Distinct epigenomic landscapes of pluripotent and lineage-committed human cells.

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Public Summary:
There are over 200 different human cell types, each with a unique function. For example, embryonic stem (ES) cells have the unique ability to differentiate to nearly any cell type, in contrast to terminally differentiated fibroblast cells which serve the specific function of providing the structural framework of connective tissues. Despite these dramatic functional differences, both ES cells and fibroblasts share the same genome sequence. Rather, it is thought that epigenetic modifications, such as methylation of DNA and post-translational modifications of histones, contribute to the unique gene expression profile of each cell type, and therefore to unique cellular functions. But how much epigenomes differ remains unclear. Here, we confirm that epigenomic landscapes in hESCs and lineage-committed cells are drastically different. By using techniques to map various epigenetic modifications in ES cells and fibroblasts, we find that nearly one-third of the genome differs in chromatin structure. Most changes arise from dramatic redistributions of repressive histone modifications, which form blocks that significantly expand in fibroblasts. Our results provide new insights into epigenetic mechanisms underlying properties of ES cells and differentiation.

Scientific Abstract:
Human embryonic stem cells (hESCs) share an identical genome with lineage-committed cells, yet possess the remarkable properties of self-renewal and pluripotency. The diverse cellular properties in different cells have been attributed to their distinct epigenomes, but how much epigenomes differ remains unclear. Here, we report that epigenomic landscapes in hESCs and lineage-committed cells are drastically different. By comparing the chromatin-modification profiles and DNA methylomes in hESCs and primary fibroblasts, we find that nearly one-third of the genome differs in chromatin structure. Most changes arise from dramatic redistributions of repressive H3K9me3 and H3K27me3 marks, which form blocks that significantly expand in fibroblasts. A large number of potential regulatory sequences also exhibit a high degree of dynamics in chromatin modifications and DNA methylation. Additionally, we observe novel, context-dependent relationships between DNA methylation and chromatin modifications. Our results provide new insights into epigenetic mechanisms underlying properties of pluripotency and cell fate commitment.