Gene x Environment x Development Interactions (GEDI)
NIDA Strategic Planning Workgroup

April 28, 2015

Workgroup Meeting 1 of 5

Co-Chairs:

Naimah Weinberg, M.D. (NIDA)

Jonathan Pollock, Ph.D. (NIDA)

Agenda

- Introductions/Identification of participants
- Presentation of requested data from NIDA staff
  - References for studies presented April 17, 2015
  - Human vs. animal studies
  - Longitudinal vs. cross-sectional human studies
- Summary of major issues so far
- Questions/comments
- Action Items
  - Narrowing topics for in-depth discussions
  - Any further resources needed?
- 5 Minute Public Comment Period
- Adjourn

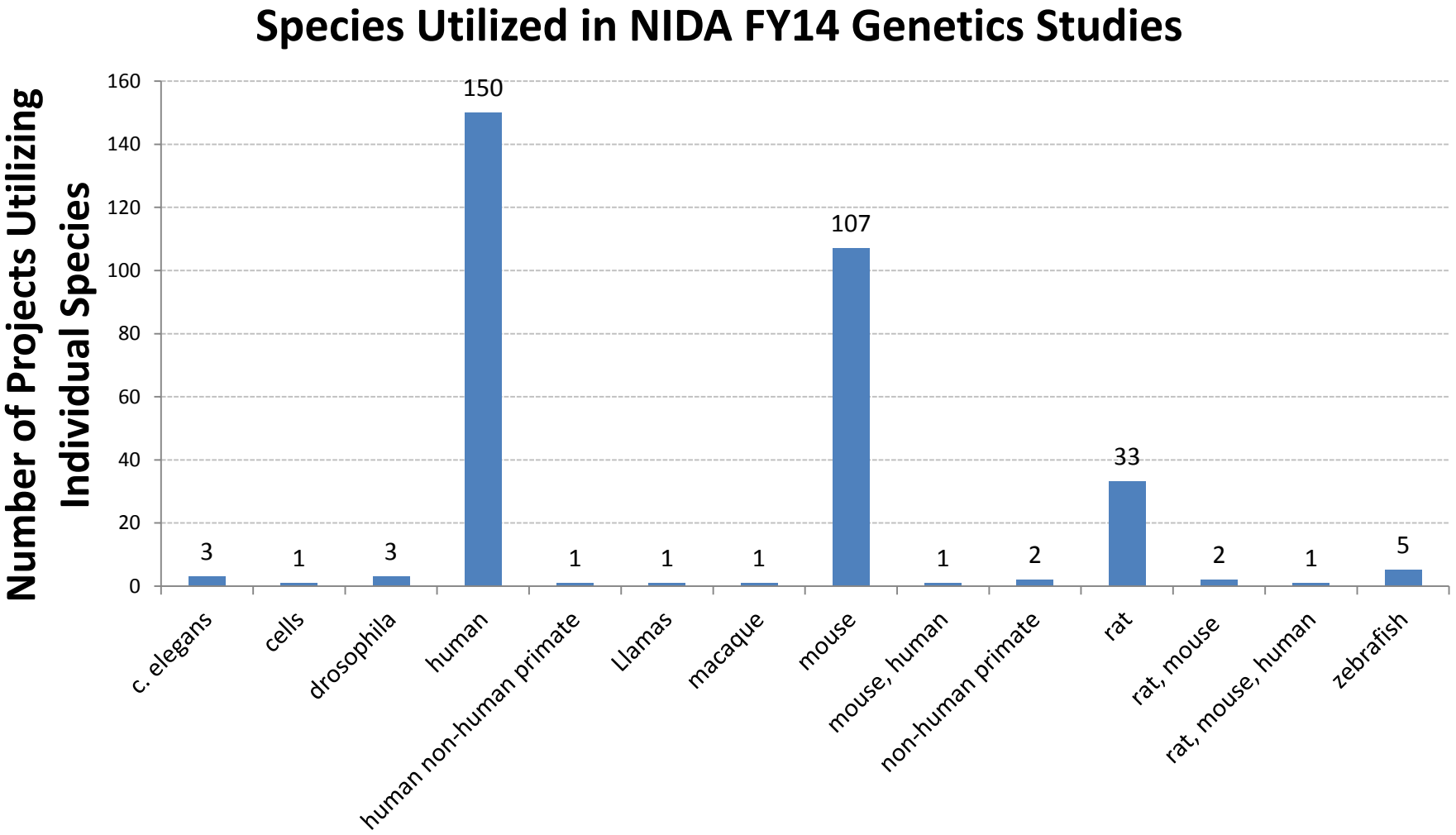
GEDI Work Group Members

NAME	AFFILIATION
WORKGROUP CHAIRS	
Naimah Weinberg, MD	NIDA
Jonathan Pollock, PhD	NIDA
EXTRAMURAL WORKGROUP MEMBERS	
Danielle Dick, PhD	Virginia Commonwealth University
Margaret Daniele Fallin, PhD	Johns Hopkins Bloomberg School of Public Health
Hugh Garavan, PhD	The University of Vermont
John Rice, PhD	Washington University School of Medicine
E. Jane Costello, PhD	Duke University Center of Developmental Epidemiology
William G Iacono, PhD	University of Minnesota
Kenneth Kendler, MD	Virginia Commonwealth University
Eric Johnson, PhD	RTI International
Gustavo Turecki, MD, PhD	McGill University
NIH STAFF	
Maureen Boyle, PhD	NIDA
Hal Gordon, PhD	NIDA
Raul Mandler, MD	NIDA
Michele Rankin, PhD	NIDA
Joni Rutter, PhD	NIDA
John Satterlee, PhD	NIDA

Requested Info: Citations

- Reference Materials GEDI.docx
  - **Citation information**– for genetic studies presented during the April 17 meeting
  - **Web resources** – hyperlinks to the web resources presented during April 17 meeting
  - **WebEx Event login instructions** – participant emails for panelist login; instructions for audio connection

Requested Info: Species Utilized in NIDA FY14 Genetics Portfolio



*311 of 331 studies reported

Requested Info: Longitudinal vs. Cross-sectional Studies

Study Characteristic	Number of Projects
Cross-sectional studies*	24
Utilizing postmortem tissue	13

*analysis restricted to R01s, FY14 NIDA Genetics portfolio

Summary of Last Meeting April 17, 2015

- Work group members suggested that NIDA consider the following recommendations:
  - Larger data sets are needed to conduct GxE research to identify associations, particularly for drugs other than nicotine.
  - Examination of phenotype and environment is needed.
  - Prioritize data-sharing on phenotyping.
  - Longitudinal study design and sophisticated causal modeling could be used to advance understanding of etiology/causality.
  - Training future GEDI investigators will require a multidisciplinary approach.

Feedback from GEDI Panelists: Dr. Turecki

- Research areas to prioritize:
  - Research examining epigenetic mechanisms of addiction (epigenetic mark modification, temporal dimensions and avenues for intervention)
  - Studies examining cell type specific epigenetic markers in peripheral and CNS tissues
  - Translate epigenetic mechanisms of addiction identified in animals to humans.
  - Examine the potential of small, non-coding RNAs as biomarkers for addiction phenotypes
- Resources needed:
  - Generation of epigenomic reference maps from different brain regions at cell-level resolution
  - Biobanks of both human and animals tissues are essential
  - Increased sequencing capacity and bioinformatics/computational resources to analyze concomitant, multiple marks
- Benchmarks to achieve:
  - Consistency of research findings between different labs and across animal models and related human phenotypes
- Training needs:
  - Increased bioinformatics training
- Technologies to leverage:
  - CRISPR for targeted epigenetic modification
  - Optogenetics
  - More efficient vector systems

Feedback from GEDI Panelists: Dr. Johnson

- Research areas/actions to prioritize:
  - Genotyping the many existing samples that lack sufficient funding
  - Large-scale GWAS comparison of epigenetics in brain tissue between those addicted vs. non-using controls
  - Identify biomarkers for addiction
  - Require broad sharing of environmental risk factor and phenotype data
  - Expand basic research across the spectrum of genomics to other omics to provide insights into HIV + SUDs
  - Bring discovery science tools (e.g., Omics) to real world treatment settings using large numbers of patients to focus discovery on clinical outcomes
  - Leverage ABCD study biospecimens for linking omics to imaging
- Resources needed:
  - Increased funding; targeted RFAs
  - Revise dbGaP requirements to allow sharing of environmental and phenotype data
- Benchmarks to achieve:
  - The number of new samples genotyped under the NIDA existing samples (Smokescreen) project.
  - Tracking number and success of new awards addressing each targeted area
  - Tracking the impact of data sharing through citation counts for the shared data sets
  - Count the number of newly shared data sets and resources made available to the research community for each targeted area
  - Count the number of new, replicated genetic discoveries
- Training needs:
  - Bioinformatics to integrate data across domains and leverage publically available resources effectively
- Technologies to leverage:
  - Metabolomics
  - Wearable sensors

Reminder: Workgroup Charge

- Develop strategic priorities for increasing our understanding of gene x environment x development interactions in substance use research.
  - Identify measureable objectives for each priority
  - Specify benchmarks for gauging progress toward each objective
- Deliverable: 3-5 page summary of recommendations for NIDA on GEDI research for the next 5 years
- Completion date: **by Friday June 26th**

Cross-cutting Themes to Consider During Strategic Planning

- The workgroup should also consider these cross cutting themes as appropriate
  - Training needs (training of clinicians common theme in RFI comments)
  - Addressing sex and gender issues
  - How to leverage technology advances
  - Leveraging innovations from other fields

GxExD Interaction Challenges

- Quantitative phenotypes
- Methods to quantify environmental variables and responses
- Statistical methods to analyze GxE that overcome multiple comparison problems, harmonize data
- Appropriate animal models to identify epistasis, pleiotropy, gene-development interactions
- Translating findings in animals to humans

GEDI Gaps and Opportunities

- What research opportunities exist that NIDA should develop/expand? Prioritize.
- What are potential new areas of research? Prioritize.
- What resources are needed?
- What are the training needs?
- Are there any other gaps and opportunities that NIDA should consider?

Plan to Accomplish Research Goals

- Charge to the GEDI workgroup:
  - Identify research priorities
  - List objectives for each priority
  - Identify benchmarks to measure progress towards each objective

Questions about what the workgroup is charged to do?

Workgroup Logistics

- Meet biweekly on Tuesdays from 3-4 pm EDT via WebEx
- All correspondence should be sent to: NIDAOSPCPlanning@mail.nih.gov
- A Dropbox folder has been created to store files to share with the group – you should have received an email to collaborate via Dropbox. (*Dropbox serves as a means to avoid sending attachments and as an archive of the GEDI strategic planning process. You do not have to use it if you don't want to, but all documents generated throughout the process will be placed there*.)

Meeting Wrap-up

- Action items for next meeting
  - Workgroup homework
- Public comment period – 5 minutes
- Adjourn

***Next Meeting – 3:00-4:00 pm EDT, Tuesday, May 12, 2015**