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Chromatin regulatory circuits in mammalian early development

Multicellular organisms rely on diverse epigenetic mechanisms to precisely decode their genomes, allowing the derivation and maintenance of a variety of cell types. A primary epigenetic process involved in facilitating gene regulation is the organization of the chromatin structure. Here I focus on the organization, dynamics and regulation of chromatin, and the role these play in orchestrating cellular fate decisions and commitment. First, I will present my work focused on the study of the transcriptome and chromatin organization of *in vivo* mouse Inner Cell Mass (ICMs) and evaluation of how well the *in vitro* ES cell model captures the *in vivo* state. Next, I will discuss our efforts to identify the principles governing the organization of Chromatin Regulators (CRs)—the enzymes controlling the structure of the epigenome. I will then present recent work leveraging new technologies I have developed for profiling chromatin structure to demonstrate a key role for the CR histone deacetylase SIRT6 in regulation of ES cell fate. Finally, I will discuss my plans to develop and apply innovative tools for characterizing the structure, function, and temporal dynamics of chromatin during development and differentiation. Altogether, my studies highlight the importance of chromatin regulation during development, identify similarities and distinctions between *in vivo* state and the ES *in vitro* model system, and elucidate key concepts regarding the organization and function of CRs.