National Institutes of Health
U.S. Department of Health and Human Services

LINCS Consortium Kick-Off Meeting

October 27-28, 2011
Legacy Hotel, Rockville, MD

Purpose: To gather all PIs (new and current) of the LINCS consortium to present research efforts and plans, and to work along with NIH program staff to structure a successful LINCS program.

Background: Contemporary biomedical research is progressing from characterizing the activities of individual molecules to acquiring a deep understanding of the complex functional interactions that exist among such molecules as they are found in cells, as components of biological networks and systems. Understanding biological networks in the context of small molecule drugs and RNA interference perturbations can lead to the development of novel therapies that aim to target biological networks. *The Library of Integrated Network-based Cellular Signatures (LINCS) Program directly addresses this by using high-throughput approaches to systematically search for and catalog robust rules (signatures) that identify the effects of exposure to small molecule and RNAi perturbations on biological networks in human cells.*

LINCS, beginning its 2nd year of a 3-year pilot, has the following basic scientific aims: (1) to generate large amounts of data in standardized high-throughput modes, (2) to use data integration and informatics methods to infer robust generalizable rules about biological networks, and (3) to drive advances in new high-throughput data generation capabilities and novel algorithms for data integration and visualization. The initial awards (two U54 centers) under the LINCS program were made as demonstration projects to assess the ability to populate the LINCS data matrix of *Cell Type X Perturbations X Phenotypic Assays* in a cost-efficient and high-throughput manner and to assess the value of doing so. The LINCS program recently awarded eight UO1s from two FOAs intended to complement the U54 centers' production-scale efforts by supporting the development of new approaches for data generation and analysis, so that present limitations do not constrain future research. Two small collaborative RO1 supplements were also awarded to introduce additional expertise, cell types, and interests to the LINCS program, and to explore in a small pilot the best possible way to perform these activities while at the same time generating useful scientific data that could become part of the LINCS data matrix.

This LINCS consortia meeting brings together all PIs (U54, U01, RO1) for the first time to begin to seriously address how to integrate multi-dimensional assays into a single coherent LINCS database, to identify promising new assays that could be included in a full-scale LINCS program, to develop new tools to visualize and analyze the complex LINCS database, and to develop strategies to incorporate new expertise and biomedical science areas while also generating a resource of general usefulness to the scientific community.

AGENDA

Day 1: Thursday, October 27

8:00-8:30 a.m.	**Registration and Continental Breakfast**
8:30-9:10 a.m.	**SESSION 1**
	Welcome and Programmatic Items

Moderator: Jennie Larkin

8:30-8:40 a.m. **LINCS and the Common Fund**
James Anderson, Director, DPCPSI

8:40-9:00 a.m. **NIH's LINCS Vision**
Alan Michelson, NHLBI

9:00-9:10 a.m. **Meeting Goals and Expected Outcomes of LINCS Consortia**
Jennie Larkin, NHLBI

9:10-2:50 p.m. **SESSION 2**

PI Overviews and Discussion of LINCS Science
Moderator: Ajay Pillai, NHGRI

LINCS teams will highlight grant proposals and research to identify network strengths, expertise, team interests, lacks/overlaps, and expected outcomes. Teams are listed alphabetically.

9:10-10:20 a.m. ***U54 Centers***

Broad Center, Todd Golub (20 min)
"Integrating Immediate-early and Transcriptional Signatures of Cellular Responses to Ligands and Drugs"

Harvard Medical School Center, Peter Sorger, (20 min)
"*Pharmaco Response Signatures and Disease Mechanism*"

Joint U54 Project, Aravind Subramanian, & Mario Niepel, (10 min)
"*Linking the phosphoproteome and transcriptome in oncogenic signaling pathways*"

Panel discussion with U54 leaders (20 min)

10:20-10:50 p.m. ***R01 supplement awardees*** *(10 min talk, 5 min discussion)*

Robert Bao, Massachusetts General Hospital
"Signaling network alterations in mitochondrial disease"

Evan Snyder, Sanford-Burnham Research Institute
"Disease-in-a-Dish": The ability of stem cells to model pathophysiology in vitro & facilitate molecular profiling & drug discovery"

10:50-11:05 a.m. **BREAK**

11:05-12:20 p.m. ***UO1 grantees*** *(15 min talks)*

Advanced Technologies for Detection of Perturbation-Induced Cellular Signatures
Moderator: Jerry Li, NCI

Andrea Califano, Columbia University
"Unlocking the potential of compound synergy and personalized medicine by experimental and computational analysis of compound signatures in distinct genetic backgrounds"

Jacob Jaffe, Broad Institute
"Accelerated Protein Signaling Signatures: Highly Multiplexed Assays to Monitor Perturbations of Serine/Threonine Phosphosignaling"

Deirdre Meldrum, Arizona State University-Tempe
"Novel live cell microarray to contribute single-cell metabolic biosignatures to LINCS"

Kathryn Miller-Jensen, Yale University
"Single Cell Protein Signatures for Systems Oncology"

Panel discussion (15 min)

12:20-1:20 p.m. **LUNCH/poster viewing**

1:20-2:35 p.m. Computational Tool Development and Integrative Data Analysis for LINCS
Moderator: Jennie Larkin, NHLBI

Andrea Califano, Columbia University
"Novel computational systems biology approaches to elucidate the genetic basis of compound synergy"

Mario Medvedovic, University of Cincinnati
"Integrative statistical methods and tools for analysis of perturbation signatures"

Stephan Schurer, University of Miami School of Medicine
"LINCS Information FramEwork (LIFE) to Integrate and Analyze Diverse Datasets"

Xiaobo Zhou, Methodist Hospital Research Institute
"itNETZ: The Integrative and Translational Network-based Cellular Signature Analyzer"

Panel discussion (15 min)

2:35-2:50 p.m. **BREAK**

2:50-4:15 p.m. **SESSION 3**
Implementing the LINCS Network –Structure of Collaborations
Session Moderator: Todd Golub

2:50-3:35 p.m. **UO1 Breakouts**
A. Structure of U01 Computation Collaborations
Moderator: Andrea Califano

Points of Discussion:

- How can we define a structure for effective UO1 data exchange and collaboration?
- Are there other large-scale NIH activities that the U01 should cross-interact with?
- What computational methodologies and tools are still missing to fully achieve the stated LINCS goals?

- Are there additional data modalities that may dramatically improve the ability of computational approaches to elucidate mechanisms of cellular response to exogenous perturbations?
- Should we select some established platforms to integrate our tools in to achieve maximum community traction?
- Since some of the tools will be extremely data and computationally intensive, should we consider the issue of tool deployment on cloud or grid infrastructure? E.g. should we consider an alliance with Amazon or Google?

B. Structure of U01 Technology Development Collaborations
Moderator: Deirdre Meldrum

Points of Discussion:

- How can the U01 technology groups effectively collaborate and leverage their technologies?
- Are there experiments that can be performed that combine several U01 technology platforms?
- Are there new technology developments that could be pursued that easily leverage technologies currently funded in the U01s?
- Of the technologies funded for this program, are there gaps in the technologies needed for data production?

3:35-4:05 p.m. **Structure of U54/UO1 Collaborations**
Moderators: Andrea Califano, Todd Golub, Deirdre Meldrum, Caroline Shamu

Points of Discussion:

- What are the needs or recommendations of the U54 centers in terms of technology development so that the next generation, high-throughput platforms are most readily adapted by the U54s?
- How can the TechU01s maintain close communications with the U54s to that they stay on track to deliver the most useful technology and data for the U54s and LINCS?
- How should UO1 and U54 groups exchange information and data?
- How to implement a data exchange pipeline so that Comp UO1 groups can plan their work accordingly?
- How will information about data formats (e.g. image file formats) be exchanged?
- Data Working Group Metadata Standards – short and long-term goals, and strategies for gathering input from within LINCS and from the larger community.

4:05-4:15 p.m. **BREAK**

4:15-6:45 p.m. **SESSION 4**

Implementing the LINCS Network – Data Analysis, Dissemination of Information and Outreach

Moderators: Andrea Califano, Deirdre Meldrum, Peter Sorger, Aravind Subramanian

Points of Discussion:

- Who will use LINCS data, for what purpose, and how do we facilitate this use? Consider short and long-term scenarios.
- Ways to link to other large-scale validation studies to get more information on when cellular contexts recapitulate in vivo data?
- Outreach structure and efforts?

5:15-6:45 p.m	**Concurrent Sessions**
5:15-5:45 p.m.	Session 3 and 4 moderators meet for Summaries
5:15-5:45 p.m.	NIH – ESP closed session - quick recap of the day
5:15-6:45 p.m.	Poster viewing/Cash bar
6:45 p.m	**General Session ADJOURNS**
7:00 p.m.	**DINNER** (PI/ESP, post-doc dinners)

Day 2: Friday, October 28

8:00-8:30 a.m.	**Breakfast** (Special Room for PIs and ESP)
8:30-10:05 a.m.	**SESSION 5**
	Day 1 Summary
	Presenters: Todd Golub and Peter Sorger
8:30-8:45 a.m.	**Summary of LINCS Science Achievements & Future**
8:45-9:45 a.m.	**Breakout reports and Implementation of Working Groups**
9:45-10:05 a.m.	**BREAK/Consortia Photo**
10:05-12:00 p.m.	**SESSION 6**
	LINCS-related programs at NIH (15 min talks)
	Moderator: Jennie Larkin
10:05-10:55	NCI programs, Jennifer Couch, NCI Single cell analysis, Andrea Beckel-Mitchener, NIMH Tox 21 project, Raymond Tice, NIEHS
10:55-11:00 a.m.	**Remarks by the next chair of the LINCS Steering Committee**
11:00 a.m.	**General Session ADJOURNS**
11:00-12:00 p.m.	**NIH – ESP executive session**