Karl Tryggvason, Madridge J Cancer Stud Res. 2018
http://dx.doi.org/10.18689/2640-5180.a3.005

Generation of Clinical Quality HESC-Derived Cells on Laminin Matrices for Regenerative Medicine

Karl Tryggvason
Duke-NUS Medical School, Singapore

Human embryonic stem cells (HESC) are considered the gold standard as a cellular source for regenerative medicine. The HESC's are obtained from supernumerary human *in vitro* fertilization (IVF) embryos that cannot be used for infertility treatment. FDA and EMA require that therapeutic HESC-derived cells should be differentiated under fully human and defined conditions, the differentiation protocols should be highly reproducible, the transplanted cells should exhibit normal function *in vivo* and improve function of the tissue to be repaired. Also, the cells should not be tumorigenic. We developed a technique for clonal establishment and expansion of HESCs on stem cell niche laminins LN-511 or LN-521 from 8-16-cell IVF embryos under fully xeno-free and chemically defined conditions. Important from an ethical standpoint is that the IVF embryos need not be destroyed like when making cell lines from the inner cell mass of human blastocysts. By culturing the pluripotent HESCs on specific cell type specific recombinant laminins, we can differentiate the cells to various lineages such as endothelial cells, cardiomyocytes and progenitors, retinal RPEs and photoreceptor progenitors. Cardiomyocyte progenitors injected into the heart infarction region of mice for human cardiomyocyte fiber bundles resulting in improved heart function. Also, laminins specifically present in the matrix surrounding photoreceptors allow generation of progenitor cells that express typical photoreceptor markers. The differentiated cells not exhibit signs of teratoma formation. Together with a major pharmaceutical company, we are developing HESC-derived cell lines for treatment of heart injury and macular degeneration.

Biography:

Karl Tryggvason, MD, PhD is Professor at Duke-NUS Medical School, Singapore and Duke University, North Carolina, as well as Senior Professor at Karolinska Institutet in Stockholm. His research concerns the molecular nature, biology and diseases of basement membranes (BM), a special compartment of the extracellular matrix. His group has cloned almost all human BM proteins and clarified genetic causes of many BM-associated diseases, such as Alport and congenital nephrotic syndromes, junctional epidermolysis bullosa and congenital muscular dystrophy, as well as studied matrix metalloproteinases, including the discovery and crystal structure of MMP-2. His group has produced most laminins as recombinant human proteins and currently the group mainly studies how different laminin isoforms influence cell growth and stem cell differentiation. Tryggvason has published over 400 research articles. He is a member of the Finnish Academy of Sciences and the Swedish Royal Academy of Sciences, and has served for 18 years as a member of the Nobel Assembly and Committee for Physiology or Medicine at the Karolinska Institute. He has received several international awards, and he is co-founder of Bio Lamina AB, Stockholm, that produces laminins for cell biology and cell therapy purposes.