2021 Genetic Resources Core Facility (GRCF)
Virtual Symposium
Seminar Agenda
April 14, 2021, 9 am – 5 pm

9:00 -9:55 am

Opening Plenary Session, 'A new method to spatially map large volumes of human tissues and tumors at single-cell resolution (CODA)'

Sponsor: Genetic Resources Core Facility

Denis Wirtz

Vice Provost for Research
TH Smoot Professor, Chemical and Biomolecular Engineering, Pathology, Oncology
Director Johns Hopkins Physical Sciences-Oncology Center
Johns Hopkins University and Johns Hopkins School of Medicine

Abstract: A multidisciplinary team of students and faculty in the Departments of Chemical Engineering and Pathology have developed a new method (CODA) to map extremely large volumes of human tissues, organs and tumors at single-cell resolution. Hundreds-to-thousands of thin sections serially cut and stained with standard hematoxylin and eosin are automatically annotated using a trained Deep Learning segmentation algorithm. Annotated sections are then locally and globally aligned and re-assembled into a digital volume for analysis. As a first test of CODA, healthy pancreatic tissues, precursor lesions and tumors were reconstructed to determine the 3D complex topology of blood vessels and epithelial ducts, fat content, the architecture of stromal matrix, and immune cell infiltration. CODA revealed new types of precursor lesions (PanINs), not readily detectable in standard 2D sections. Other applications of CODA includes 3D assessments of the remodeling of the lung in COVID, the pancreas in diabetes, and the developing heart in the mouse embryo.

10:00 - 10:55 am

Title: 'Unveil the immune response to cancer and infectious disease with powerful immunoassays'

Sponsor: ThermoFisher Scientific

Sigrun Badrnya

Ph.D., Manager Product Development

Abstract: Uncovering the interactions between the immune system and cancer cells or pathogens is key for understanding and controlling both cancer and infectious disease. The evolving research field of immuno-oncology focuses on an individual's immune system as potential innovative treatment approaches to combat cancer. Immune checkpoint molecules have been identified as critical players in the regulation of NK cell- and T cell-mediated immune responses. Thus, the systematic analysis of crucial soluble immune stimulatory and inhibitory factors using multiplexing high-throughput immunoassays will help to shed light on the regulation of checkpoint pathways and to monitor response to immunotherapeutic treatment. Likewise, innovative assay formats to characterize the humoral response to infection are urgently needed as the novel human coronavirus SARS-CoV-2 and the associated respiratory disease COVID-19 continue to evolve worldwide. Simple, rapid and multiplex high-throughput assays will enable researchers to assess the prevalence of SARS-CoV-2 infection and to examine the immunological memory and potential protective immunity of previously infected or vaccinated individuals. Moreover, analyzing the level of a broader panel of immunomodulatory markers will allow researchers to decipher the complex interplay of soluble mediators accounting for the so-called cytokine storm or cytokine release syndrome (CRS), an overactive state of the immune system that is a common complication associated with SARS-CoV-2 infection.

11:00 - 11:55 am

'Enhancing Transcript Detection Sensitivity for a Range of Sample Types'

Sponsor: New England Biolabs

Siva Chavadi

Ph.D., NGS Field Application Scientist

Abstract: The expanding range of RNA-seq applications and technologies increasingly face the challenge of extremes of low input amounts and degraded samples. RNA samples can include a large dynamic range of transcript expression, and highly expressed transcripts with minimal biological interest can dominate readouts, masking detection of more informative low-abundance transcripts. Our RNaseH-based method for depleting abundant RNAs is optimized for high performance with both FFPE samples and high-quality inputs. Probe sets developed for this method include rRNA from human, mouse, rat and bacteria, and also globin transcripts from blood. We also launched a customizable approach to enrich for RNAs of interest by eliminating any unwanted RNAs across different species. For samples composed of single cells or picogram amounts of total RNA, detection of low-abundance transcripts is challenging but can be achieved by full-length transcript sequencing using a robust method incorporating template switching and enzymatic
fragmentation to provide uniform transcript coverage.

12:00 - 12:55 pm

Title: 'The QIAcuity Digital PCR System'

Sponsor : QIAGEN

Louis Lichten

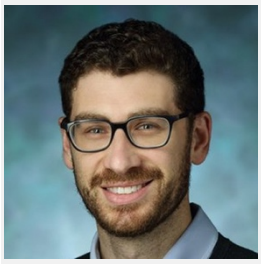
Ph.D., Sr Customer Solutions Manager

Abstract: Digital PCR (dPCR) is a highly viable solution for copy number variation (CNV) detection, rare mutation detection and quantification, validation of NGS results, and applications alike. However, currently available solutions are either very complex to operate, or lack a scalability option for users with variable throughput and flexible workflow needs. Unlike current systems relying on droplet generation, QIAGEN's offering of fully integrated walkaway instrument options and multiple plate configurations with increased partitions can potentially solve throughput, speed, and usability challenges. In this talk, we will first present the improvements that the QIAcuity offers over existing systems. Then reveal how the QuantiNova LNA PCR Assays provide highly sensitive and accurate locked nucleic acid (LNA)-enhanced digital PCR quantification for mRNA and lncRNA targets, detecting even the smallest expression changes at the lowest concentrations.

1:00 - 1:55 pm

Keynote Address: ‘A natural single-guide RNA repurposes Cas9 to autoregulate CRISPR-Cas expression’

Sponsor: Genetic Resources Core Facility



Joshua W Modell

Ph.D., Assistant Professor, Johns Hopkins University School of Medicine, Molecular Biology and Genetics

Abstract: CRISPR-Cas systems provide prokaryotes with acquired immunity against viruses and plasmids, but how these systems are regulated to prevent autoimmunity is poorly understood. We show that in the S. pyogenes CRISPR-Cas system, a long-form transactivating CRISPR RNA (tracr-L) folds into a natural single guide that directs Cas9 to transcriptionally repress its own promoter (Pcas). Further, we demonstrate that Pcas serves as a critical regulatory node. De-repression causes a dramatic 3,000-fold increase in immunization rates against viruses; however, heightened immunity comes at the cost of increased autoimmune toxicity. Using bioinformatic analyses, we provide evidence that tracrRNA-mediated autoregulation is widespread in type II-A CRISPR-Cas systems. Collectively, we unveil a new paradigm for the intrinsic regulation of CRISPR-Cas systems by natural single guides, which may facilitate the frequent horizontal transfer of these systems into new hosts that have not yet evolved their own regulatory strategies.

2:00 - 2:55 pm

Title: ‘Genomics in 2021 and Beyond’

Sponsor: Illumina

Dan Gheba

Executive Sequencing Specialist, Illumina, Inc.

Abstract: Basic and translational research is the driving force behind Illumina's mission to improve human health by unlocking the power of the genome. In collaboration with the resources at the JHU GRCF, advances in Illumina technology are creating simpler library preparation, more cost-effective sequencing, and easier to understand data analysis tools. Please join us for a webinar around 2021's hottest topics in genomics and learn how the latest Illumina innovations can drive your research forward.

3:00 - 3:55p m

Title: 'Advancing Immunotherapeutics Research with Immuno-oncology Cell Line Panels and Milliplex Multiplexing Assays'

Sponsor: MilliporeSigma

M. Zulfiquer Hossain

Ph.D., Research Technology Specialist, Advanced Genomics and Cell Models

Amy R. Johnson

Ph.D., Field Application Scientist, Immunoassay Platform Solutions

Over the past decade, immunotherapeutics have emerged as a promising approach for the treatment of a variety of diseases including cancer. In this webinar, we'll discuss cutting-edge tools for immunotherapeutics research. Variable expression of tumor-associated antigens and MHC polymorphism in patient cell populations make it difficult to predict when and why a specific immunotherapy might fail. We utilized our advanced cell engineering workflow to generate cell lines with controlled levels of tumor-associated antigens or mono-allelic expression of specific MHC/HLA molecules. These genetically modified cell lines can be used as controls in validated assays or for the development of new assays to test candidate immunotherapies. Our immuno-oncology cell lines are thus designed to simplify evaluation of immunotherapeutic strategies through cell-based assays and immunoassays.

In these complex biological systems, multiple interconnected mechanisms are involved in simultaneously producing a cellular response to disease or therapeutic intervention. This response can be quantified by measuring biomarkers such as cytokines, hormones, and signaling proteins. Multiplexing enables researchers to more fully understand the complexities of their biological systems by assessing multiple biomarkers in a single sample, thus increasing throughput and saving precious sample. We will discuss how Milliplex multiplexing immunoassays can be easily integrated into any study to facilitate your immunotherapeutics research.

Collectively, our innovative physiologically relevant tools can help provide deeper insight into the function and performance of novel immunotherapeutic approaches.

4:00 - 4:55 pm

Title: 'Next Generation Sequencing confirmation with Droplet Digital PCR'

Sponsor: Bio-Rad Laboratories

Scott Hauenstein

Ph.D.

Abstract: Next Generation Sequencing (NGS) excels as a discovery technique and is ideal for performing global analyses. By looking at all possible targets, NGS allows for the discovery of new molecules or pathways that were not known to have a specific biological function. However, once new targets have been identified they must be confirmed using an alternative testing mechanism. Droplet digital polymerase chain reaction (ddPCR™) was developed to provide high-precision, absolute quantification of nucleic acid target sequences with a wide range of applications. Compared to traditional real time PCR, ddPCR has an increased signal-to-noise ratio and allows for the removal of PCR efficiency biases. As a result, ddPCR can be used to analyze events that require a high level of sensitivity. The advantages of ddPCR make it an ideal platform for orthogonal validation of NGS data.