

Report 52: Opportunities in Translational Animal Models

Convener: Tom Vogt

Brief History: Animal models represent a powerful experimental approach across a range of research questions in environmental health. The choice of which animal models to pursue is driven by the specific biological question to address. The questions posed were: 1) does the NIEHS have a comprehensive and integrated approach to the selection and use of translational animal models, 2) are there opportunities for new approaches to improve relevance to environmental health, and 3) is there opportunity or value to broaden a focus on traditional animal approaches to animal population type approaches.

Discussion Highlights:

- An important health research area is understanding genetic variation to risk susceptibility and health and disease
- The rodent models represent a rich source of historical data, advanced experimental manipulation, well characterized profiles, and cost containment.
- The group championed that there is a valuable opportunity to broaden the use of emerging mouse genetic reagents to mine the value of genetic variation and to look to relate the genotype: phenotype response to the understanding of human variation in risk, response, and health. Specifically the group championed investment in the mouse *genetic diversity outcross* and the *collaborative cross* as enhancements to gaining understanding to the efforts focused on an inbred strain or F1 strain for screening and testing.
- In consideration of the potential resource ramifications of multiple strains by multiple experimental tests (single agents, dosing regimens, complex mixtures etc.) the group suggested there needs to be consideration of use of higher throughput screens in simpler model organisms, increased effort in modeling and simulation, and increased efforts in integrating human variation data with the model organism variation to prioritize experiments with highest human health impact.
- Outside the traditional experimental model discussion explored the potential value of “eco-toxicity” in natural populations to explorations of companion animal studies as a correlative read-out for shared living environment with humans. One exploration was regarding companion animals in common environment with similar health responses (allergies). There was a strong sentiment that the value proposition would best focus resources on human and experimental translational model research.
- It was unclear to the group what is the level of coordination and communication between NIEHS activities in translational animal models with the strategies and activities of ex-USA efforts (Western Europe etc).

Recommendations:

- Strategically explore and exploit the emerging datasets on correlating human variation to health by an increased use of genetic diversity in the rodent model to address questions in environmental health. Grapple with the real value and the challenge of looking to develop new approaches against the inertia of large data sets collected in single species and/or strains.
- For translatability in the rodent model in addition to leveraging genetic variation fully explore the use of genetically engineered approaches to “humanize” the response to xenobiotics by germline engineering of Phase 1 and Phase 2 metabolizing genes in the rodent model.
- Strategically develop an overarching approach across the span of experimental model organisms (from bacteria to nonhuman primates) so that the information, infrastructure, communication, and governance are in place to efficiently and effectively address the questions of highest importance.
- Seek a strategic approach that has the NIEHS divisions to work in an integrated fashion in the translational animal models approach to addressing questions in environmental health—shared goals and shared datasets.
- Seek a strategic approach that is maximizes the efforts of other groups in advancing the strategic translational animal models capability (e.g. Computational Toxicology at EPA, rodent genetic resources and uses, systems biology data, etc.)

Discussion Participants:

Christopher Bradfield, Gina Goulding, Michele LaMerrill, Richard Mural, Robert Sills, Thomas Vogt, and Richard Woychik