Special lecture 3

Exploring the physical genome

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The human genome is a 2 meter long object compacted and sequestered into a ~5 micron nucleus. We have develop divers methods, including ATAC-seq and single cell ATAC-seq to explore the ~2% of the genome open to the binding of trans-acting regulatory proteins. We have applied these methods to understanding human gene regulation in health and disease. I will discuss applications of open chromatin analysis in cancer, blood development, and development of human fetal brain and heart. Open chromatin maps in these tissues also provide direct interpretability of the impact of both rare and common human genetic variation on regulatory elements in the genome, as well as impacted genes.

William Greenleaf is a Professor in the Genetics Department at Stanford University School of Medicine, with a courtesy appointment in the Applied Physics Department. He is a member of Bio-X, the Biophysics Program, the Biomedical Informatics Program, and the Cancer Center. He received an A.B. in physics from Harvard University in 2002, and received a Gates Fellowship to study computer science for one year in Trinity College, Cambridge, UK. He then returned to Stanford to carry out his Ph.D. in Applied Physics in the laboratory of Steven Block, where he investigated, at the single molecule level, the chemo-mechanics of RNA polymerase and the folding of RNA transcripts. He conducted postdoctoral work in the laboratory of X. Sunney Xie in the Chemistry and Chemical Biology Department at Harvard University, where he was awarded a Damon Runyon Cancer Research Foundation Fellowship, and developed new fluorescence-based high-throughput sequencing methodologies. He moved to Stanford as an Assistant Professor in November 2011. Since beginning his lab, he has been named a Rita Allen Foundation Young Scholar, an Ellison Foundation Young Scholar in Aging (declined), a Baxter Foundation Scholar, and a Chan-Zuckerberg Investigator. His
highly interdisciplinary research links molecular biology, computer science, bioengineering, and genomics a to understand how the physical state of the human genome controls gene regulation and biological state. Efforts in his lab are split between building new tools to leverage the power of high-throughput sequencing and cutting-edge microscopies, and bringing these new technologies to bear against basic biological questions of genomic and epigenomic regulation. His long-term goal is to unlock an understanding of the physical “regulome” — i.e. the factors that control how the genetic information is read into biological instructions — profoundly impacting our understanding of how cells maintain, or fail to
maintain, their state in health and disease.