**Live Short Research Talk Session**

October 21, 2020 10:00 a.m. EDT

**Talk 1**

**Title:** ExoToxChip: A Toxicogenomics tool for chemical prioritization and environmental management

**Speaker and co-authors:** Doug Crump3, Markus Hecker2, Jessica Head1, Natacha Hogan2, Jeff Xia1, Gordon Hickey1, Steve Maguire4, and Niladri Basu1

1 McGill University, Montreal, QC Canada, 2 University of Saskatchewan, Saskatoon, SK, Canada, 3 Environmental and Climate Change Canada, National Wildlife Research Centre, Ottawa, ON, Canada, 4 The University of Sydney Business School, Sydney, NSW, Australia

**Abstract:** Chemical contamination of our natural ecosystems is one of the planet’s greatest threats. The EcoToxChip project ([www.ecotoxchip.ca](http://www.ecotoxchip.ca)) aims to develop and commercialize PCR arrays (EcoToxChips) and a data evaluation tool (EcoToxXplorer.ca) for the characterization, prioritization, and management of environmental chemicals. EcoToxChips for 3 model species used in ecological risk assessment (fathead minnow, Japanese quail, *Xenopus laevis*) and 3 native species of concern (rainbow trout, double-crested cormorant, leopard frog) are being developed via collaboration with Qiagen. EcoToxChip gene selection is an integrative process based on 3 main approaches: 1) toxicology (literature/expert knowledge); 2) regulatory (genes familiar to regulators); 3) bioinformatics (RNAseq, machine learning). Project deliverables provide a solution to pressing problems in the field of ecological risk assessment and guidance to diverse end-users with regard to the adoption of toxicogenomics tools.

**Talk 2**

**Title:** An eMERging target for cancer therapy

**Speaker and co-authors:** Macy Yemsratch Akalu, Sourav Gosh, and Carla Rothlin

Department of Immunobiology, Yale School of Medicine, New Haven, CT, USA

**Abstract:** The discovery of T cell checkpoints and their blockade to facilitate anti-tumor immunity has revolutionized oncology. We, and others, have discovered molecules that function as checkpoints in innate immune cells. Innate immunity is an obligate prerequisite for adaptive immunity; therefore, innate immune checkpoint blockade (CPB) will not only complement T cell CPB in responders, but may even convert T cell CPB non-responders to responders. One such innate immune checkpoint is the receptor tyrosine kinase MERTK, which is expressed in tumor-associated macrophages. I will present our findings with myeloid cell-specific ablation of Mertk in two mouse models of anti-tumor immune responses– one model in which this ablation is sufficient for driving a robust anti-tumor response, and another in which this fails to promote anti-tumor immunity. I will describe cellular and molecular immune correlates (including scRNAseq, TCR seq) that correspond to a successful anti-tumor response.

**Talk 3**

**Title:** Differential expression of miRNAs in mesenchymal stromal cell-derived exosomes from improved function outcome after ischemic heart failure: A biorepository evaluation of the Focus CCTRN Trial.

**Speaker and co-authors:** Lourdes I. Chacon, Fernanda Mesquita, Mohammad Hassan Virk, and Camila Hochman-Mendez

Department of Regenerative Medicine Research, Texas Heart Institute, Houston, TX, USA

**Abstract:** Mesenchymal stromal cells derived from bone marrow (BM-MSCs) have been considered promising candidates for regenerative medicine therapies for more than 20 years, but to date cardiovascular clinical trials of MSC-based therapies have demonstrated only modest improvement. However, the mechanisms underlying why some patients improve and others do not remain undefined. Although MSC survival after transplantation remains a challenge, several studies have reported that BM-MSC-mediated paracrine effects and delivery of exosomes may be therapeutically relevant. We hypothesized that MSC-derived exosomes from patients with cardiac functional improvement contain factors that promote cell survival, proliferation, and cardiac protection. Here, we compared exosomes (derived from MSCs that had been expanded from BM-MNCs used for autologous transplantation) from two cohorts of disease- and age- matched consented patients with ischemic cardiomyopathy enrolled in the FOCUS-CCTRN trial—those with improved (cohort1, n=3) or worsened (cohort2, n=3) functional outcome in three primary endpoints: left ventricular (LV) ejection fraction, LV end-systolic volume, and maximal oxygen consumption. MicroRNA-seq analysis identified 16 upregulated and 12 downregulated miRNAs in cohort 1 when compared to cohort 2. Using DIANA-Mir Path v.3.0, we identified 3,522 experimentally validated gene targets. Gene set enrichment analysis identified enrichment for fatty acid biosynthesis and metabolism, Hippo signaling pathway, protein processing in endoplasmic reticulum, adherent junction, cell cycle, endocytosis, RNA transport and degradation, estrogen-signaling pathway, regulation of actin cytoskeleton, Prolactin signaling pathway, Focal adhesion, Notch-signaling pathway, p53-signaling pathway, insulin-signaling pathway and HIF-1-signaling pathway in the targets of upregulated miRNAs. The downregulated miRNAs were related to extracellular matrix-receptor interaction, protein processing in endoplasmic reticulum, cytokine-cytokine receptor interaction and antigen processing and presentation. Thus, the identified miRNAs differentially expressed in patients with an improved functional outcome that may play a role in the molecular mechanisms that underlie in cardiac repair in patients with ischemic cardiac disease. Moreover, these finding indicate that not all autologous cell products may be competent therapy candidates for cardiac repair These results warrant further investigation to confirm the effects of the identified differences on the target genes, which could improve the prognosis and unveil new therapeutic approaches.