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Control of Human Embryonic Stem Cell Pluripotence and Fate Choice

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Human embryonic stem cell (hESC) lines have been established from at least 200 different blastocyst-stage embryos and several earlier-stage embryos. Based on our large-scale molecular analyses, using gene expression microarray and global DNA methylation assays, we have observed that diverse hESC lines are remarkably similar to each other and very unlike any other cell type, including stem cells derived from somatic tissues. This is a surprising result, given that the large number of hESC lines we have analyzed were cultured under a variety of conditions in different laboratories in several countries. The existence of a unique hESC molecular "profile" suggests that pluripotence is a stable biological state that can tolerate a wide range of variation in culture techniques. We are linking gene expression, epigenetic, microRNA, and proteomic analyses of undifferentiated hESC and differentiated derivatives to identify the key elements that maintain hESC in a pluripotent state. Our results will help the design of methods to maintain hESC pluripotence and guide selection of hESC cell lines for generation of the ideal cell types for cell therapy.