



# John Lawrence Seminar

## Translating Cancer Genomics to Precision Oncology



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Large-scale, cancer multi-omics projects such as the TCGA and the ICGC, enabled by the advent of next-generation sequencing (NGS), have generated significant information on the structure of the genome of many cancers, the mutational signatures emerging during the development of the disease, recurrent cancer driver genes and mutations, and the accompanying gene expression and methylation changes. Most analysis to date have focused on the coding regions of the genome, but recent efforts to expand these to the genome-scale have made significant progress that I will discuss. This information has led to a better understanding of the etiology of the disease and the development of targeted therapies, which are more effective in tumors harboring certain somatic alterations. Hence, the use NGS to identify molecular biomarkers in tumors to support clinical decisions is rapidly becoming the standard of care for refractory patients. We also are beginning to understand the molecular underpinnings of resistance to therapy, how to monitor its emergence, and strategies to overcome it. As we move to the clinical applications of cancer genomics, it becomes apparent that the experimental strategies and informatics tools used on the research settings are ill suited for the clinical needs. This includes making the proper trade-off between the fraction of the genome sequenced and depth of coverage needed to handle tumor heterogeneity and detecting low frequency somatic variants. Additionally, dealing with poor samples and damaged DNA in FFPE specimens, extremely diluted tumor cell-free DNA in patient's plasma, and the lack of matched normal/germline samples requires improvements in the targeted enrichment chemistries and bioinformatics analysis paradigms. I will discuss strategies to overcome these challenges, including new algorithms to identify somatic mutations in the lack of matched germline from next-generation sequencing data, and how reference materials can be used to validate both algorithms and the targeted resequencing assays as we translate cancer genomics technologies into clinical practice.

**Tuesday  
Nov. 15 at 4:00 PM**

**717 Potter St.  
Rm. 977-141**

**Hosts: A. Snijders/J.-H. Mao, Biological Systems & Engineering Division**