EMERGING SCIENCE FOR ENVIRONMENTAL HEALTH DECISIONS

AGENDA

The Promise of Single Cell and Single Molecule Analysis Tools to Advance Environmental Health Research

MARCH 7-8, 2019

THE NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE

LECTURE ROOM, 2101 CONSTITUTION AVENUE NW, WASHINGTON, DC 20418

THIS WORKSHOP WILL BE WEBCAST

HOW SIMILAR ARE THE CELLS within a particular tissue? Most analytical tools study cells and their molecular contents in bulk, providing information about the average cell and molecular complexes. Now, emerging findings suggest these traditional approaches could miss important differences between the cells in a sample, rare cell types like cancer stem cells or drug-resistant bacteria, and the opportunity to capture a cell in a fleeting transitional state.

Over the past decade, new single cell and single molecule analysis tools have led to advances that isolate single cells, technologies that can assay each cell's DNA, RNA, proteins, and metabolites, and imaging tools that map cell contents and their molecular interactions. These tools promise new insight on the differences in function between individual cells and molecules, the organization and timing of responses to stimuli, how cells interact as components of a complex system, and how these interactions may change with age, disease, and exposure to environmental stressors.

This workshop will explore the current status of this rapidly evolving field of study, review the preliminary use of single cell and single molecule analysis tools in environmental health studies, and investigate the resources needed to make the data generated most useful to the biomedical and public health fields and to regulatory decision makers.

THURSDAY, MARCH 7, 8:30 AM–5:00 PM

8:00 ***Registration***

8:30 Welcome and Opening Remarks
- **Keegan Sawyer**, National Academies of Sciences, Engineering, and Medicine
- **Kim Boekleheide**[§†], Brown University, Co-Chair of the Standing Committee
- **Linda Birnbaum**, National Insitute of Environmental Health Sciences

8:45 Workshop Overview—**Norbert Kaminski**[§†], Michigan State University, Chair of the Organizing Committee

Session 1 Enabling Single Cell and Single Molecule Research and Exploring the Toolbox

Moderator: **Ramnik Xavier**[§], Broad Institute

9:00 Overview of the Promise of Single Cell and Single Molecule Technologies—**Ramnik Xavier**[§], Broad Institute

9:35 Cell Atlases as roadmaps to understand tumors—**Orit Rozenblatt-Rosen**, Broad Institute

10:05 Digital detection of molecules–the new frontier in biomarker analysis—**M. Selim Ünlü**[§], Boston University

10:35 ***Break***

(continued)

[§] Member of the workshop Organizing Committee for The Promise of Single Cell and Single Molecule Analysis Tools to Advance Environmental Health Research.

[†] Member of the Standing Committee on the Use of Emerging Science for Environmental Health Decisions.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Register at
http://dels.nas.edu/envirohealth

THURSDAY, MARCH 7 (CONTINUED)

Session 2 The Promise and Uses of Single Cell and Single Molecule Technologies

Moderator: **Lesa Aylward**[§†], Summit Toxicology, LLP

10:50 Mass Spectrometry Based Single Cell Metabolomics and Imaging for Environmental Health Research—**Vasilis Vasilou**, Yale School of Public Health

11:15 Single-molecule fluorescence microscopy enables super-resolution imaging of DNA replication and repair in living bacterial cells—**Julie Biteen**, University of Michigan

11:40 Multiplex Imaging for Single Cell Mechanistic Analysis of Steroid Receptor Functions—**Michael Mancini**, Baylor College of Medicine

12:05 ***Lunch***

1:05 Single cell analysis work-flows: the usual and unusual—**Lana Garmire**, University of Michigan

1:30 Convergence of single cell assays, bioinformatics and simulation to study tissue injury and regeneration—**Rajanikanth Vadigepalli**, Thomas Jefferson University

1:55 Lessons from the Pulmonary Fibrosis Cell Atlas—**Naftali Kaminski**, Yale School of Medicine

2:20 Panel Discussion with Session 2 speakers

3:00 ***Break***

Session 3 Exploring Barriers, Challenges, and Limitations

Moderator: **Sudin Bhattacharya**[§], Michigan State University

3:15 Comprehensive Integration of Single Cell Data—**Rahul Satija**, New York University

3:45 Latent manifolds for single cell data: normalization, batch correction, density estimation—**Barbara Engelhardt**, Princeton University

4:15 Single cell genomic study design and controlling for unwanted technical and biological variation—**Yoav Gilad**, University of Chicago

4:45 Day 1 Closing Remarks—**Sudin Bhattacharya**[§], Michigan State University

5:00 ***Adjourn***

FRIDAY, MARCH 8, 8:30 AM–12:30 PM

8:30 Welcome—**Norbert Kaminski**[§†], Michigan State University, Chair of Organizing Committee

8:35 The Human Cell Atlas—**Aviv Regev**, Broad Institute (*Remote presentation*)

9:20 Identifying and rationally modulating cellular drivers of enhanced and diminished immunity—**Alex Shalek**, Massachusetts Institute of Technology

9:50 ***Break***

Session 4 Considerations for Application in Environmental Health

10:05 Dose Response Modeling at the Level of Single Cells and Single Molecules: From Concepts to 'Applications'—**Melvin Andersen**, ScitoVation LLC

10:15 PART 1: IDENTIFYING MODES OF ACTION

- **Lana Garmire,** University of Michigan
- **Michael Mancini,** Baylor College of Medicine
- **Vasilis Vasilou**, Yale University

10:30 Panel Discussion with Part 1 speakers

(continued)

§ Member of the workshop Organizing Committee for The Promise of Single Cell and Single Molecule Analysis Tools to Advance Environmental Health Research.

† Member of the Standing Committee on the Use of Emerging Science for Environmental Health Decisions.

11:15 **PART 2: APPLICATION IN RISK ASSESSMENT**

- **Melvin Andersen**, ScitoVation LLC
- **Patrick McMullen**†, ScitoVation LLC
- **Rajanikanth Vadigepalli**, Thomas Jefferson University

11:30 Panel Discussion with Part 2 speakers

12:15 Closing Remarks—**Norbert Kaminski**§†, Michigan State University, Chair of Organizing Committee

12:30 ***Adjourn Workshop****

---

* The Emerging Science for Environmental Health Decisions Committee Business Meeting is from 1–4pm. This meeting is open to Committee, Government Liaisons, and workshop participants.

§ Member of the workshop Organizing Committee for The Promise of Single Cell and Single Molecule Analysis Tools to Advance Environmental Health Research.

† Member of the Standing Committee on the Use of Emerging Science for Environmental Health Decisions.

Workshop Organizing Committee

This workshop was organized by the following experts: **Norbert Kaminski**†, Michigan State University; **Lesa Aylward**†, Summit Toxicology, LLP; **Sudin Bhattacharya**, Michigan State University; **Kim Boekelheide**†, Brown University; **M. Selim Ünlü**, Boston University; **Ramnik Xavier**, Broad Institute

For more information and to subscribe for updates, please visit http://dels.nas.edu/envirohealth

Emerging Science workshops are free and open to the public.

About Emerging Science for Environmental Health Decisions

The National Academies' Standing Committee on the Use of Emerging Science for Environmental Health Decisions (ESEHD) examines and discusses issues on the use of new science, tools, and research methodologies for environmental health decisions. The ESEHD committee is organized under the auspices of Board on Life Sciences and the Board on Environmental Studies and Toxicology of the National Academies of Sciences, Engineering, and Medicine, and sponsored by the National Institute of Environmental Health Sciences.