

ILSI/HESI Genomics Committee: Overcoming Challenges to Share Data on Non-Proprietary Compounds

Current Committee leadership:

Syril Petit, HESI

Cindy Afshari, Amgen

George Orphanides, Syngenta

Database Steering Committee:

Jennifer Fostel, LMIT, NCT

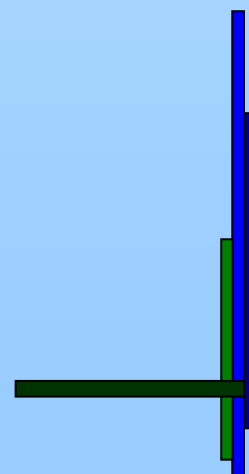
Mike Lawton, Pfizer

ILSI / HESI Genomics Committee

- ILSI = International Life Sciences Institute
- HESI = Health and Environmental Sciences Institute
- Genomics Committee = Technical Committee on the Application of Genomics to Mechanism-Based Risk Assessment

ILSI / HESI Genomics Committee



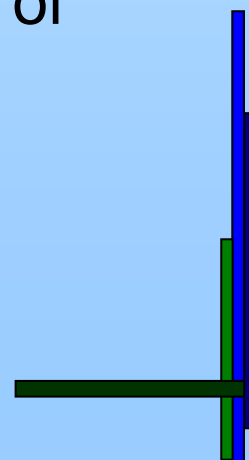
- The mission of HESI's Technical Committee on Application of Genomics to Mechanism-Based Risk Assessment is to advance the scientific basis for the development and application of genomic and proteomic methodologies to risk assessment.
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Long-term objectives:

- Provide a scientific forum to facilitate further development and advances in genomics and proteomics methodologies to **increase the utility of gene expression data for mechanism-based risk assessment**
- Facilitate a broad-based, multinational **collaboration** involving academic, governmental and industrial institutions
- **Develop public information** of interest to the specialist user and the scientific community at large – to include details of experimental design, materials and methods, and study results
- Contribute to the **greater understanding of toxic mechanisms** and identification of appropriate **biomarkers** so that the toxicity observed in animals and the extrapolation of these observations to humans results in meaningful risk assessment
- Contribute to the **development of publicly available databases**, to include details of experimental design, methods, and study results

Technical Challenges



- Genomics Committee formed in 1999
 - Technical challenges at that time:
 - No public databases available
 - Technology not validated; multiple array platforms
 - Lack of standard tools, methods, study designs
 - Lack of robust analysis tools
 - Lack of consensus on interpretation; relevance of single gene change
 - Uncertain regulatory applications, environment
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Scientific Questions:

- Can known pathways and mechanisms of toxicity can be associated with gene expression profiles?
- Can this information be used for risk assessment?
 - develop data using well-characterized toxicants with well-known mechanism of toxicity under controlled conditions
 - evaluate gene expression changes in the context of other toxicity measures
 - use the information obtained to identify potential biomarkers and interspecies extrapolation issues
 - help to build consensus on optimal approaches for interpretation of gene expression data and its application to risk assessment

Four Working Groups

- **Hepatotoxicity:**
 - 2 agents, 2 doses, 3 times, 2 in-life studies
 - 14 institutions, 7 array platforms
- **Nephrotoxicity:**
 - cisplatin, gentamicin, puramycin, 2 doses, 3 times
 - 8 institutions, 6 array platforms
- **Genetic Toxicity:**
 - 14 genotoxicants, 5 array platforms
- **Database Steering Committee**
 - oversee contract with EBI to extend ArrayExpress

Data “ownership” not an issue

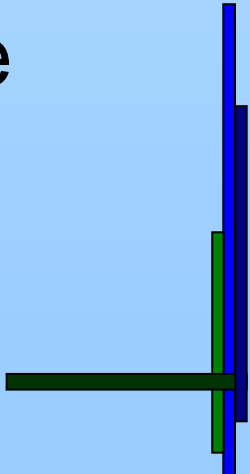
- Committee members agreed that the data and tissue / RNA samples from the in-life studies were to be shared with all participating members of the Committee.
- Individual labs “owned” the data they generated but committed to sharing outcomes with the Committee, and to publishing data jointly.
- All data were to be made publicly available per HESI Committee requirements
- Some microarray sequence probes were considered to be proprietary.
 - these reporters were not identified to the public

Data transfer became an issue

- Development of database infrastructure followed generation of data, often with significant **time lag**
- Transfer of data (originally) was a very **manual** process
- Committee members were new to large-scale data exchange / management; some **inefficiencies** surfaced as a result

Current status



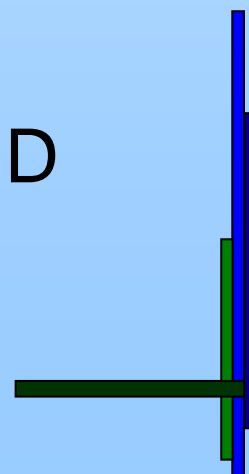
- Tox/MIAMExpress, web interface to EBI curation database, used to load data from **several thousand hybs**
 - Tox/MIAMExpress captures treatment information, clinical chemistry and histopathology observations about the sample.
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Data sharing, current projects

- Gathering data from current members for retrospective analysis
- How to manage donor identity
 - what if “my” data are the outlier?
- How to facilitate data transfer
 - if it’s not easy as pie I don’t have time
- How to maximize benefit
 - What does sharing data do for me?

Managing donor identity



- Anonymize the donors to the public.
 - only identify the institutions within the Committee
 - How to provide useful information that will not spill the beans?
 - If company X is the only one using array type Y, then array type will disclose the ID
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Facilitating data transfer



- Make it rapid
 - close in time to the data generation / sharing (have the DB ready)
 - make it electronic as much as possible
- Make it conform to standards
 - controlled vocabularies commonly used within the donor community is a bonus
 - use a standard form for data submission

What is the benefit to me?

- Support the public good
- Understand “how I stack up”
- Address questions I couldn’t answer alone
- Provide a standard analysis platform, comparator data
- Provide useful, validated analysis tools

Acknowledgements.....



- HESI
 - Cyril Petit
 - Candace Hamilton
 - Genomics Committee
 - Cindy Afshari, George Orphanides (current co-chairs)
 - Bill Pennie, Pete Lord (previous co-chairs)
 - Mike Lawton (co-chair of Database Working Group)
 - EBI (European Bioinformatics Institute)
 - Susanna-Asunta Sansone
 - Philippe Rocca-Serra
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