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Immunomodulatory Properties of Human Amnion Epithelial Cell in Support to Allogenic Transplantation without Immunosuppression

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Placental amnion tissue has been used for decade in clinical practice, while amnion--derived cells has been proved successful only recently. We reported that human amnion epithelial cells (hAEC) from term placenta are not tumorigenic, have immunomodulatory and anti- inflammatory properties and once transplanted differentiate into functional hepatocyte-like cells. In preclinical studies with immune-competent mice, hAEC engrafted and survived without administration of immunosuppressive drugs, resulting in correction of metabolic liver diseases (iMSUD and PKU) and reversal of acute liver failure. Immunogenicity of the hAEC has been confirmed on purified immune effector cells (T-, B- and NK-cells).

Placental expression of non-canonical HLA proteins has been identified as key regulator in maternal-fetal immune-toleration. Amnion characteristically lacks HLA class 2 expression, and expresses both class 1a and 1b. We measure HLA-G and HLA-E expression both as membrane-bound and soluble isoforms. Recently, purinergic mediators, such ATP and NADPH, hydrolyzed by plasma membrane nucleotidases, have been identified to regulate immune cell response. High level expression of ecto-enzymatic axis and non-canonical HLA molecules likely play a key role in immunological tolerance and long-term acceptance of the human xeno-cell graft in immunocompetent mice. Based on their safety and the successful preclinical studies, approval was granted to begin banking of hAEC under cGMP condition at Karolinska Institute, and to perform hAEC transplants on 10 patients with liver disease without immunosuppression.

Biography:

Dr. Roberto Gramignoli, PhD, is presently is an Assistant Professor at Karolinska Institute, Department of Laboratory Medicine Stockholm, Sweden. From May 2012 - Dec 2014 he obtained Postdoc Position in Karolinska Institute, Department of Laboratory Medicine Sweden. From Jul 2007 - Apr 2012 he was a visiting fellow at University of Pittsburgh, Department of Pathology Pittsburgh, United States. And from Nov 2002 - May 2008 he was a research fellow at Fondazione IRCCS Ca' Granda - Maggiore Policlinico Hospital, Regenerative Medicine Area (Riparazione e Sostituzione di Cellule, Organi e Tessuti) Milano, Italy. In Apr 2000 - Jul 2002 he was an undergraduate student, from National Research Council, Milan, Italy.

Dr. Roberto's primary interest has always been to investigate human liver biology, pathology and disease; in particular, human liver cells (hepatocytes) transplantation as an alternative treatment to liver diseases. Gramignoli's group was the first facility approved for clinical HTx, and they performed infusions in patients with metabolic liver diseases. His group optimized methods to isolate human hepatocytes in GMP conditions; they identified several roadblocks that prevent a more successful implementation of HTx, including paucity of human hepatocytes. They investigated alternative sources, such as fetal liver cells, iPS and placental amnion epithelial (AE) cells. Encouraged by the lack of tumorigenicity and the expression of genes that could correct human metabolic liver diseases, in addition to immunomodulatory and anti-inflammatory effects, Gramignoli's group proved efficacy of human AE cells in several preclinical models, leading to AE cell banking for clinical purposes.

Skills and Expertise:

Cell Culture Molecular Biology, Cell Biology Tissue Engineering, Gastrointestinal Diseases, Stem Cell Biology, Liver Diseases, Clinical Trials, Regenerative Medicine, Hepatocellular Carcinoma, Stem Cells, Liver Cirrhosis, Liver Cirrhosis Hepatobiliary, Surgery Liver Transplantation, Transplantation Biliary Tract Diseases, Liver Surgery Pancreatic Diseases, Hepatitis Liver Failure Cholangiocarcinoma, Liver Diseases and Immunology, Pluripotent Stem Cells, Embryonic Stem Cell, Liver Regeneration Cell Therapy, Transplant Surgery, Cell Transplantation, Radiofrequency Ablation, Hepatocytes Stem Cell Therapy, RFAH epatoblastoma.