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University of Colorado, Denver
Anschutz Medical Campus

Series – 72

- Date & Time - April 06, 2022 (13:30-14:30 JST | 10:00-11:00 IST)
- Venue - [Zoom](#)
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Competing for DNA

DNA packaged in dynamic chromatin harbors all the information required for life. While the genetic information in a lung cell and a heart cell is the same, what makes them different is which parts of the genome are active in each cell type. One of the key determinants of cell-type-specific gene activation is the function of Transcription Factors (TFs) which bind to DNA in a sequence-specific manner. The DNA segments that drive gene regulation are referred to as cis-regulatory elements (CREs) or enhancers. Nucleosomes, the basic unit of chromatin, compete with TFs to occupy CREs. Thus, probing how TFs bind their functional sites and compete for DNA against nucleosomes can help us understand fundamental processes that drive both development and disease. Using high-resolution mapping of TF footprints and single-molecule mapping of multiple TF binding events, we dissect enhancer structure in *Drosophila* S2 cells. We find that cooperative binding of TFs is at distances that suggest no protein-protein interactions. Most TFs are tissue-specific, thus they can be used as probes to monitor diseases. For instance, more than two-thirds of breast cancers in women are estrogen-receptor (ER)-positive, where ER functions as a TF. But, currently, the only way to monitor cancer phenotypes is to perform routine painful biopsies. Alternatively, we propose that we can do this in a minimally invasive manner by using free-floating DNA referred to as cfDNA in plasma. cfDNA survives in plasma primarily due to protein protections, predominantly by histone complexes and transcription factors (TFs), thus carrying the chromatin blueprint of their cells-of-origin. We exploit this information to define tumor state-specific ER binding using mouse models. These sites reflect chromatin signatures of ER binding associated with FOXA1. Moreover, chromatin accessibility at cfDNA-inferred ER binding sites separate TCGA breast cancer cohorts by their ER phenotype.