Gramignoli R, Arch Gen Intern Med 2019, Volume 3 | DOI: 10.4066/2591-7951-C2-026

# MOLECULAR MECHANISMS IN SUPPORT OF ALLOGENIC PLACENTA-DERIVED STEM CELL TRANSPLANTATION WITHOUT IMMUNOSUPPRESSION

**Gramignoli R**
Karolinska Institute, Sweden

Placenta is a non-controversial and readily available source of stem cells for regenerative medicine. Author previously reported that human Amnion Epithelial (AE) stem cells from term placenta are not tumorigenic, have immunomodulatory and anti-inflammatory properties. In preclinical and clinical studies, AE engrafted and survived without administration of immunosuppressive drugs, resulting in correction of metabolic diseases or reversal of acute and congenital diseases. During the past years he studied and identified molecular pathways driving AE immune regulatory capacity. He performed surface screening of AE cells, profiling all the molecules commonly described on stem and somatic cells. Amnion characteristically lacks HLA-II expression and expresses HLA-Ia and non-polymorphic HLA-Ib (responsible for maternal immune-toleration of the fetus). He quantified the level of expression of HLA-Ib molecules both as membrane-bound and soluble forms and he quantified the level of expression of all known plasma membrane nucleotidases, recently identified as important regulators in immune cell response. AE cells constitutively express all ecto-enzymes and their activity was confirmed on purified immune effector cells (T-, B- and NK-cells). He concluded that high level expression of ecto-enzymatic axis and HLA-G plays a key role in immunological tolerance and long-term acceptance of the human xeno-cell graft in immune-competent mice. The ability to treat the most common (liver) diseases with one stem cell therapy without the administration of immunosuppressive drugs could be a "game-changer" and will greatly expand the number of patients who could benefit from cellular therapies. Based on AE safety and successful preclinical transplants, approval was granted to begin banking AE cells under cGMP condition at Karolinska Institute and to perform AE transplants on 10 patients with liver disease.

## BIOGRAPHY

Gramignoli R is specialized in medical genetics and has a PhD in Molecular and Translational Medicine. During his post-graduate studies at University of Pittsburgh, he identified and proposed new solutions for roadblocks limiting clinical hepatocyte transplantation. Due to the paucity of human hepatocytes, he investigated alternative sources, such as iPS and placental stem cells. Working with his Mentor Dr Strom, they became the first group to get approval for isolation and clinical infusion of human hepatocytes and Amnion Epithelial (AE) stem cells. Over the past years, they have accumulated evidences on the potential of AE cells in several models of congenital liver diseases and as supporting therapy in fulminant hepatic failure. Based on safety and efficacy, in addition to AE immunomodulatory and anti-inflammatory effects, they are in the process to start a phase I/IIa clinical trial for liver disease and to create the first placenta stem cell bank.

roberto.gramignoli@ki.se

Note: