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*The stem cell genomics project*

The molecular mechanisms that regulate the formation, self-renewal, and differentiation of stem cells remain at best poorly understood. The full exploitation of the potential of stem cells will require a complete understanding of the genetic factors that specify stem cell identity, and that regulate the commitment towards specific differentiated cell lineages. Therefore, we propose to define the spectrum of genes that define the identity and regulate the plasticity of embryonic and adult stem cells. This is the overarching goal of the Stem Cell Genomics Project. We will work primarily with human and mouse embryonic, neural, muscle, and marrow stem cells, and utilize high-throughput genomic analyses towards achieving this objective. A variety of stem cells will be isolated using a range of methodologies from both embryos and from a variety of adult tissues. We will employ emerging technologies to conduct expression microarray analysis on as few as 1–10 cells. Cluster analysis of multiple stem cell isolates and their immediate downstream differentiated derivatives will identify genes that are enriched or specifically expressed within the stem cell compartment. This data will then be used as a baseline to investigate the changes in gene expression that occur early during stem cell commitment and differentiation. To facilitate gene discovery and to complement the microarray analysis, we will employ serial analysis of gene expression (SAGE). A proteomics approach will be employed to monitor protein expression profiles from both immature stem cells and differentiated cells. Full exploitation of the stem cell expression data will be facilitated by the mounting of a web site for the dissemination and analysis of data (StemBase). This approach will facilitate large-scale reiterative analysis to elucidate hierarchical molecular regulatory mechanisms during stem cell commitment as well as stratification of subtle differences in stem cell states or identities.