American Institute for Medical and Biological Engineering

National Institute of Biomedical Imaging and Bioengineering

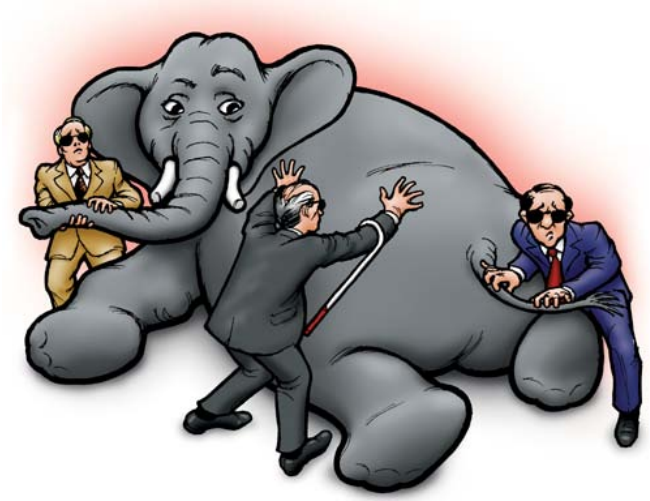
AIMBE/NIH Summit on Validation and Qualification of New In Vitro Tools and Models for the Pre-Clinical Drug Discovery Process

Session 2: Latest Technologies for Pre-clinical Regulatory Science.

12:50 – 1:00 PM	**Introduction** *Rosemarie Hunziker, Ph.D., NIBIB/NIH , moderator*
1:00 – 1:40 PM	**Experience using PBPK Models in Clinical Pharmacology Reviews** *Ping Zhao, Clinical Pharmacology CDER/FDA*
1:40 – 2:10 PM	**Functional in vitro Systems for Drug Discovery** *Mike Shuler, Ph.D., Cornell University*
2:10 – 2:40 PM	**Organs on Chips** *Donald Ingber, MD, Ph.D., Wyss Institute/Harvard*
3:00 – 3:30 PM	**Liver Construct for Drug Screening and Toxicity** *Dawn Applegate, Ph.D., CEO RegeneMed*
3:30 – 4:00 PM	**Stem Cell Technologies for Pre-clinical Drug Discovery** *Nick Thomas, Ph.D., GE Healthcare*
4:00 – 4:30 PM	**Pre-clinical Imaging Technologies** *John Elliott Ph.D., NIST*

Drug/Biologic/Device Approval

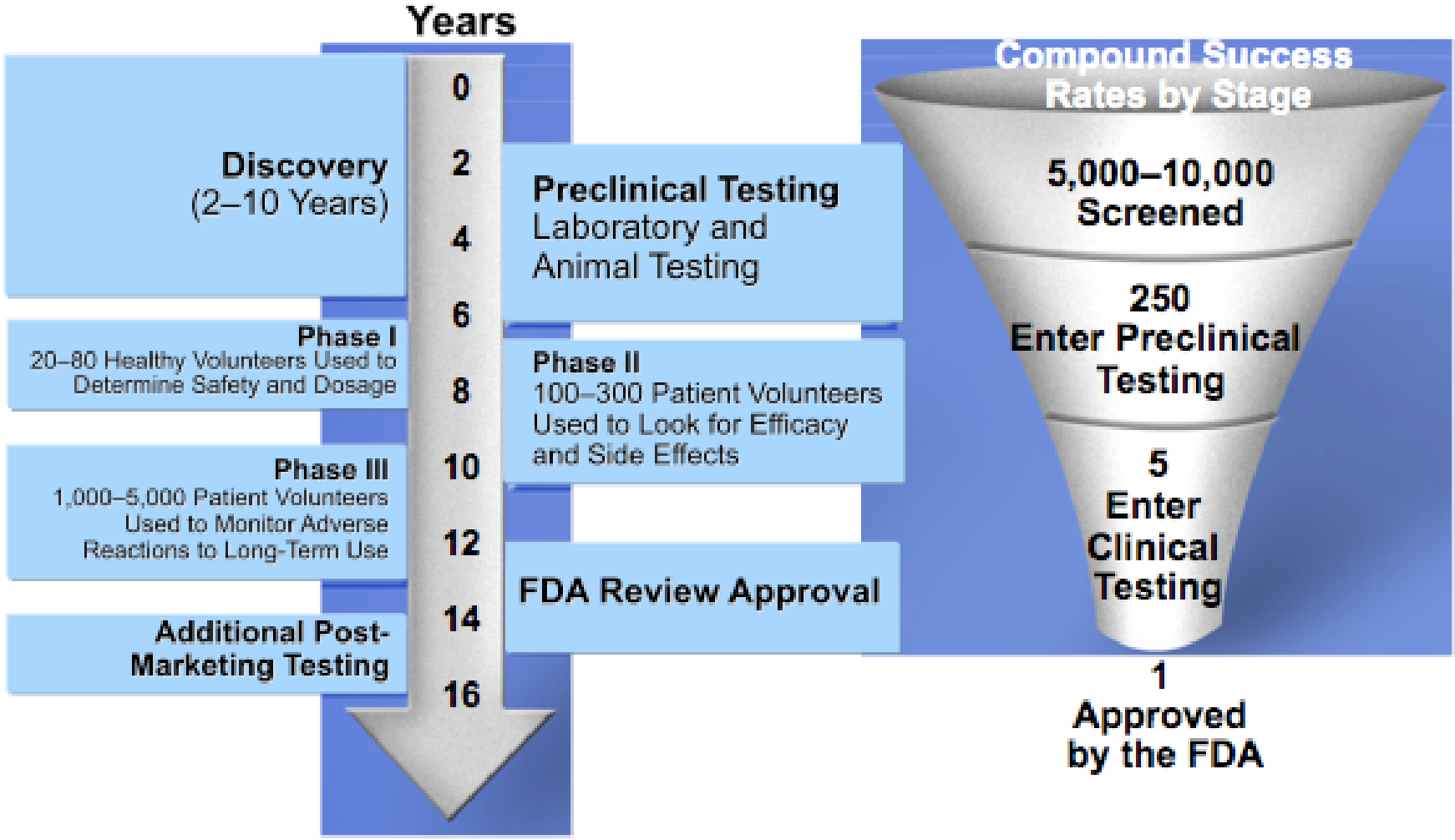
Validation? Qualification? Tools/Assays? Necessary/Sufficient?



- highly complex
- confusing
- culturally inscrutable
- difficult to navigate
- often frustrating

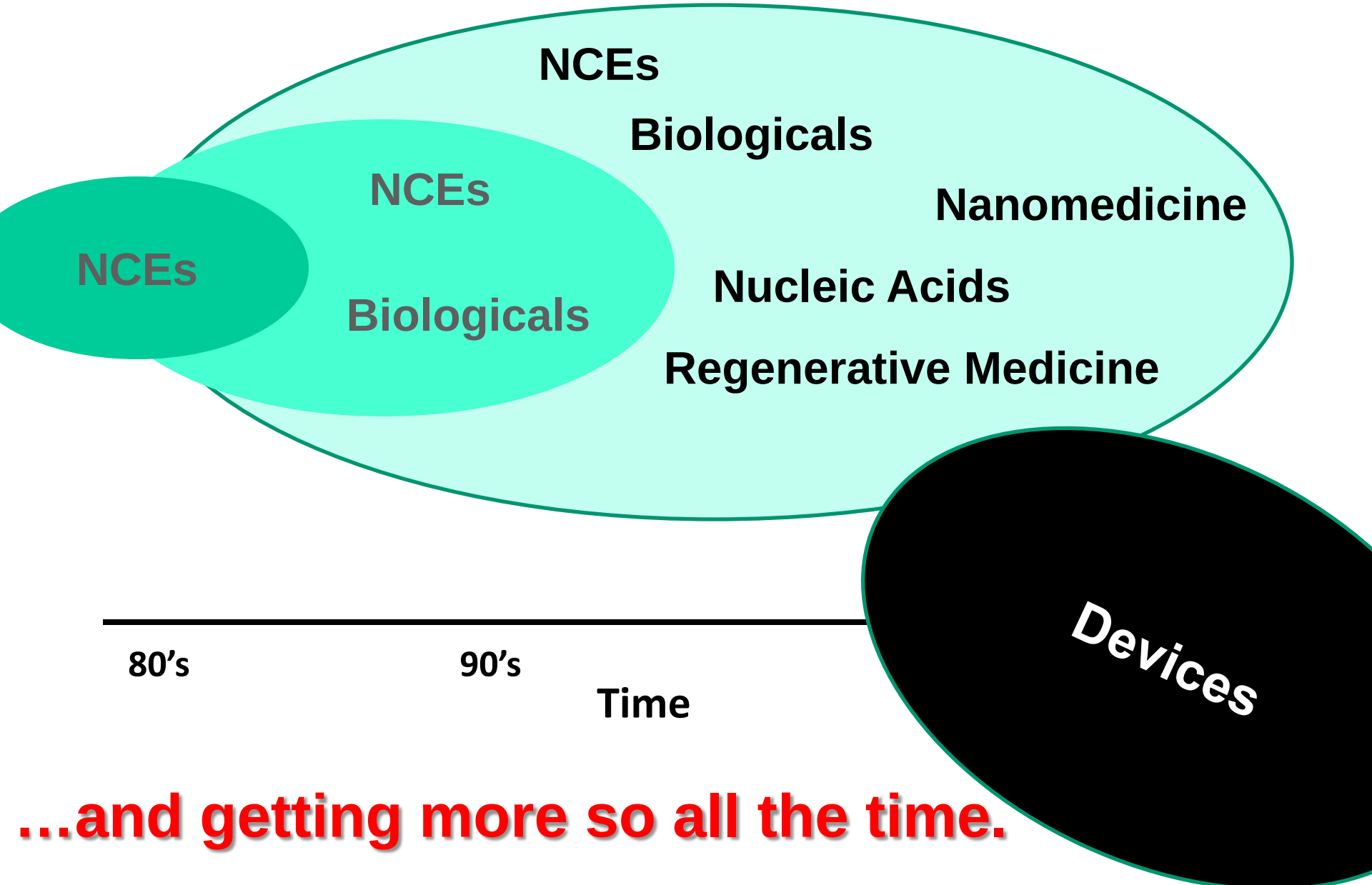
- robust
- reliable
- standardized
- persistent
- legally defensible

Drug Development is Long, Risky, and Expensive…



…and getting more so all the time.

Products are Increasingly Complex…



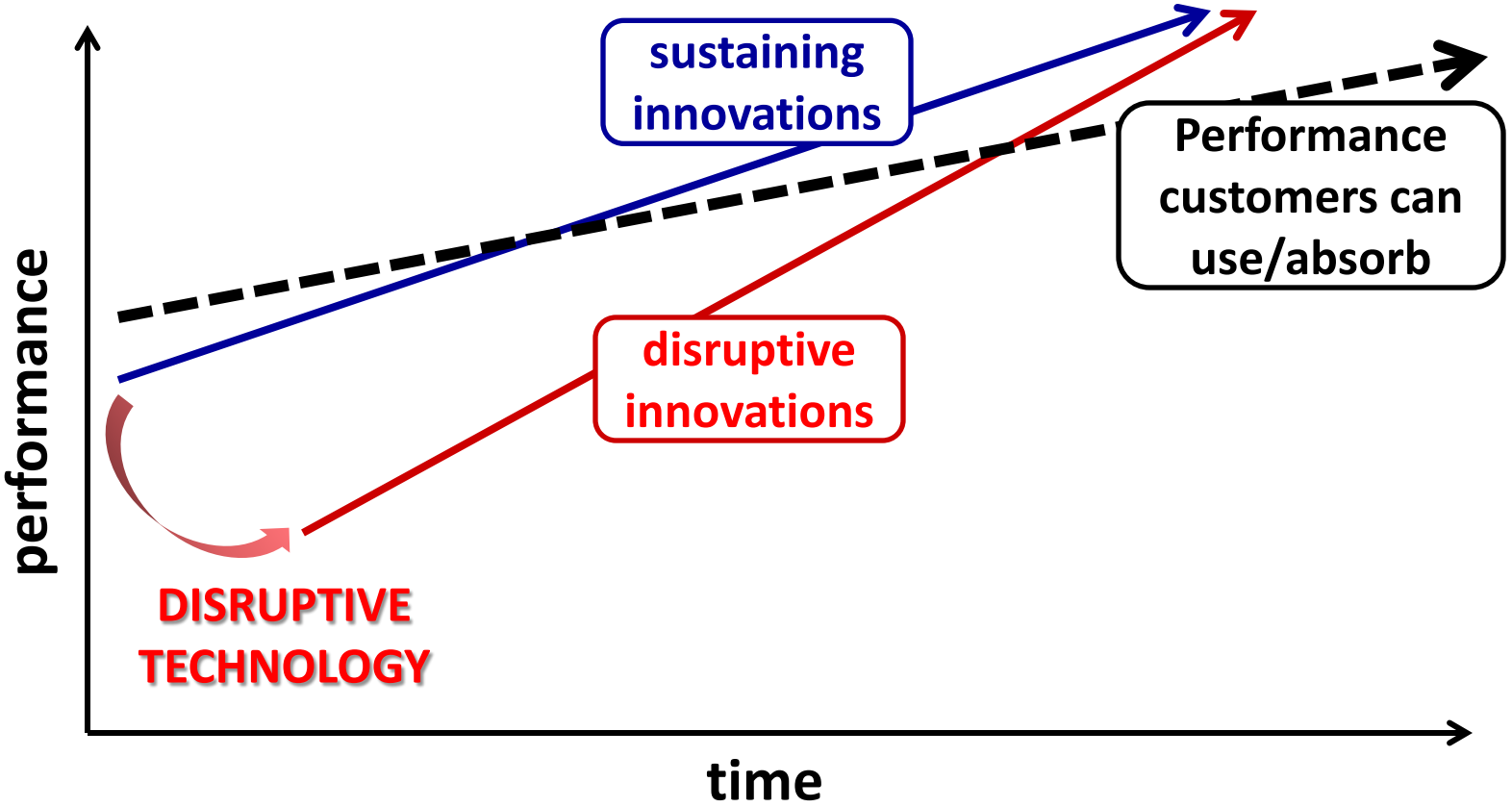
…and getting more so all the time.

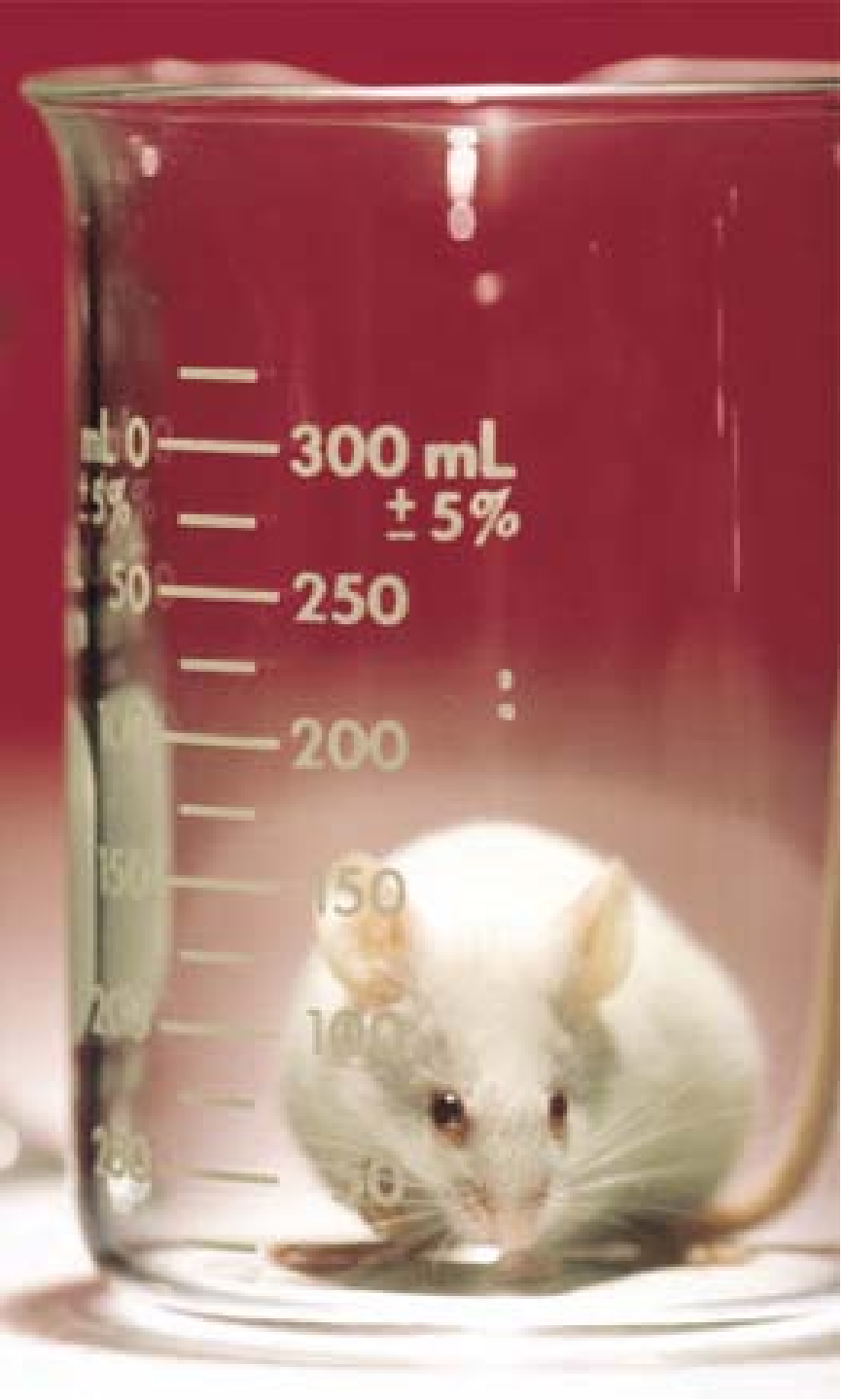
Phase IV (post-marketing) Studies Are Part of Drug Development…

- Screen for rare adverse events in larger populations
- Assess longer-term exposure
- Expand indications or target populations
- Reveal drug-drug interactions
- Compare idealized to actual clinical practice
- “Phase V” can address comparative effectiveness

…and here to stay.

New Technologies are needed for New Challenges





Advanced ADMET: Thinking Outside the Mouse…

- Quantitative Structure-Activity Relationships (QSAR) and Quantitative Structure-Property Relationships (QSPR)
- Drug-drug interactions
- Controlled Release

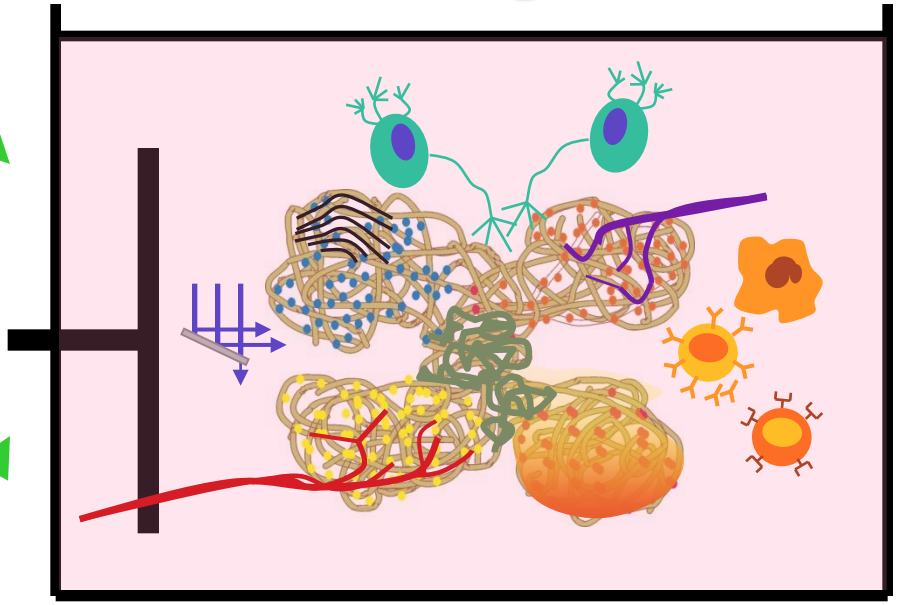
… with modeling and simulation.

Scale-up for Cell-based Assays

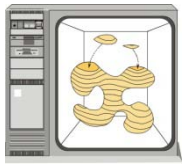
STEM CELLS may be more

- **Robust**
- **Reliable**
- **Standardized**
- **Productive**
- **Storable**
- **Versatile**

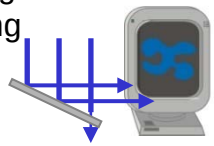
Organotypic Tissue Model from Common Building Blocks



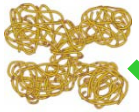
Computational Design
- systems integration
- multi-scale modeling
- simulation
- feedback



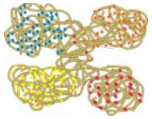
Functional Readout
- real-time, label-free, non-destructive sensing
- imaging



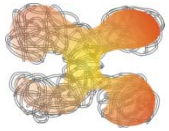
Scaffold
- purified ECM
- synthetic polymers
- composites



Cells
- stem/progenitor
- differentiated
- mixed cell types

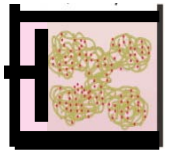


Structure
- porosity
- topography
- stiffness

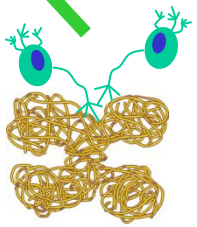


Spatial/Temporal Patterning
- cytokine gradients
- controlled release

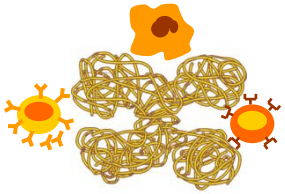
Perfusion
- embedded channels
- vascularization



Bioreactors
- optimized culture conditions
- biomechanics



Innervation
- signal propagation
- coordinated response



Host Response
- generalized inflammation
- specific immunity

Technologies for Today's Discussion: *Where Do They Fit?*

American Institute for Medical and Biological Engineering

National Institute of Biomedical Imaging and Bioengineering

AIMBE/NIH Summit on Validation and Qualification of New In Vitro Tools and Models for the Pre-Clinical Drug Discovery Process

Session 2: Latest Technologies for Pre-clinical Regulatory Science.

12:50 – 1:00 PM	**Introduction** *Rosemarie Hunziker, Ph.D., NIBIB/NIH , moderator*
1:00 – 1:40 PM	**Experience using PBPK Models in Clinical Pharmacology Reviews** *Ping Zhao, Clinical Pharmacology CDER/FDA*
1:40 – 2:10 PM	**Functional in vitro Systems for Drug Discovery** *Mike Shuler, Ph.D., Cornell University*
2:10 – 2:40 PM	**Organs on Chips** *Donald Ingber, MD, Ph.D., Wyss Institute/Harvard*
3:00 – 3:30 PM	**Liver Construct for Drug Screening and Toxicity** *Dawn Applegate, Ph.D., CEO RegeneMed*
3:30 – 4:00 PM	**Stem Cell Technologies for Pre-clinical Drug Discovery** *Nick Thomas, Ph.D., GE Healthcare*
4:00 – 4:30 PM	**Pre-clinical Imaging Technologies** *John Elliott Ph.D., NIST*