Session 3: SWOT Analysis

Imaging
Tox21
Genomics

Imaging for safety assessment

- Strengths
  - Longitudinal study design and minimal invasiveness
  - Acceptance of imaging by the medical community enhances its utility as a translatable pre-clinical biomarker
- Weaknesses
  - No standardized approach
  - ~~Deficits in quantization~~
    - Can be highly quantitative.
- Opportunities
  - Broader applications due to recent advances in resolution and standardization of approaches
- Threats

Tox21: high-throughput screening

- Strengths
  - Capability to test thousands of chemicals for toxicity-related activity in human cells
  - Very small amounts of compound are needed for screening
  - Rapid generation of test data
  - Eliminates or greatly reduces use of animals
  - Large number of cell lines
  - MOA information
- Weaknesses
  - High throughput screens currently lack means to provide bioactivation
  - Small number of suitable assays for genotoxicity endpoints
  - Compounds that can be tested are limited to those that are DMSO-soluble, nonvolatile, stable in solution for a period of time, etc.
- Opportunities
  - Ability to develop approaches to assess, on a wide-spread scale, differential susceptibility
  - Ability to identify susceptible subpopulations using genomic assays and approaches like the 1000 genomes project

Tox21: high-throughput screening

- Threats
  - Challenges inherent in anchoring the compound profiles generated using these technologies to results obtained in “gold standard” traditional tests for genotoxicity with sufficient accuracy to be acceptable to regulatory agencies
  - Selection of appropriate cellular pathways or endpoints to be screened
  - Bioinformatics and analyses

Genomics approaches

- Strengths
  - Query large swaths of biological space in one assay
  - Pathway / mechanistic info
- Weaknesses
  - In vivo genomics dependent on animals
  - Ability to interpret complex data
  - Variability (time-dependent, platforms, dose)
  - Lack of mechanistic anchoring (more correlative data)
- Opportunities
  - High dimensionality allows for querying of large amount of biological space including genotoxicity and beyond (i.e., one assay to query all)
  - Potential to rapidly identify a no effect dose that will define a bottom end on any traditional toxicity study
- Threats
  - Metrics (i.e., genes and pathways) are different than traditional endpoints and no model is 100% predictive of an outcome
    - If it is no possible to change metrics (i.e. pathology to pathways) this will significantly hinder development in the regulatory arena

- Future in vivo models used for imaging genotoxicity
- Throughput of imaging technologies
- Use of radioactive labels for studies
    - Relatively low amt