

## Epigenomics

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### Synopsis:

Uniquely human biological traits ultimately derive from changes that occurred in the human genome during the six million years of divergence from our closest relative, the chimpanzee. Traditionally, studies of the genomic basis of human-chimp divergence have focused on sequence differences in protein-coding and regulatory regions. We hypothesize that, in parallel to DNA changes, stable differences in the epigenomes of human and chimp contribute to the divergence of the two species. Accordingly, the goal of this study is to identify genome-wide epigenomic differences between human and chimp. Demonstration of the existence of stable epigenetic differences between species would open a new field in the study of species evolution. While the epigenome may be defined as the layer of molecular modifications of the genome, including cytosine methylation, histone modifications and associated chromatin proteins, as an initial approach we propose to determine the broad patterns of cytosine methylation in both genomes in a single well-defined cell lineage. This has not been feasible until now because technological limitations have prevented a whole epigenome analysis. To address this challenge, we plan to adapt Solexa massively parallel sequencing technology to a modified protocol for the detection of cytosine methylation. Consequently, this proposal has a two-fold aim: (a) the development of methods for cost-effective whole genome methylation analysis and (b) the production of a catalog of methylation differences between human and chimp. These differences will likely identify regions whose functions have changed during the divergence of the two species. This catalog will enable scientists to investigate a previously unexplored mode of human evolution (epigenetic inheritance) and help prioritize regions responsible for phenotypic differences underlying uniquely human biology.