UCLA Engineering
HENRY SAMUELI SCHOOL OF
ENGINEERING AND APPLIED SCIENCE

BIOENGINEERING

PRESENTS

“Synthetic Genome Regulation for Cell and Tissue Engineering"

THURSDAY, November 4th, 2021
12:00 – 1:00 PM
Zoom Link: https://ucla.zoom.us/j/96241974712

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ABSTRACT:

Molecular heterogeneity is emerging as a critical feature of multicellular life. While single-cell analyses have revealed the existence of cell-to-cell variation in the levels and activities of the molecules responsible for gene regulation, the source of such variation is still poorly understood. The Downing Lab studies how genome replication contributes to epigenetic heterogeneity across stem cell populations. We recently developed a new sequencing method (Repli-Bisulfite Sequencing) that enables analysis of DNA methylation within newly replicated strands of DNA over time. Using this method, we discovered that much of the methylation heterogeneity observed within human embryonic stem cells (hESCs) is temporal in nature and associated with DNA replication. Here, we employ bioinformatic analyses to explore how properties of post-replication DNA methylation dynamics relate to well-established features of the genome and the broader chromatin landscape. Our findings reveal that unique patterns of methylome replication associate with distal regulatory regions throughout the genome, enrich for cytosine residues dynamically methylated across cell types, and coincide with the location of stem cell-specific transcription factor binding and chromatin architectures. We also find correlations between sub-cell cycle kinetics in DNA methylation and the divergence of bulk methylation patterns observed during multiple cell generations and natural aging. Taken together, our studies suggest that (epi)genome replication may act as an important source of (temporal) regulatory variation in hESCs while, simultaneously, conferring susceptibility to epigenetic drift throughout the human lifespan. Our lab is also interested in understanding how the chemical and biophysical microenvironment influences adult cell behavior and phenotype through epigenetic gene regulatory mechanisms. We hope to use this information in the design of next-generation biomaterials. The second part of this presentation will describe how focal adhesions and cell-mediated forces contribute to inefficiencies observed during the acquisition of stemness from somatic cell states.

BIOGRAPHY:

Tim Downing has been on the faculty at UC Irvine since 2016 and holds a primary appointment in the Department of Biomedical Engineering. He also holds a courtesy appointment in the Department of Microbiology & Molecular Genetics. Tim received his B.S. in Chemical Engineering in 2008 from Northwestern University and Ph.D. in Bioengineering from UC Berkeley in 2013 under the mentorship of Dr. Song Li. As a Ford Foundation and UNCF/Merck Fellow, Tim completed his postdoctoral training in stem cell epigenomics with Dr. Alexander Meissner at Harvard University and the Broad Institute (Cambridge, Massachusetts). The Downing Lab focuses on understanding gene regulation during tissue development, regeneration, and disease progression. Building on this information, the lab also aims to develop molecular tools and biomaterials to synthetically regulate the epigenome for better control over cell fate and behavior. Tim is a 2019 NIH (DP2) New Innovator Award recipient and a 2020 recipient of the “Rising Star” Award from the Cellular and Molecular Bioengineering (CMBE) Special Interest Group within the Biomedical Engineering Society (BMES).