Extending the usefulness of extraembryonic mesenchymal stem cells in regenerative medicine: expression of novel markers, immunoregulatory molecules, and novel differentiation capacity

Giampiero La Rocca[1], Rita Anzalone[1], Melania Lo Iacono[1], Simona Corrao[1], Francesca Magno[1], Tiziana Loria[1], Antonino Di Stefano[2], Marilena Colombo[2], Pantaleo Giannuzzi[2], Giovanni Zummo[1], Felicia Farina[1]

[1] Department of Experimental Biomedicine and Clinical Neurosciences, Section of Human Anatomy, University of Palermo, Italy
[2] Fondazione "S. Maugeri", IRCCS, Istituto Scientifico di Veruno (NO), Italy

Mesenchymal stem cells (MSC) are considered promising tool in regenerative medicine applications. Even if they are already applied clinically, their extended characterization is being increasingly viewed as a needed feature, in order to avoid contrasting results when translating "in vitro" experiments to "in vivo" approaches. We recently demonstrated in human MSC isolated from the umbilical cord matrix (HEMSC) the expression of novel markers indicative of their stemness, as well as differentiative and immune properties [1].

HEMSC were cultured and subject to multiple molecular and morphological analyses to determine the expression of markers of interest.

Undifferentiated HEMSC expressed immunoregulatory molecules, both surface antigens and secreted cytokines. In addition to the differential expression of B7 co-stimulators (CD80+/CD86-), HEMSC expressed pregnancy-specific immunomodulatory molecules, together with non-classical type Ib MHC antigens. In fact, besides HLA-A and HLA-G, HEMSC expressed both HLA-E and HLA-F, two tolerance-promoting HLAs, involved in attenuating NK- and T-cytotoxic responses. In the continued characterization of these cells, we assessed the expression of endoderm-related molecules, suggestive of their possible transdifferentiation towards hepatocytes. In addition to HNF4α and endoderm-related GATA factors (GATA-4,-5,-6), undifferentiated cells expressed also albumin, cytokeratins 18 and 19, and further hepatocyte-enriched transcription factors (as HNF1α, and HNF1β), thus suggesting the possibility to be successfully differentiated towards hepatocytes [2].

The immunological and differentiative properties of human extraembryonic MSC are under intense investigation. Our data suggest that HEMSC bear new markers and have a hypoimmunogenic phenotype which can be a favoring factor to ensure the engraftment of "in vivo" transplanted cells.

References

[1] La Rocca et al. (2009) Histochem Cell Biol.
[2] Anzalone et al. (2010) Stem Cells Dev.

Key words
Mesenchymal stem cells, umbilical cord, immunogenicity, hepatocyte differentiation