Placental Stem Cells – Interview with Dr. Ornella Parolini of IPLASS

February 26, 2016 By Cade Hildreth (CEO)


Dr. Ornella Parolini, President of IPLASS

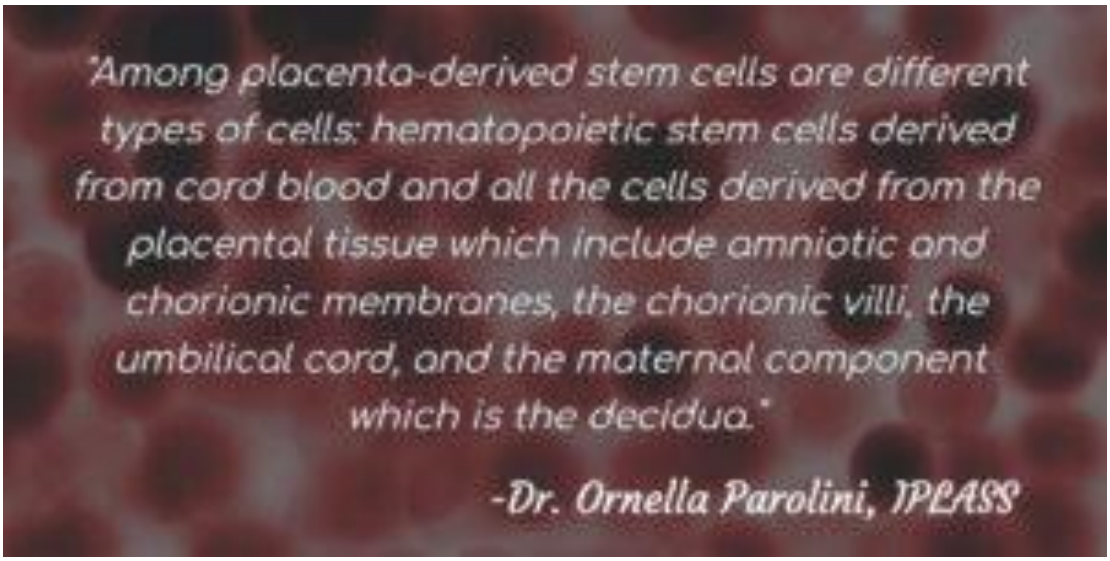
This is an interview with Dr. Ornella Parolini, Director of the E. Menni Research Center in Brescia, Italy, and President of the International Placenta Stem Cell Society (IPLASS).

In this interview, we discuss her pioneering research on human placental stem cells. Her research focuses on the immunomodulatory, anti-inflammatory, and antifibrotic properties of amniotic and chorionic membrane-derived cells.

Interview with Dr. Parolini of IPLASS

Cade Hildreth: How were placental stem cells first discovered?

Dr. Parolini: First, I would like to clarify the cells we are talking about. Among placenta-derived stem cells are different types of cells: hematopoietic stem cells derived from cord blood and all the cells derived from the placental tissue which include amniotic and chorionic membranes, the chorionic villi, the umbilical cord, and the maternal component which is the decidua.



Hematopoietic stem cells possess characteristics which typically define stem cells; they are clonogenic, possess the capacity to self-renew, and can differentiate towards multiple lineages. On the other hand, we should be careful in defining the other cells, such as stromal cells from the amniotic and chorionic tissue and epithelial cells from the amniotic membrane, as entirely stem cells, even if within these populations there are cells which possess stem cell characteristics

These cells were identified many years ago and their existence has been known for some time. However the first demonstration of their stem cell potential was around 2004 and we demonstrate that these cells can be transplanted without signs of immunological rejection (Bailo et al., Transplantation 2004). "In an editorial of our 2004 paper, Peter Heeger made a point to underline the infancy of the field at that time, and to highlight the interest of the transplantation community in keeping updated on bright future of perinatal tissues in transplantation applications (Heeger, Transplantation 2004)."

My idea to investigate placenta for its potential in regenerative medicine is summarized in an old slide that I often present, which shows the two pillars of cell transplantation,: one representing stem cell potential, and the other is referred to the ideal situation in an allogeneic transplantation, which is lack of rejection. I think placental cells combine these two features as their early embryological origin suggests the hypothesis of a high stem-cell potential, and the fact that the placenta contributes to the development and growth of an allogeneic fetus during pregnancy favors the idea that cells from the placenta could possess some intrinsic, peculiar immunological characteristics.

Cade Hildreth: What are the advantages of placental stem cells over other stem cell types?

Dr. Parolini: The placenta as a source of cells provides additional benefit when compared to other tissues. It is easy to procure, with no harm to the mother or baby. There are also no ethical issues associated with obtaining placenta, since it is considered

biological waste after birth. Its early embryological origin suggests the presence of cells with higher "stemness" potential.

A significant advantage of the placenta is the high cell yield, and the fact that placental cells have been less exposed to infections (they come from an infection-naïve environment), thus rendering disease transmission less-likely.

Cade Hildreth: What inspired you to start the International Placental Stem Cell Society (IPLASS)?

Dr. Parolini: The idea to investigate placenta to as a source of stem cells started more than 15 years ago, and after a few years, I realized that this topic was starting to spark the interest of other colleagues too. I organized the International workshop on Placenta-Derived Cells in 2007. The aim was to put together people that started working in this field in order to find consensus on terminology, phenotype, and main properties of cells isolated from different regions of placenta (Parolini et al, Stem Cells 2008), and of course to also meet each other and to define our area of interest for building collaborations.

In September 2009, the International Placenta Stem Cell Society (IPLASS) was founded to help strengthen the research in this field. Since then, we have had three biannual meetings, the first in Brescia, the second in Vienna and the third in Granada. Our next meeting will be in Riyadh (Saudi Arabia), and we will have many symposia within other meeting societies.

Cade Hildreth: What is the mission of the International Placental Stem Cell Society?

The main purpose of the society is to promote and advance research on placenta-derived stem cells, and this includes basic and clinical research using these cells and their derivatives.

Cade Hildreth: What are current goals that you have for the organization?

Dr. Parolini: I want everyone working in this field to know IPLASS, so that they can both contribute to and obtain benefit from the society. I would like it to springboard collaborative research.

IPLASS holds society meetings every two years, but I would also like to have smaller sessions whereby IPLASS members can present their work at other national or international, related society meetings. These satellite symposiums will be important in expanding the IPLASS network.

Cade Hildreth: What is the current focus of your own research?

Dr. Parolini: Currently my research is focused on understanding the mechanisms of the therapeutic effects of placental stem cells. My group has shown their therapeutic benefit in preclinical models of different diseases with underlying aberrant inflammatory processes, such as fibrosis and autoimmune diseases. In particular, we were one of the first groups who showed that these effects are mostly due to paracrine mediators produced by the cells which act on endogenous cells to induce tissue repair and/or regenerations.

So now we are also trying to understand which factors are responsible for therapeutic benefit, as we might even envisage a cell-free treatment, that would have the advantage of not only avoiding cell transplantation, but could also promote the differentiation of resident stem cells in the damaged tissue.

Cade Hildreth: What do you see as the future of placental stem cells and how they will impact society in 10-15 years?

Dr. Parolini: In 10 years I think the regenerative potential of placental cells will be clear. This would be thanks to preclinical and clinical trials with documented results.

Besides regenerative medicine, I also think that we will find a wider use for these cells, and this will be further supported considering the ease in obtaining them and lack of ethical concerns. I see a bright future for placental cells.

Cade Hildreth: What, if any, are current clinical applications of placental stem cells? If they have not yet reached the clinic, when do you anticipate that they will?

Dr. Parolini: I think we have to distinguish between what are now considered established clinical uses (approved and marketed for therapy) and investigative clinical trials. Currently, there are no approved and marketed placental cell therapies, but this is

probably a matter of time since there are many clinical trials being performed, some of which have reported beneficial results.

Besides the trials mentioned by Kyle Cetrulo in his interview, other ongoing clinical trials are being carried out with cells from different placental regions. These include cells manufactured by companies, such as Pluristem (PLX-PAD: Placental expanded adherent stromal cells) which are being tested in patients with pulmonary arterial hypertension, or Celgene (PDA-001/-002, human placenta-derived stem cells HPDSC) who have tested placental cells in patients with Crohn's disease and rheumatoid arthritis, and more recently in patients with multiple sclerosis.

Other institutions, such as Prince Charles Hospital of Brisbane and Karolinska Institutet, are testing placental derived MSC and decidual cells, respectively, in patients with idiopathic lung fibrosis, or graft versus host disease. Another interesting clinical trial is the one published in 2011 which tested placental MSC in patients with type II diabetes (Jiang et al, 2011).

I think its worth noting that Stemnion has developed amnion-derived cellular cytokine solution, which is being tested in patients with radiation-induced dermatitis, and will soon be tested in patients with dry eye syndrome and radiation-induced dermatitis. This strengthen our preclinical observation which show that conditioned medium from these cells could indeed replace cell based therapy (Rossi et al. 2012, Cargnoni et al. 2014, Pianta et al. 2015).

Most of these have been focused on evaluating the safety of placental cells and factors, but we should expect soon to begin seeing results on the therapeutic effectiveness too.