Recombinant Laminins Drive the Differentiation and Self-Organization of hESC-Derived Hepatocytes.

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Abstract

Stem cell-derived somatic cells represent an unlimited resource for basic and translational science. Although promising, there are significant hurdles that must be overcome. Our focus is on the generation of the major cell type of the human liver, the hepatocyte. Current protocols produce variable populations of hepatocytes that are the product of using undefined components in the differentiation process. This serves as a significant barrier to scale-up and application. To tackle this issue, we designed a defined differentiation process using recombinant laminin substrates to provide instruction. We demonstrate efficient hepatocyte specification, cell organization, and significant improvements in cell function and phenotype. This is driven in part by the suppression of unfavorable gene regulatory networks that control cell proliferation and migration, pluripotent stem cell self-renewal, and fibroblast and colon specification. We believe that this represents a significant advance, moving stem cell-based hepatocytes closer toward biomedical application.

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