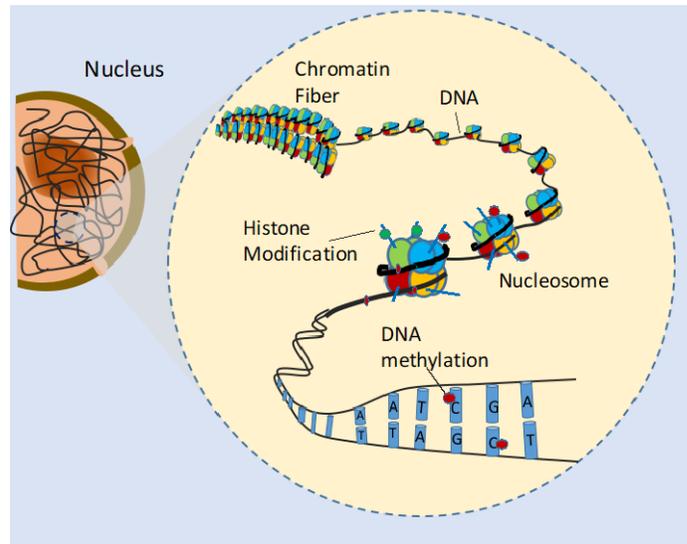




Functional Organization of the Human Genome



The 3-dimensional architecture of chromosomes in eukaryotic cells enables long-range communication between enhancers and promoters, and contributes to spatiotemporal gene expression programs in multicellular species. Detailed knowledge of how chromatin architecture dynamically reorganizes during development and in different cell types is critical for studying the gene regulatory programs controlling cell fate specification and elucidating the molecular basis of human diseases. We have delineated the dynamic chromatin architecture at high resolution during key developmental stages of human cardiomyocyte differentiation from embryonic stem cells. We observed dramatic changes in chromatin compartments, topological domains and enhancer/promoter interactions, which was correlated with dynamic gene expression patterns. The chromatin loop interactions help us to predict target genes of non-coding genetic variants associated with cardiac-related traits/diseases. We also generate maps of long-range chromatin interactions centered on human promoters in a large panel of human cell/tissue types. We use this information to infer the target genes of candidate regulatory elements, and suggest potential regulatory function for non-coding sequence variants associated with a large number of physiological traits and diseases. Integrative analysis of these promoter-centered interactome maps reveals widespread enhancer-like promoters involved in gene regulation and common molecular pathways underlying distinct groups of human traits and diseases.

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Host: Dr. Michael Wilson

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