Liver Cell-based Therapies: from Hepatocyte Transplant to (Immuno-suppression-free) Placenta Stem Cell Infusions

Thursday, December 16, 2021 at 16:00

Sumary:

Dr Gramignoli graduated at Univ. of Milan (Italy) in Biological Sciences and later Specialized in Medical Genetics (Univ. of Milan). Few years later, he acquired a PhD in Molecular and Translational Medicine at University of Milan-Bicocca while working at University of Pittsburgh Medical Center (Pittsburgh, PA-USA). In 2012, Roberto was recruited at Karolinska Institute, with the specific intent to support the Scandinavian Human Hepatocyte Transplant program and implement stem cell-based strategies for liver diseases.

Roberto and his Mentor (Dr Strom) have always been on the front line for the treatment of acute and congenital liver disorders by cell-based therapies, with hepatocyte transplant as a bridge or an alternative to orthotopic liver transplantation. Working together, they became the first facility to be approved by the FDA to isolate and transplant human hepatocytes, and performed clinical transplants both at Pittsburgh and Karolinska.

Since the main limiting factor in the use of human hepatocyte as a clinical therapy is the availability of useful human hepatocytes, they focused their attention on alternative sources, with greatest results obtained by transplantation of epithelial stem (AE) cells isolated from full-term amnion membrane (human placenta). Encouraged by the lack of tumorigenicity of AE cells and the expression of genes that could correct human metabolic liver diseases, in addition to their well-known immunomodulatory and anti-inflammatory effects, they proved correction in inborn error disease preclinical models, and a supporting therapy in fulminant hepatic failure model. Preclinical data suggests that, although not the patient's own cells, AE cells survive long-term and do not require immunosuppression. In support to allogenic use of AE cells without immunosuppression, they identified and described molecular pathways constitutively expressed by AE cells which may lead to a new, unlimited source of allogeneic stem cells for regenerative medicine approaches, not only liver-specific. These preclinical results stimulated the creation of AE cell bank for clinical purposes and a phase I/IIa clinical trial

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