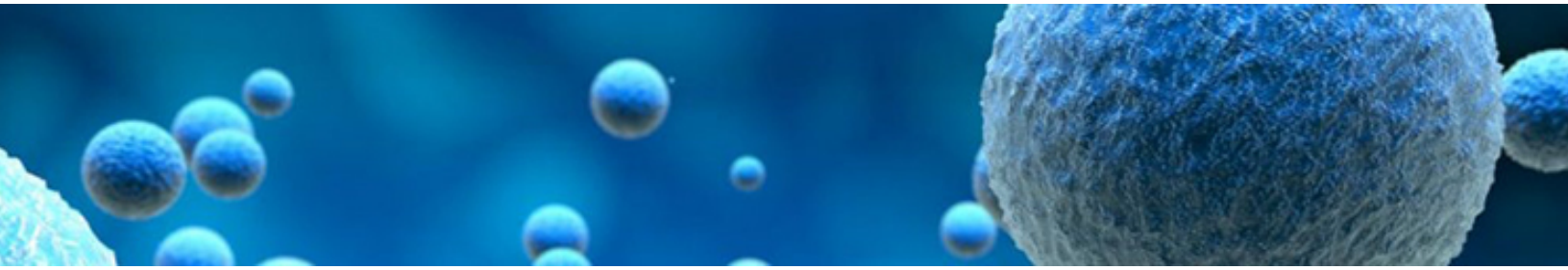


Workshop on Extracellular Vesicles, Exosomes, and Cell-Cell Signaling in Response to Environmental Stress

September 27 -28, 2021 (all times in EDT)

Workshop Purpose: Extracellular vesicles (EVs), encompassing a range of sizes and functions, are a key means of communication between cells in the same tissue and between organs. Exosomes are a type of extracellular vesicle that carry a range of types of "cargo", including small RNAs, mRNA, and proteins for signaling between cells under normal conditions, but also under stress or disease conditions. Shuttling of cargo produced in one tissue can reach distant cells or tissues and exert systemic effects. The study of exosomes and extracellular signaling is a significant focus of current study, for fundamental biological research, the discovery of new biomarkers, and for therapeutic applications. Although there have been some grants funded by NIEHS and NIH on EVs and environmental exposures, there is growing interest in identifying the roles for EVs in environmentally-related diseases, including pro-inflammatory signaling related to air pollution exposures, the transport of proteins in neurodegenerative diseases, the potential for identifying biomarkers of exposure or response, and the roles for EV signaling in other environmentally-related health conditions. The workshop will include overview talks on EV biology, development of state-of-the-art methods for EV isolation and characterization, and application of EV research to environmental exposures and disease.

September 27, 2021

10:00 am Welcome – **Rick Woychik**, Director, NIEHS

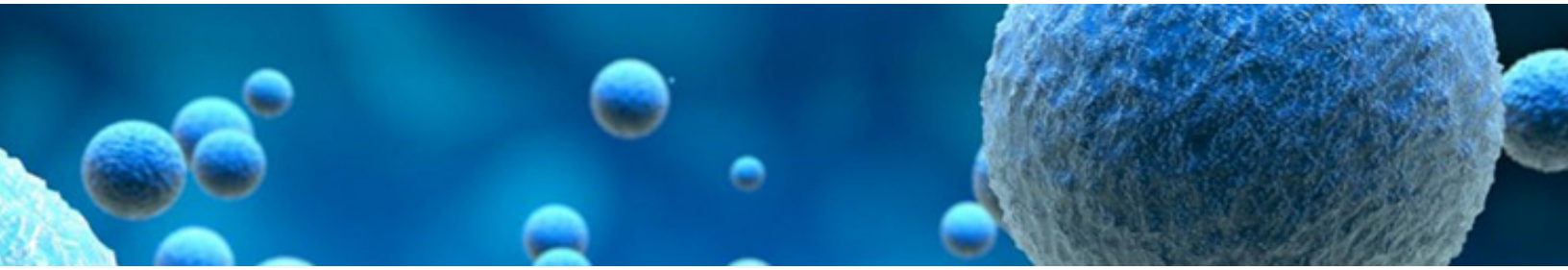
10:15 am Overview talks on Extracellular Vesicles – **Dan Shaughnessy**, NIEHS – Moderator

"Exosomes & Other EVs as Sensors of Environmental Health" – **Steven Gould**, John Hopkins University

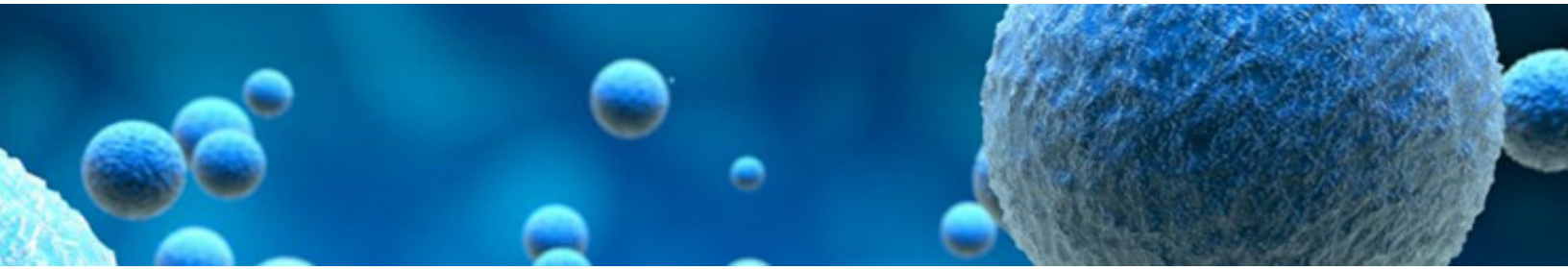
10:45 am "Overview of the NIH Common Fund Program on Extracellular RNA Signaling" – **Christine Happel**, NCATS

11:15 am "New Methods for Isolating and Characterizing Extracellular Vesicles and Their Contents" – **Jennifer Jones**, NCI

12:00 pm Break



12:30 pm	EVs and the Environment – **Jonathan Hollander**, NIEHS – Moderator
	"Extracellular Vesicles as Early Biomarkers of Environmental Toxicity - New Results and Approaches in Population-based Studies" – **Andrea Baccarelli**, Columbia University
1:00 pm	"Exosomes as Mediators of Neuroinflammation and Neurotoxicity: Translational Implications for Biomarker Discovery in Environmentally Linked Neurodegenerative Diseases" – **Anumantha Kanthasamy**, University of Georgia
1:30 pm	"Characterizing and Adapting CNS-derived Extracellular Vesicle Isolation Methods for the Study of Environmental Exposure and Disease Progression in ALS" – **Diane Re**, Columbia University
2:00 pm	Break
2:15 pm	"Exosomes as Mediators of Lung Cellular Dysfunction by Environmental E-Cigarette Chemical Exposures: Implications in Environmental-induced Lung Diseases" – **Irfan Rahman**, University of Rochester
2:45 pm	"exRNAs as Biomarkers for Pregnancy Complications" – **Louise Laurent**, University of California San Diego
3:15 pm	Discussion – **Kim McAllister**, NIEHS – Moderator
3:45 pm	Wrap-up for Day 1



September 28, 2021

10:00 am Talks on Experimental systems for EVs and Response to Environmental Stress – **Fred Tyson**, NIEHS – Moderator

10:05 am "Models for evaluating EVs In vitro models of exosomal therapies in cardiovascular disease."" – **Kit Parker**, Wyss Institute at Harvard University

10:35 am "Environmental-pollutant-induced Pathologies of Pregnancy: Modeling the Mechanistic Role of Fetal Extracellular Vesicles Using Organ-on-a-chip" – **Ramkumar Menon**, University of Texas Medical Branch

11:05 am "Bioengineering Studies of Extracellular Vesicles in the Context of Heart Toxicity and Injury" – **Gordona Vunjak-Novakovic**, Columbia University

11:35 am Overview of the ExRNA Atlas in the NIH Common Fund Program on Extracellular RNA Signaling – **Aleks Milosavljevic**, Baylor College of Medicine

12:00 pm Break

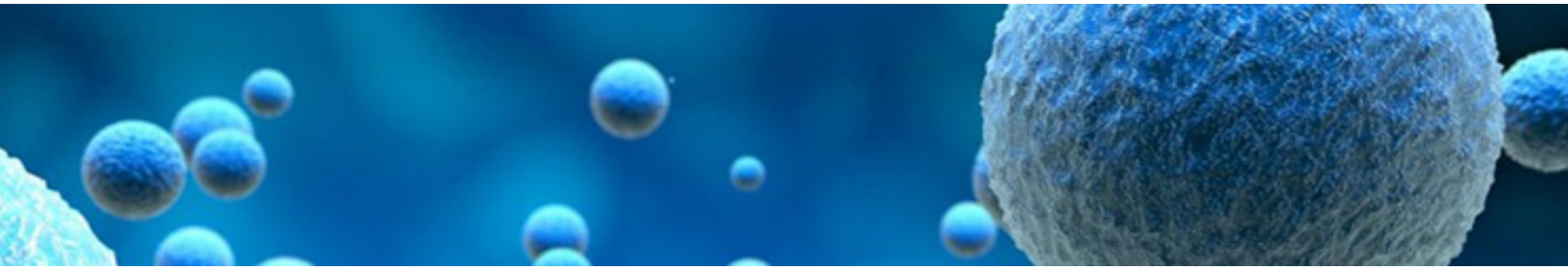
12:15 pm Panel Discussion: Experimental Systems for Studying EVs in Toxicology – **Alex Merrick**, Division of the National Toxicology Program – Moderator

Panelists: Ken Ramos, Gordona Vunjac-Novakovic, Ramkumar Menon, Merrie Mosedale.

What are the current challenges to applying the study of exosomes in toxicology research?

1. Are there ways to study EVs in archived tissues? Are there methods for isolating and storing EVs from biological samples (tissues, blood etc.) for later analyses?
2. What are the opportunities for studying EV signaling in vitro, including multi-organ models (MPS)?
3. Is there direct evidence for toxicants being carried in EVs, e.g., toxic metals? Or are the biomarkers of response to exposures mainly changes in protein or RNA content? Are there toxicant-specific EV cargos, e.g., originating in lung or liver?

1:00 pm Break



1:15 pm Panel Discussion: Studying EVs in Human Population-based Studies – **Anne Marie Jukic**, NIEHS DIR Epidemiology Branch – Moderator

Panelists: Matt Roth, Andrea Baccarelli, Louise Laurent, Diane Re, Jennifer Jones.

1. What are the barriers to using EVs as biomarkers in population-based studies? (Cost, throughput, analysis, establishing biomarker validity?)
2. Opportunities for pilot studies? Standardized methods for sample collection, EV isolation, analysis of EV cargo?
3. Are there EV-specific cargos related to specific environmental exposures? How do these vary within individuals over time or between individuals?
4. What are the practical considerations for applying exosome biology to population-based studies? Sample types (blood, CSF, ISF?) Collection and storage methods?
5. Data sharing issues? Data repositories?

2:00 pm General Discussion – research opportunities, research needs for EVs in environmental research

2:30 pm Adjourn