THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE

Department of Biomedical Informatics

Student Presentations

Esko Kautto: "Accurate Long-Read Sequencing Facilitates Variant Discovery and Detection"
High-Throughput Sequencing (HTS) revolutionized the field of genomics and has led to an immeasurable wealth of omics data. The commoditization of HTS has allowed for ever more uses, both in clinical and research environments, and has led to HTS becoming the gold standard for sequencing-based approaches. However, HTS is short-read sequencing, which suffers from technical limitations that have made detection of certain types of variants, and sequencing of segments of the genome, challenging at best. In contrast, newer third-generation single-molecule sequencing (SMS) platforms have seen tremendous technological advances in the past few years, becoming valuable tools for both genome science and clinical research. In our research, we have found that SMS has facilitated detection of pathogenic alterations and has led to a greater understanding of the complexities of structural variation in cancer genomes.

Eric Brooks:

Audrey Bollas: "RNAseq as a proxy for DNA methylation-based tumor classification"
Accurate diagnosis is critical for optimal treatment and management of cancer patients. DNA methylation-based central nervous system (CNS) tumor classification has been demonstrated to have a substantial impact on diagnostic precision, resulting in a change of diagnosis in up to 12% of prospective cases. As a basic understanding of the effects of DNA methylation on gene expression has linked methylation of CpG sites in the promoter region to a decrease in gene expression, we hypothesize that information from RNA sequencing alone can be used to perform a similar classification task as DNA methylation. Thus, the abundant analyses performed with RNA sequencing (RNAseq) can be leveraged to circumvent the need for an additional DNA methylation experiment. In addition to supplying expression information, it is possible to detect variants at the RNA level with RNAseq. Subtypes of cancer can have distinct transcriptional profiles and somatic mutations, and therefore both expression and variant data from RNAseq has the potential to improve diagnostic yield in some cancer subtypes. To this end, we propose to develop a bioinformatics method to impute DNA methylation classification from RNAseq data alone. We aim to perform the initial analysis in medulloblastoma, as there are clear subtypes defined, and then determine how extensible the method is in other tumor types. Additionally, we propose to package the classification model in a Docker container to enable application portability.

Mariame Diabate:"Multiplex Analysis of Functional Assays"
Variants of uncertain significance (VUS) are a type of missense mutation where association with disease risk is unknown. VUS are one of the most frequent types of sequence changes detected in the genome, especially for clinically underserved populations. Due to the lack of VUS information in people of color, they are limited in receiving precise clinical recommendations. The increased reporting from genetic screening of VUS has been biased against clinically underserved communities and further contributes to the large disparities in cancer outcomes for these populations. Thus, methods that classify VUS function can help address disparities in cancer outcomes. These methods could give key information for identifying the mutational drivers of disease. In the case of breast and ovarian cancer and the tumor suppressor BRCA1, pathogenic variants have shown loss of function in an assay for homology-directed repair (HDR). We hypothesize that through the functional analysis of BRCA1 VUS, we can understand the genetic diversity of variant function and predict whether a gene variant causes disease. To test our hypothesis, we will analyze the results from two HDR-based functional assays we developed to compare against existing classifications in clinical variant databases. Results from variants tested in the C-terminal of the BRCA1 give similar results between the two functional assays. Comparing the results from these assays yield high confidence results for individual data points were performance is consistence between the assays. The simple design of the cisplatin resistance-based proliferation assay, enables us to readily test VUS in other cell lines.

Friday, November 6th, 11:00am-12:00pm
Carmen Zoom