

Directed differentiation of human Embryonic Stem Cells to the endocrine pancreas lineage.

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Human embryonic stem cells (hESC) are an attractive source of replacement cells for cell therapy applications. We have developed a protocol to drive the differentiation of hESC *in vitro* to insulin-producing pancreatic cells for the treatment of type one diabetes. Our cultures are differentiated as embryoid bodies, three dimensional cell aggregates which structurally resemble the pre-gastrulation stage embryo. These cultures express genes in a sequence suggesting similarity to the ontogeny of the mammalian embryonic pancreas. This includes evidence for gastrulation and formation of the definitive endoderm, from which the embryonic pancreas emerges. In addition, only three dimensional cultures in the presence of extracellular matrix gives rise to robust and reproducible differentiation towards these endoderm-derived cells. Observations from this work suggest that the differentiation of some mature cell types may depend upon complex cell-cell and cell-matrix interactions inherent in three dimensional cell aggregates. For this reason, culture of hESCs as embryoid bodies in defined extracellular matrix may provide a powerful model for the *in vitro* reconstitution of early developmental mechanisms.

Speaker: William Rust earned his Ph.D. at the University of Nevada elucidating the mechanisms of integrin-mediated migration of metastatic breast cancer cells. For this work, he was awarded a Predoctoral Traineeship from the US Army Medical Research and Materiel Command Breast Cancer Research Program. William Rust further distinguished himself by winning the first President's Graduate Fellowship from the Graduate College of Nevada. Following his thesis work, William Rust completed a postdoctoral fellowship in the Transplantation department of Novartis Pharma AG, Switzerland, during which he investigated the mechanism of action of a novel immunosuppressant, FTY720, then in phase two clinical trials. In 2003, William Rust joined ES Cell International in Singapore and has since worked to derive insulin-secreting cells from human embryonic stem cells for the purpose of generating a cell therapy for patients of type 1 diabetes. In addition to a number of publications, William Rust has authored one granted US patent and his work in biotechnology has generated two pending patent applications. William Rust has been an avid lecturer since his first post at the University of Nevada where he taught Introductory Biology, Cell Biology and Genetics. He currently teaches Analytical Biochemistry, Pathology, and Human Genetics at SIM University and the Management Development Institute of Singapore. William Rust's research goals include understanding the early differentiation program of human embryonic stem cells for the purpose of directing lineage specification *in vitro*.