IOM Drug Forum

Strengthening a Workforce for Innovative Regulatory Science in Therapeutics Development

Story Landis, PhD September 20, 2011
The promise of regulatory science

• The FDA strategic plan outlines a commitment to incorporate the extraordinary advances being made in basic and applied sciences into advancing therapeutics development.

• Utilize human embryonic stem cells and induced pluripotent stem cells and their differentiated products for regenerative medicine

• Also use them to create “organs on a chip” to screen for safe and effective drugs

• New NIH Common Fund initiative will partner with DARPA and the FDA to develop microphysiological systems

• Addresses FDA goal of modernizing toxicology to enhance product safety
FDA/NIH Innovations in therapeutics development: Exploratory IND

- Need for innovative strategies to screen possible therapeutic candidates for cancer in humans
- Involves very limited exposure and has no therapeutic intent
- Inform decision making on target selection/dose
- Assess PK, biodistribution and target engagement
- Develop and use new Phase 0 technologies
NIH/FDA Partnership and Initiatives

• NIH-FDA Joint Leadership Council (est. 2010)
  – Six working groups currently reviewing proposals for collaboration including:
    • Regulatory Science, Training and Education
    • Drug Rescue and Repurposing; target validation efforts

• Cooperative research grant awards to advance translational and regulatory science.
The NIH-FDA Regulatory Science Initiative

• Four cooperative research grant awards, totaling ~$9 million over three years.  https://commonfund.nih.gov/regulatoryscience/overview.aspx

• The awards address four distinct, high priority areas of regulatory science:
  – A heart-lung micromachine model to test the safety and efficacy of drugs
  – Innovative approaches to adaptive clinical trial design
  – Nanoparticle characterization
  – A novel strategy to predict ocular irritancy
Heart-Lung Micromachine
Donald Ingber, Wyss Institute

GOAL

Demonstrate proof-of-principle for Integrated “Organ-on-Chip” drug screening microdevices

- Contain cultured human cells
- Recapitulate physical microenvironment of living organs
- Measure efficacy, bioavailability and adverse toxicities of therapeutic agents before they enter clinical trials

APPROACH

1. Demonstrate ability of the breathing lung on a-chip device to measure pulmonary absorption, efficacy and toxicity of aerosol-based drugs and nanotherapeutics

2. Demonstrate the ability of the beating heart microdevice to detect cardiotoxicity by measuring changes in cardiac cell contractility, electrical conduction, and tissue inflammation

3. Create an integrated heart-lung microsystem that can can assess effects of aerosolized drugs and nanotherapeutics delivered to the lung on cardiac function and toxicity in vitro
Innovative Clinical Trial Design

Project Overview
William Barsan, Univ. Michigan

• To design innovative, adaptive clinical trials for the evaluation of drugs and devices used in the emergency care of patients with acute neurological illness or injury, including:

• Identification and qualitative characterization of key steps and barriers, both intellectual and logistical, related to the acceptance and implementation of adaptive clinical trial designs among stakeholders.
Characterization/bioinformatics-modeling of nanoparticle:complement interactions
Dennis Hourcade, Washington University

Specific aims

• Develop standardized protocols using human in vitro and mouse in vivo models to characterize the capacity of lipid-encapsulated nanoparticles to activate complement.

• Develop and synthesize lipid-based nanoparticles with varying size, density, surface properties, and drug moieties.

• Develop structure-activity relationships to predict complement activation
NCATS
• Proposed National Center for Advancing Translational Sciences
  – To advance the discipline of translational science and catalyze the development and testing of novel diagnostics and therapeutics across a wide range of human diseases and conditions
  – To view drug development pipeline as a scientific problem – ripe for experimentation and process engineering: seek bottlenecks, create solutions.
  – To engage in training of translational investigators
NIH funded training

• Each NIH institute has individual and institutional training awards that support pre and postdoctoral fellows.
• NIGMS and a subset of institutes provide funds for training MD/PhD scientists.
• CTSAs offer significant training opportunities.
• The NIH intramural program also serves as a training site.