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Title: Deep Learning of Immune Cell Differentiation

Abstract: The mammalian genome contains several million cis-regulatory elements, whose differential activity marked by open chromatin determines cellular differentiation. While the growing availability of functional genomics assays allows us to systematically identify cis-regulatory elements across varied cell types, how the DNA sequence of cis-regulatory elements is decoded and orchestrated on the genome scale to determine cellular differentiation is beyond our grasp. In this talk, I'll present recent work using machine learning as a tool to derive an understanding of the relationship between regulatory sequence and cellular function in the context of immune cell differentiation. In particular, I'll present our deep learning approach (AI-TAC) to combining a large and granular compendium of epigenomic data and will describe approaches to robustly interpreting complex, black-box models in order to uncover mechanistic insights into immune gene regulation (Yoshida et al., Cell 2019; Maslova et al., PNAS 2020). Our work shows that a deep learning approach to genome-wide chromatin accessibility can uncover patterns of immune transcriptional regulators that are directly coded in the DNA sequence, and thus providing a powerful in-silico framework (an in-silico assay of sorts) to mechanistically probe the relationship between regulatory sequence and its function.