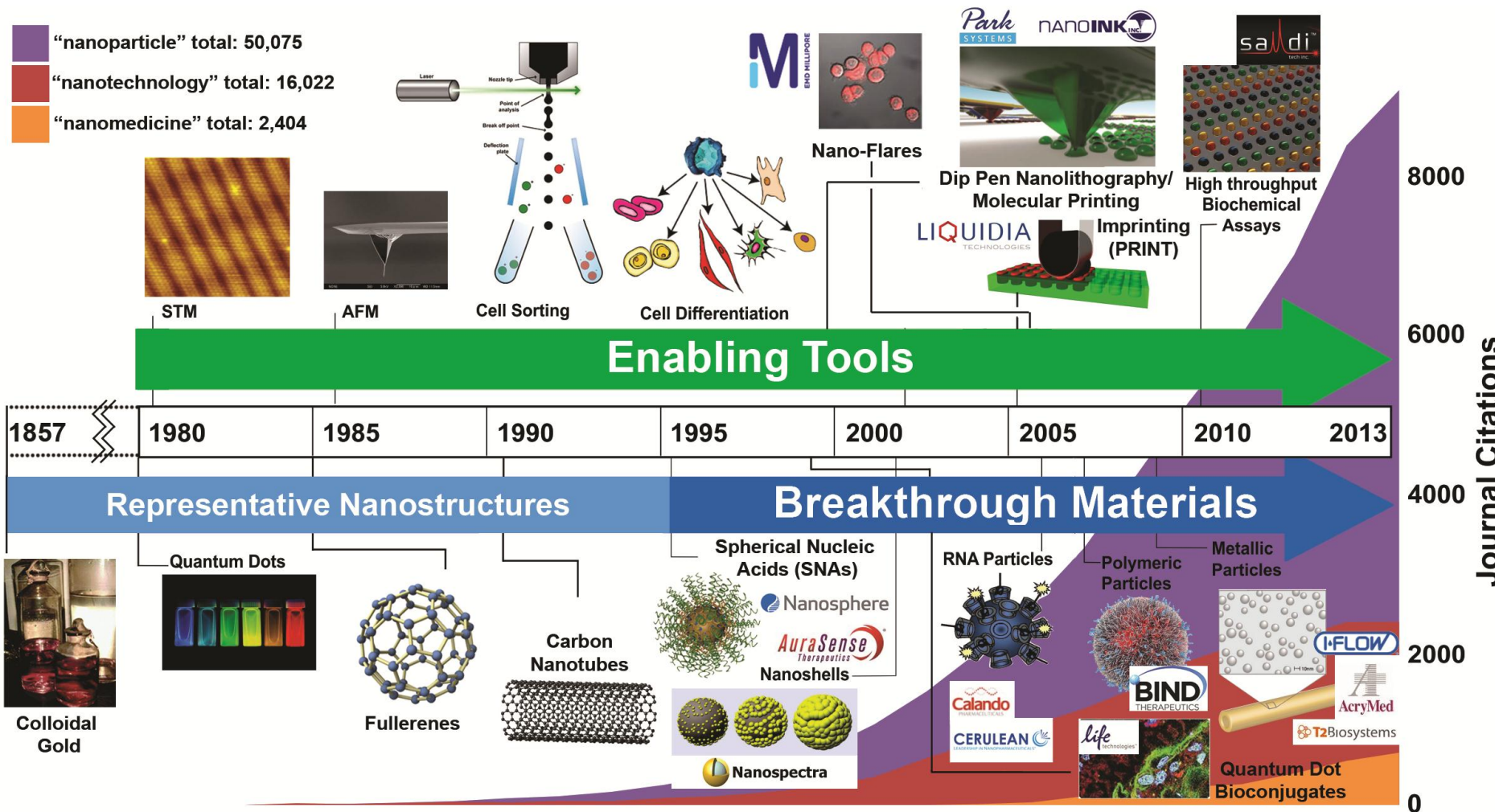


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THEN TRICK HIM INTO GIVING YOU A HIGH-FIVE AND YELL, "YOU CRUSHED THEM! AAAG!!!"



Nanomedicine: An Enduring Bridge Between Engineering and Medicine



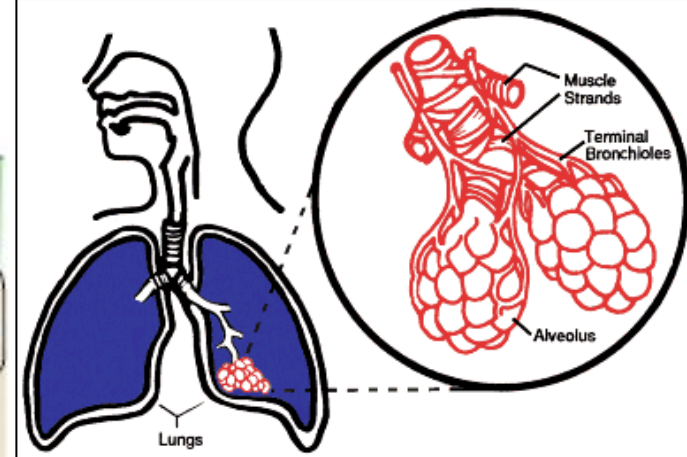
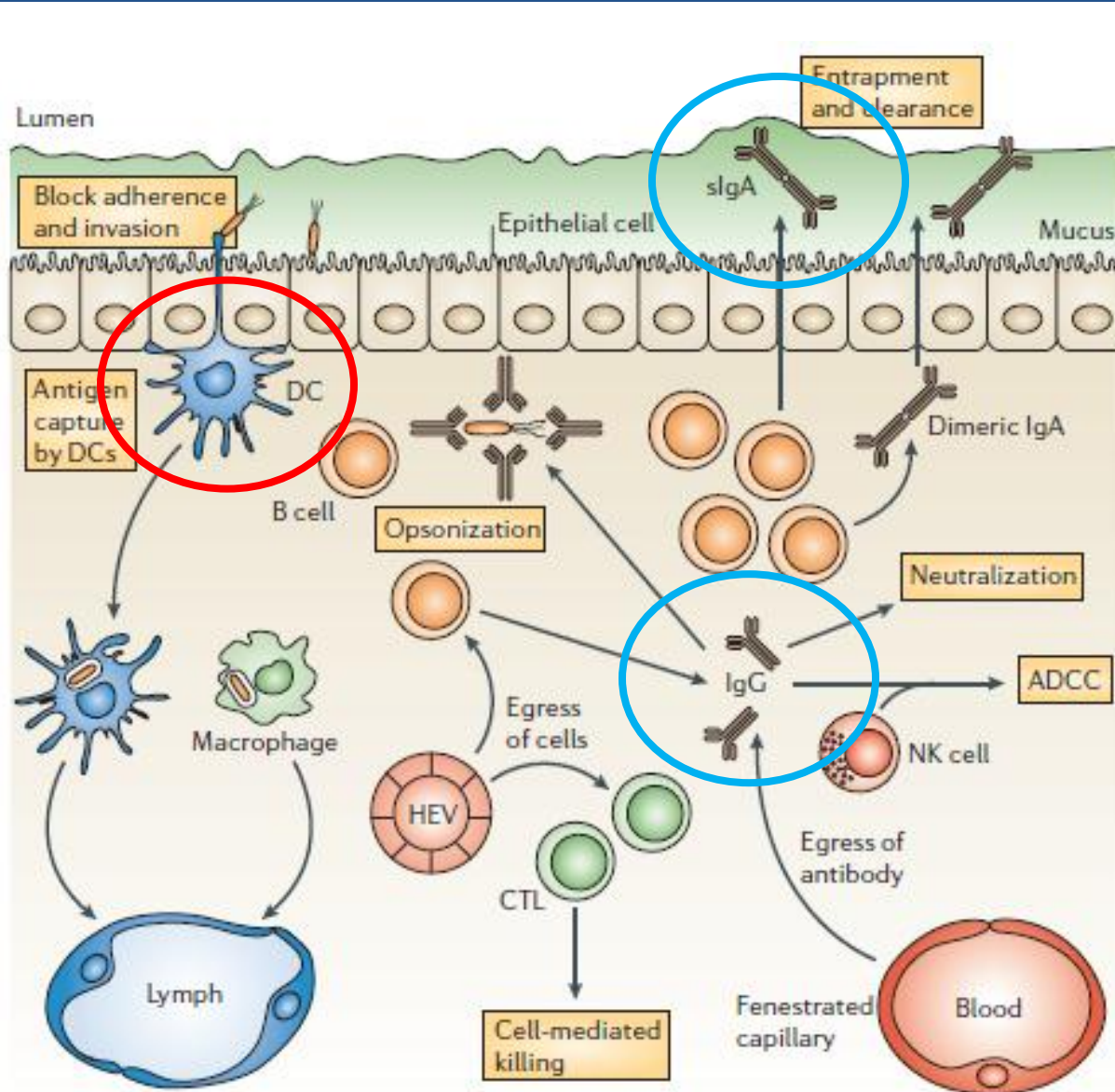
Pulmonary Delivery for Vaccines

Advantages

- Non-invasive
- Ease of access
- Eliminate cold chain storage issues
- Increased patient compliance
- Fast onset of action
- Local and systemic protection
- Harness local mechanisms

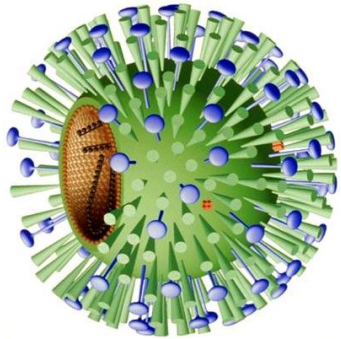


Natural Mechanisms Exist in the Lung to Initiate Protective Responses

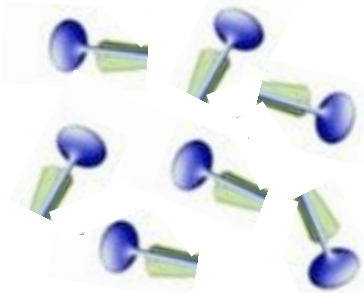


Engineered Particles are “Tailor Made” for Interacting with the Immune System

Current Vaccine Designs

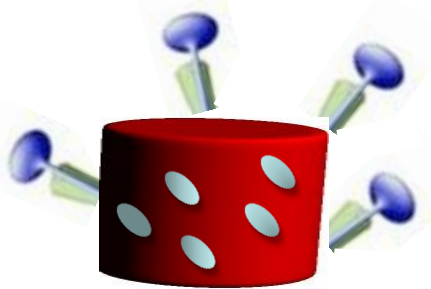


Inactivated or Live-Attenuated

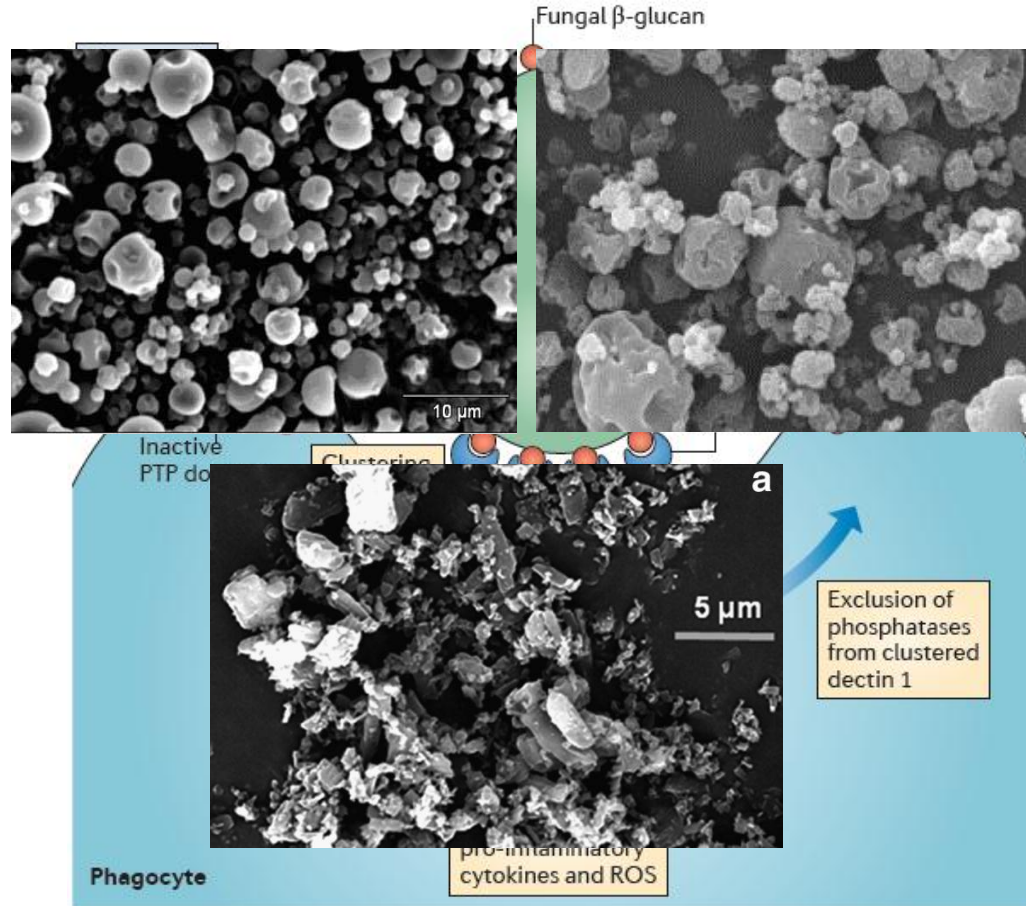


Sub-Unit Proteins

Particle Approach



Particulate Protein-Adjuvant Co-delivery

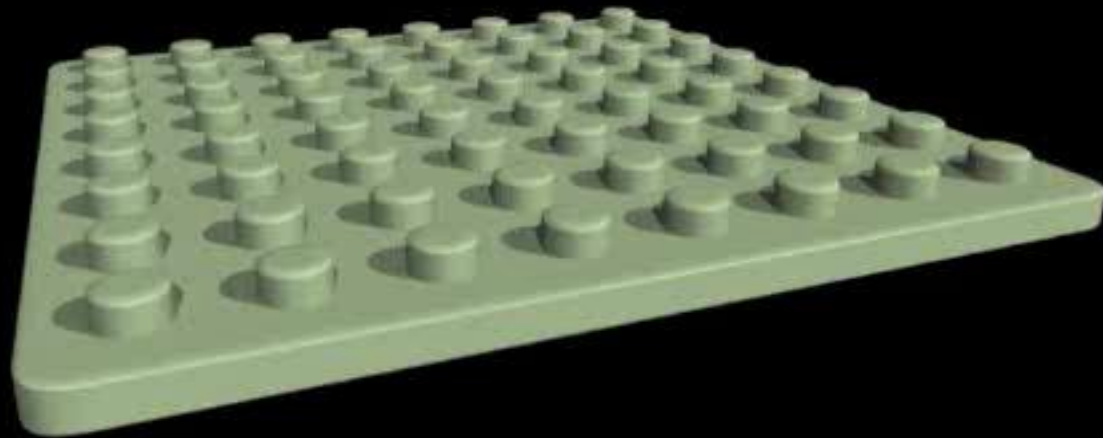




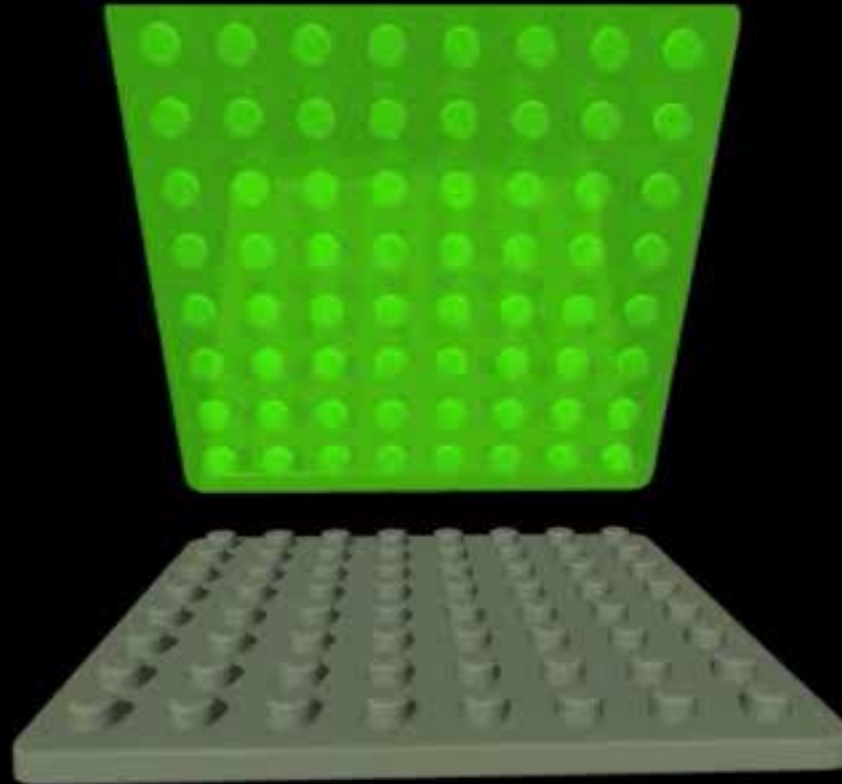
What are the critical design features to engineer an effective pulmonary particle vaccine?

How do we systematically address this?

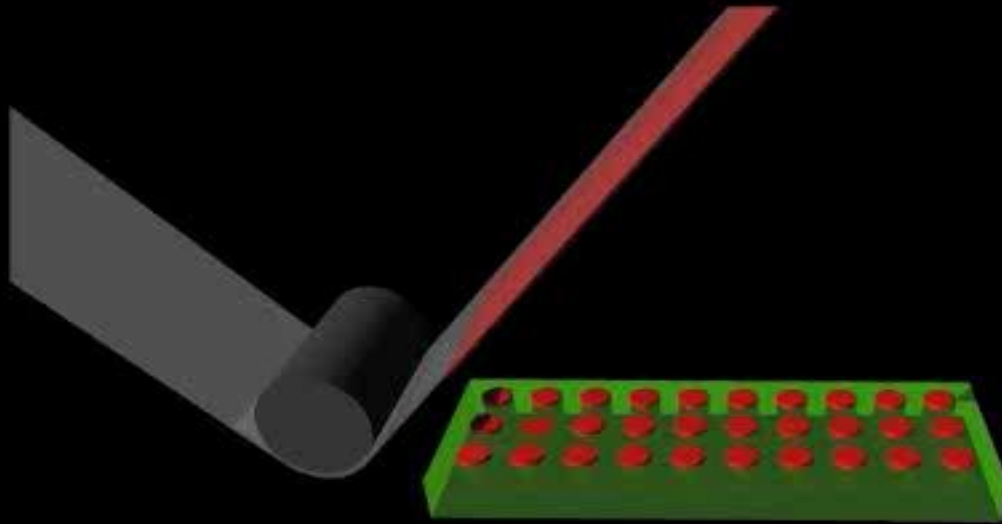
The PRINT[®] Process



The PRINT[®] Process



The PRINT[®] Process



The PRINT[®] Process

Flexible unit operations:

- Filling
- “Solidification” or curing
- Harvesting
- Stabilization and storage

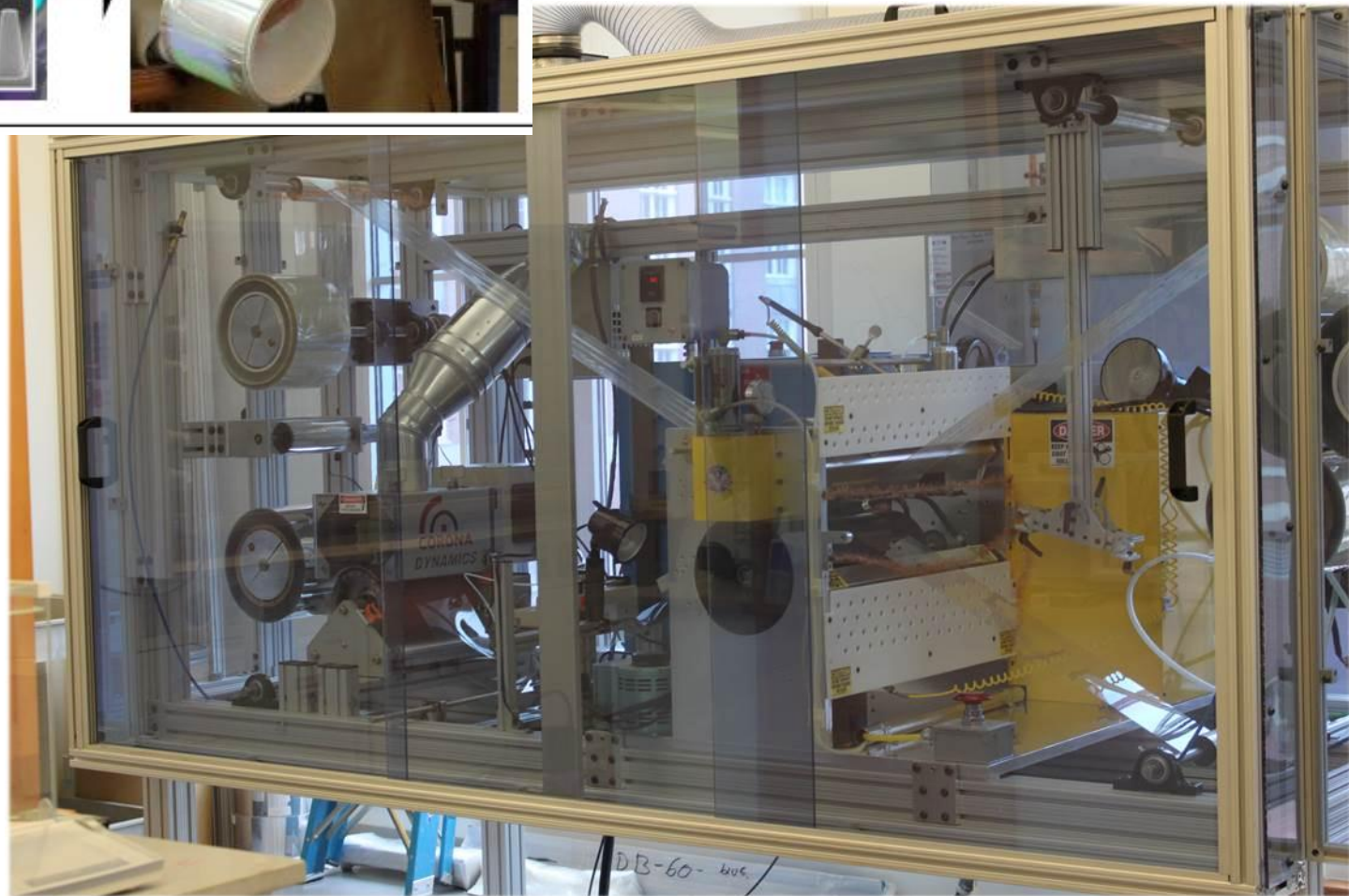
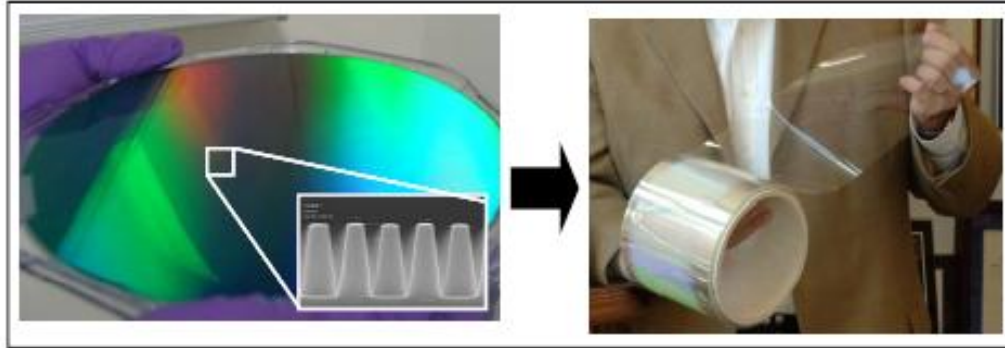
Intrinsically “dry”

Short residence time

Continuous process

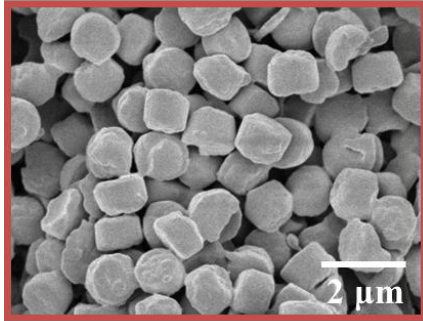


Translating the PRINT[®] Process

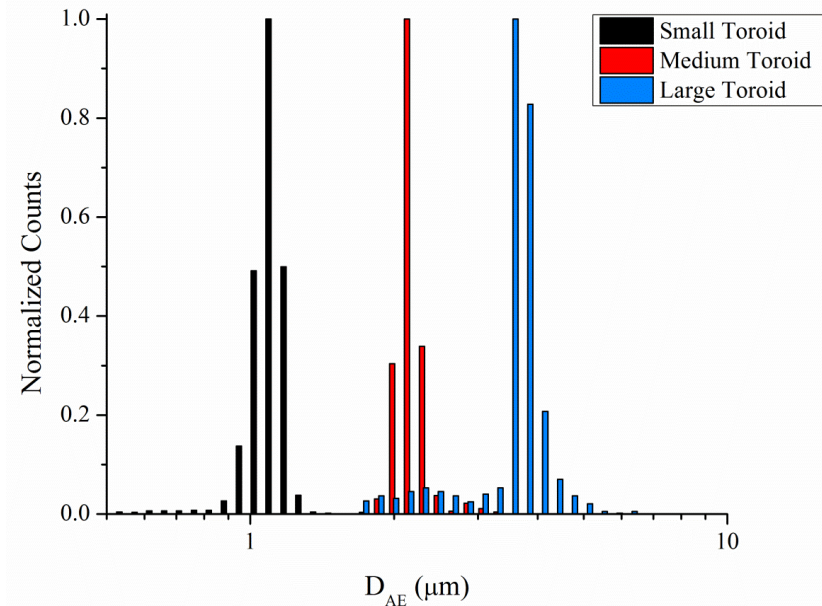
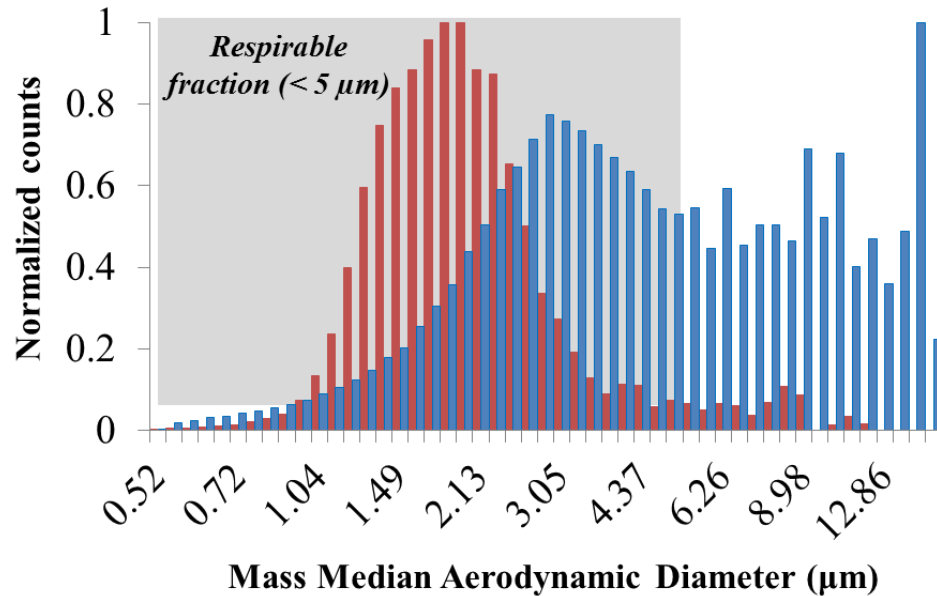
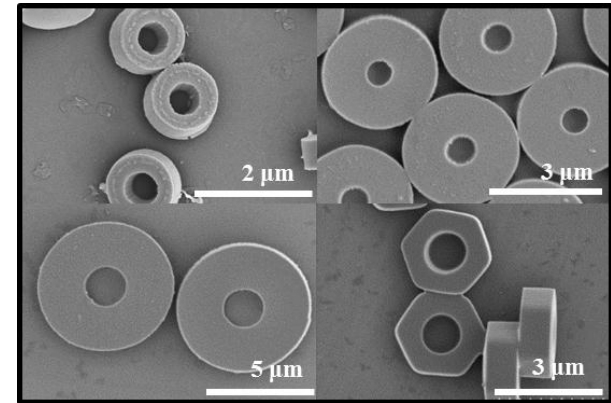
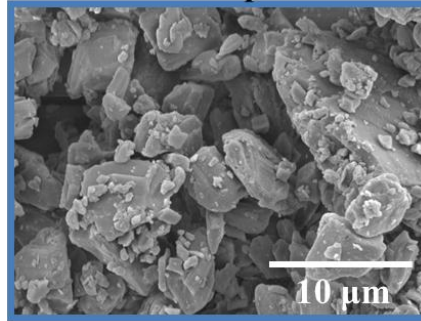


PRINT Particles Allow for Tunable Particle Deposition

1 μm PRINT cylinders

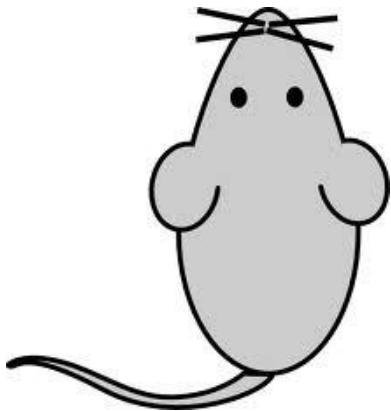


Jet milled powder



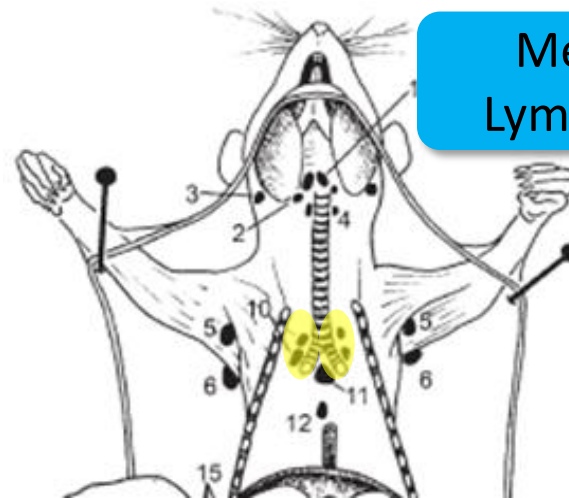
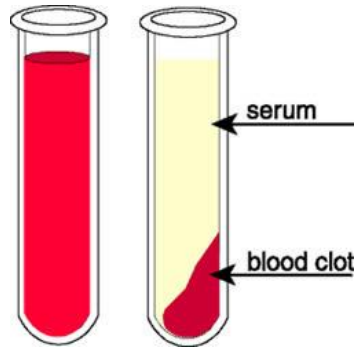
Experimental *In Vivo* Study Procedures

Instillation



Harvest

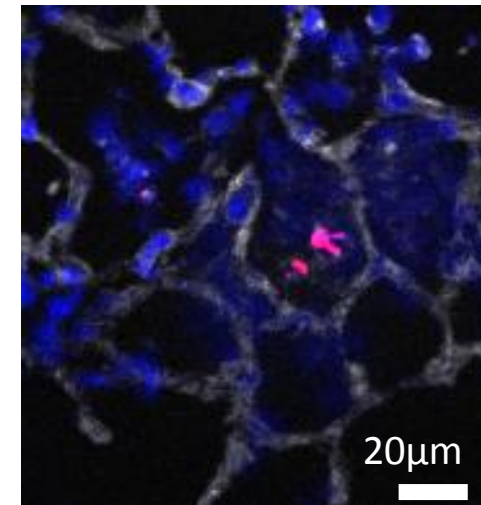
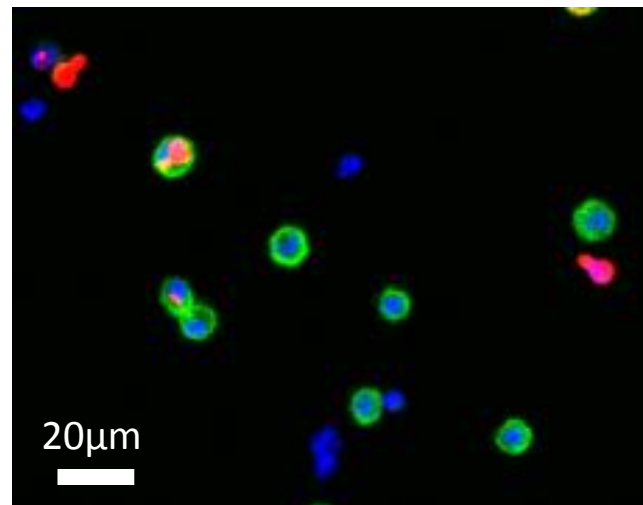
Serum



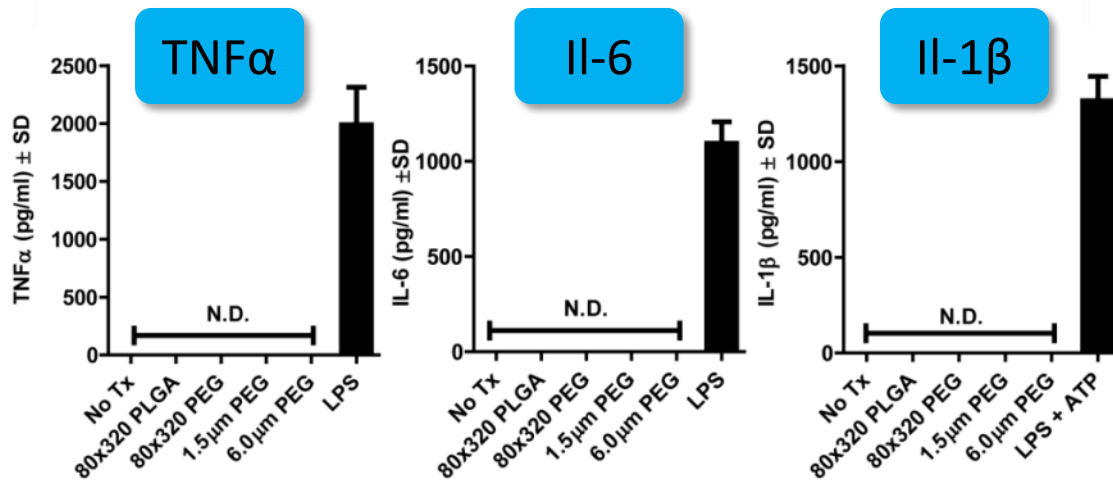
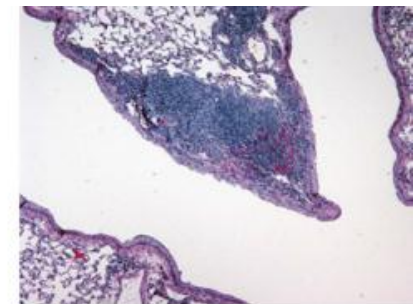
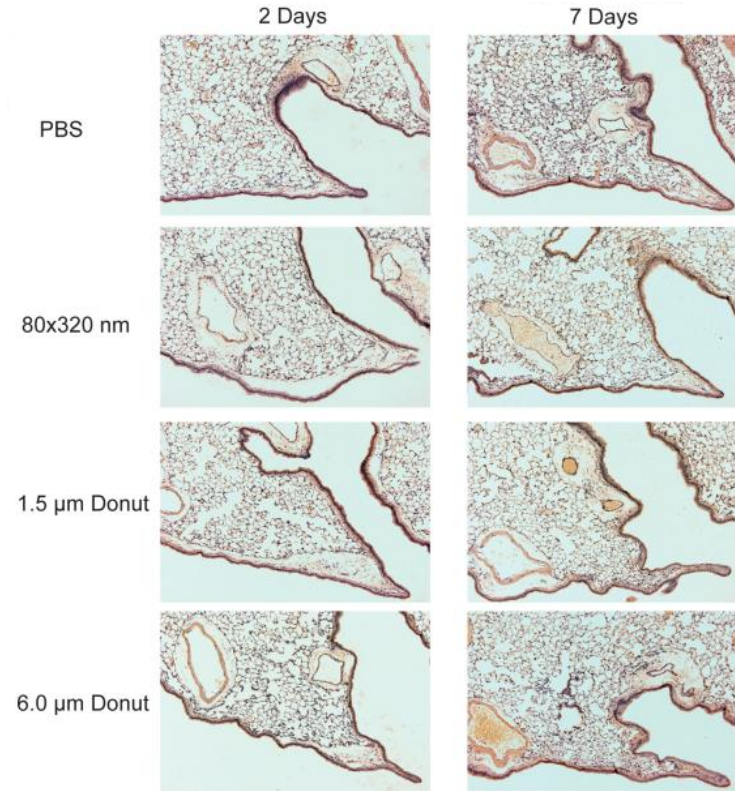
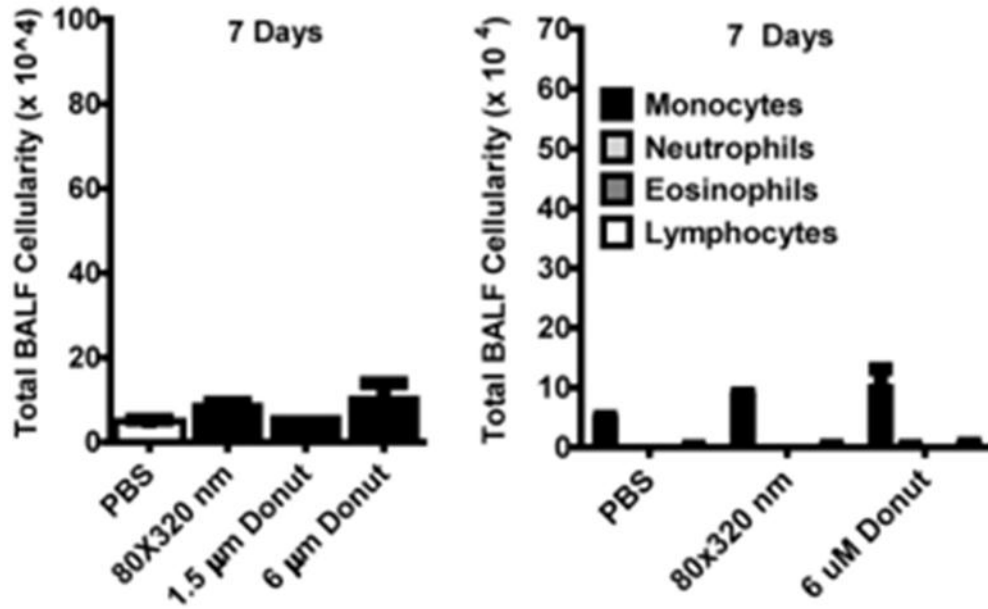
Medistinal
Lymph Nodes

BALF

Whole Lung

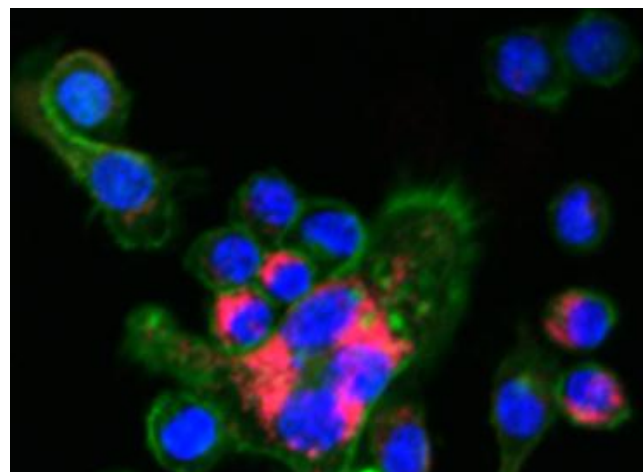
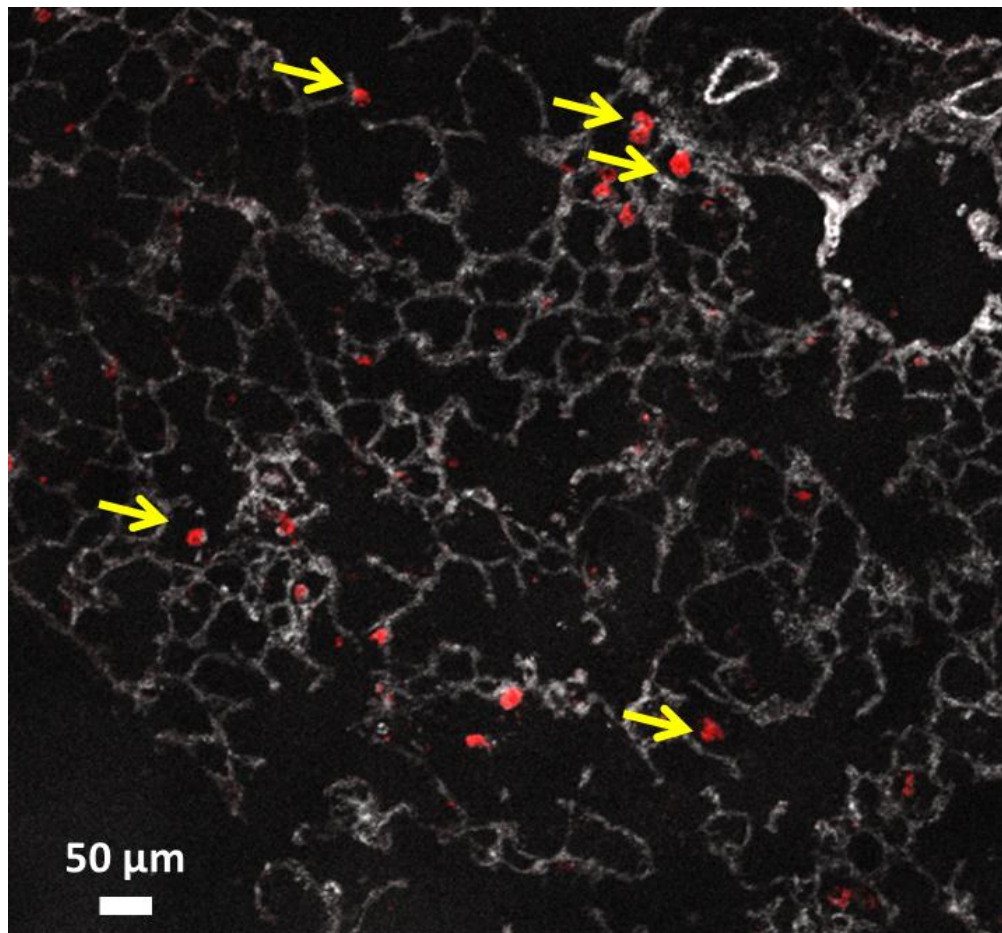


PRINT Particles are Immunologically Inert: No Inflammation or Pathology in Mouse Lungs

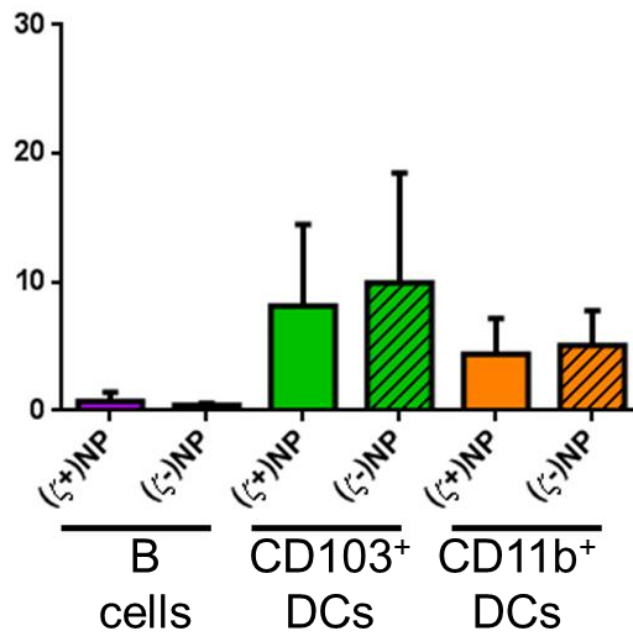


Particles Associate with Key APCs *In Vivo* and Actively Drain to Medistinal Lymph Nodes

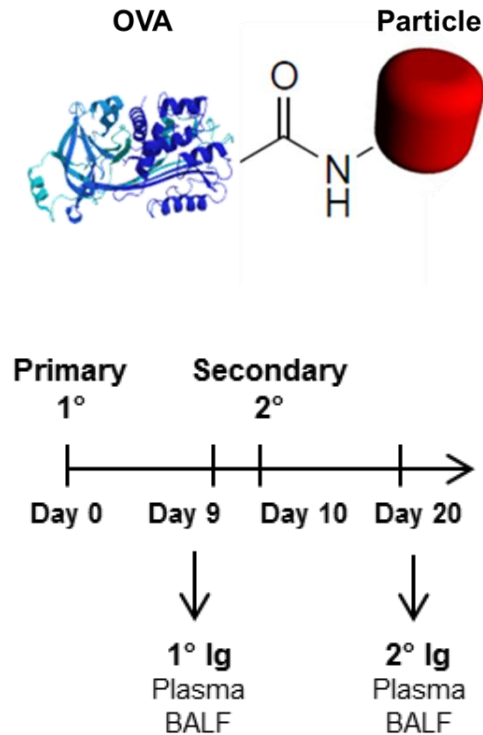
80x320nm Particles After 24hrs



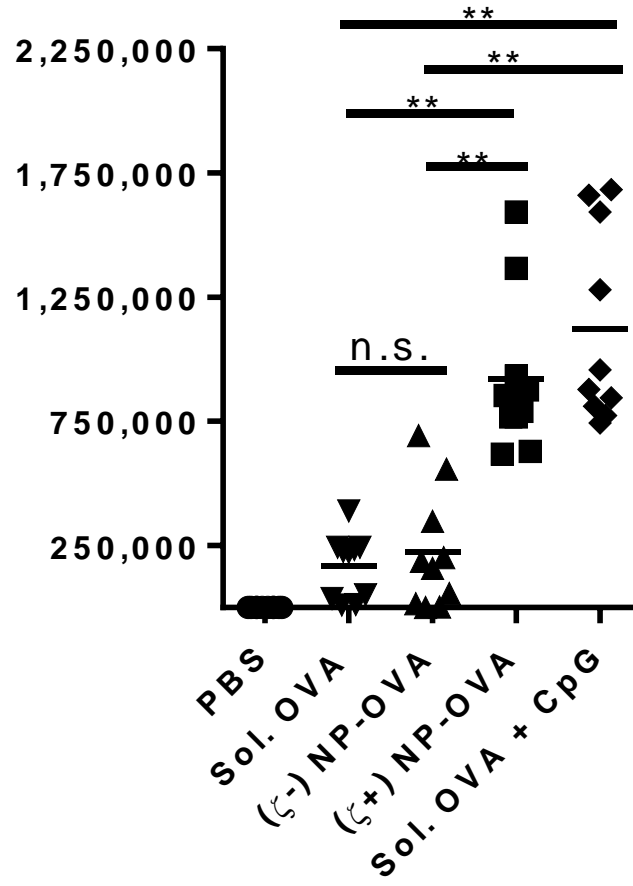
% NP+ Medistinal LN APCs After 72hrs



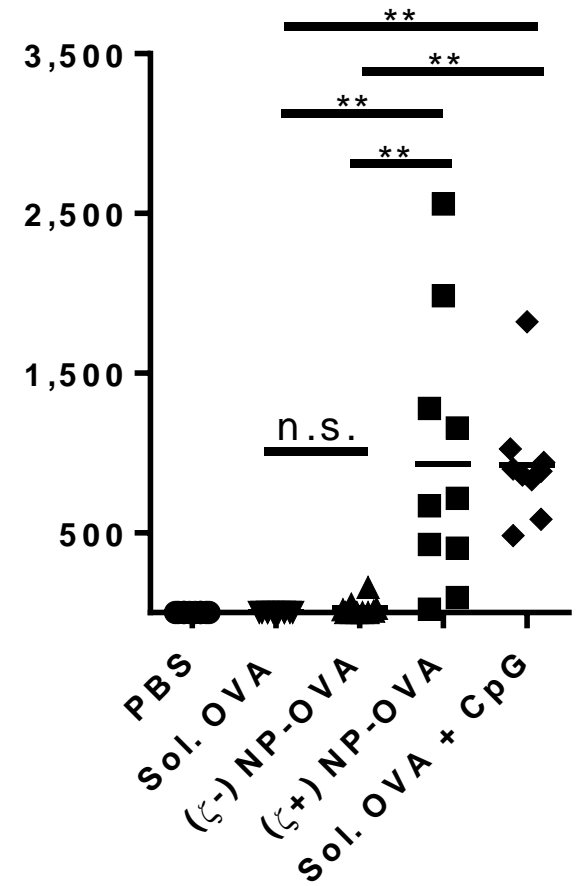
Pulmonary Immunization of Modified Particles Result in Local and Systemic Antibody Production



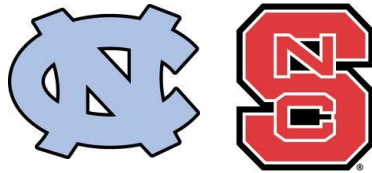
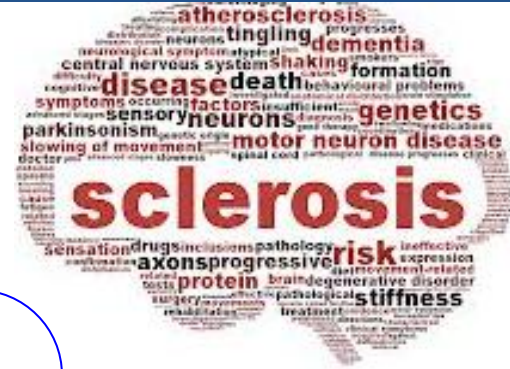
Systemic Ab IgG



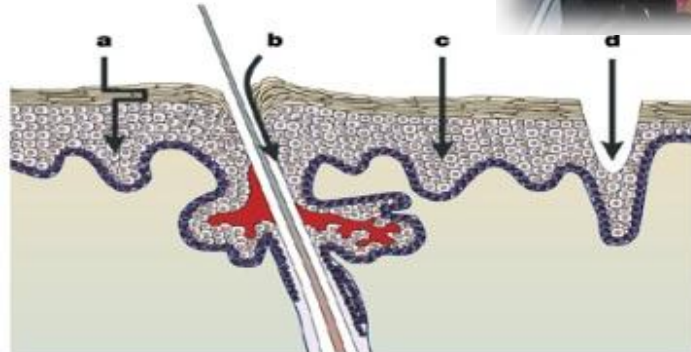
Mucosal Ab IgA



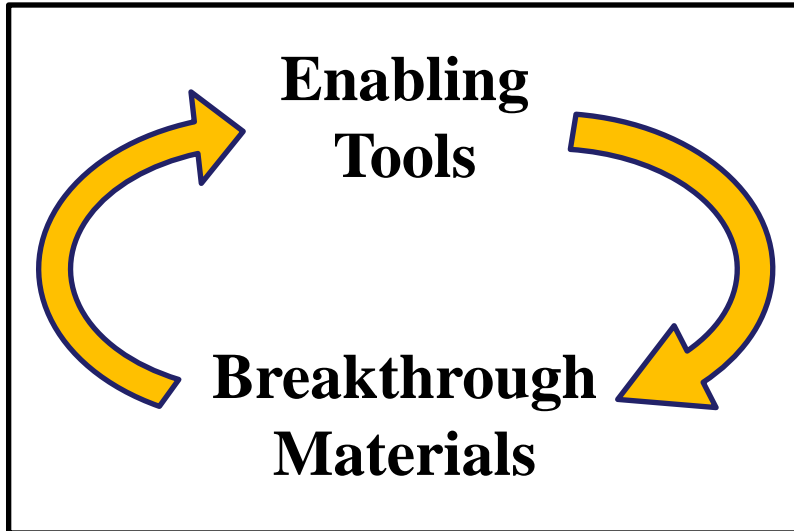
Convergent Science to Address Unmet Needs in Medicine



PRINT



Future of Nanomedicine

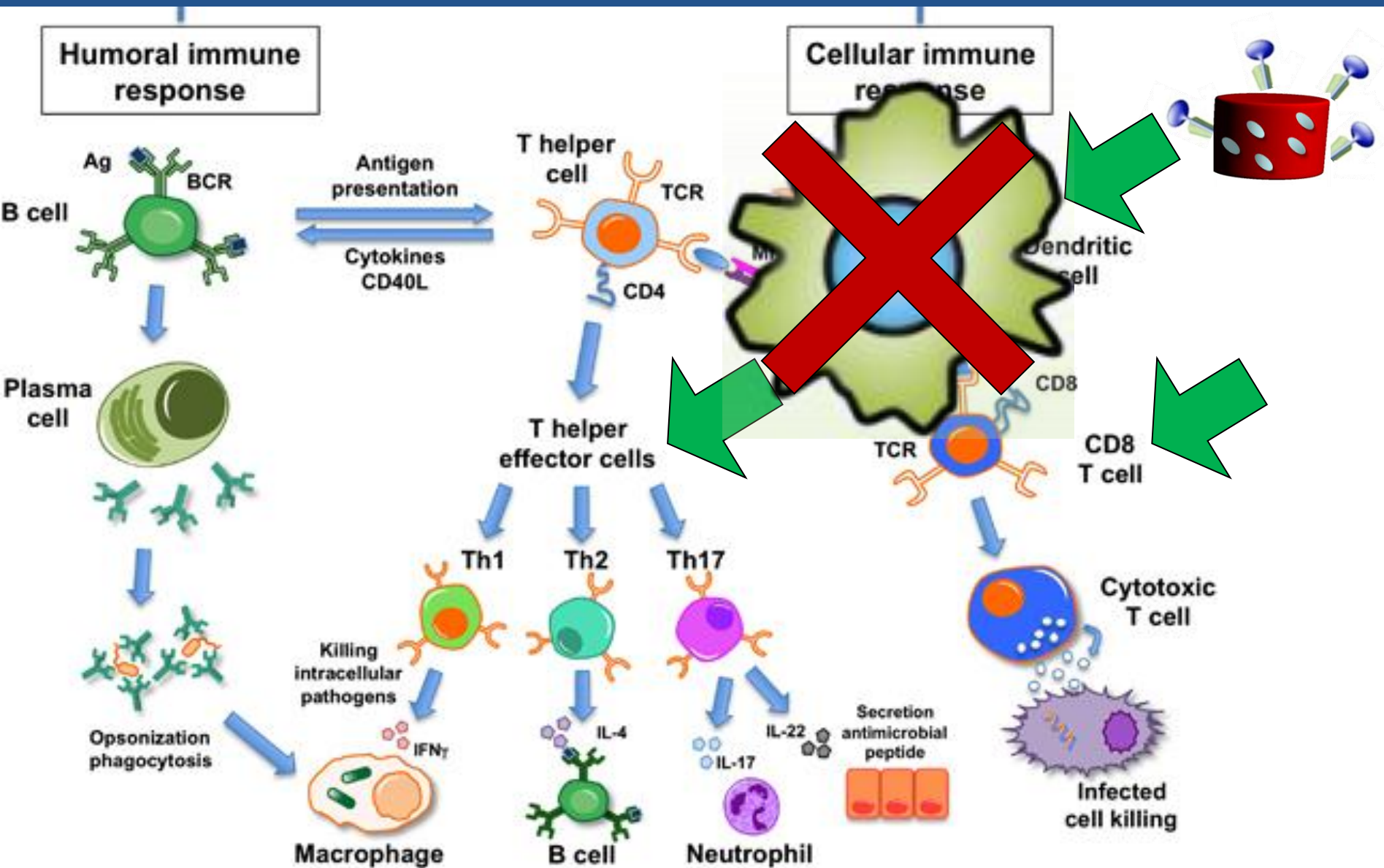


Diversity of Applications

- Cancer therapy & prevention
- Route of administration
- Theranostics
- Antibacterials
- Molecular diagnostics
- siRNA
- Autoimmune disease
- Vaccines

New Buzz Word: Immunoengineering

Future of Nanomedicine: Immunoengineering



Thank you!

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Stu Dunn

Abby Larus

David Sailer

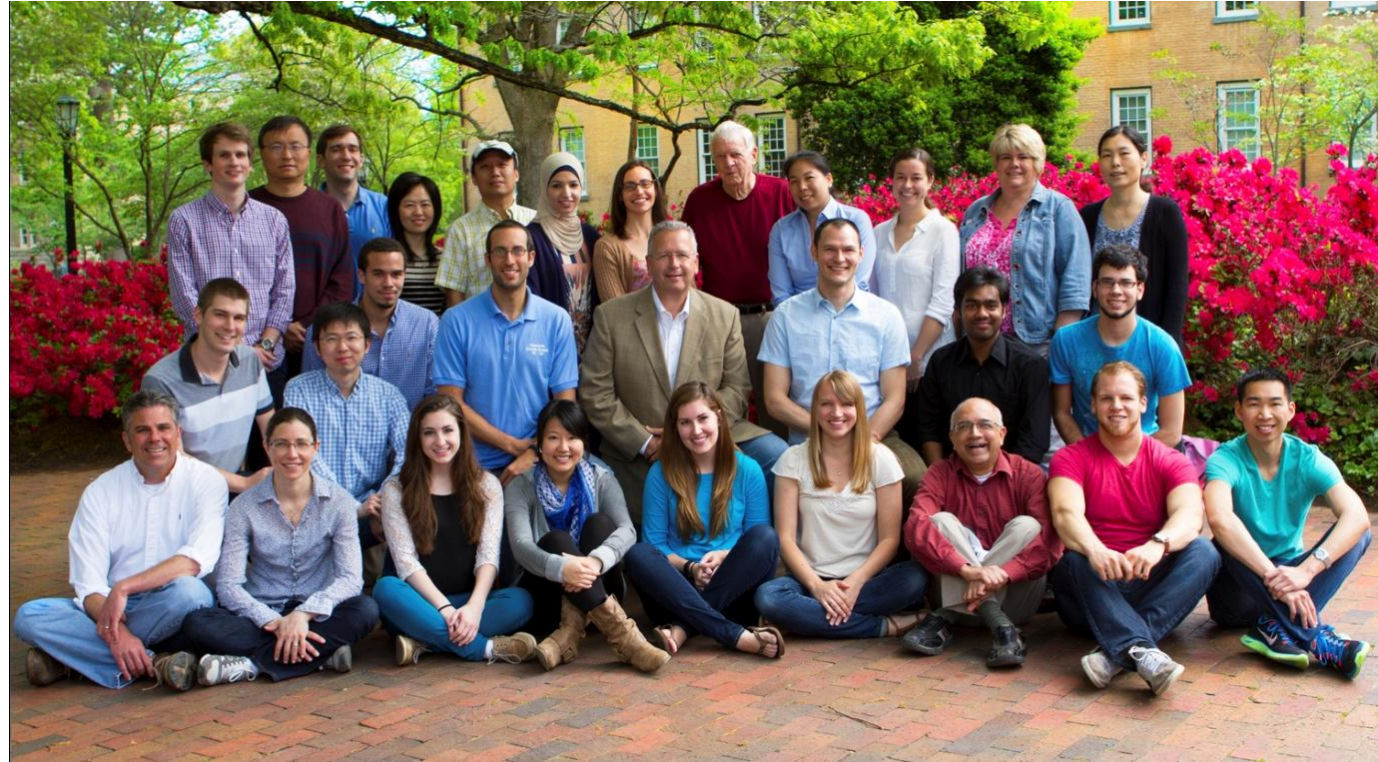
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