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Application of amniotic fluid stem cells in basic science and tissue regeneration

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The rapidly expanding field of stem cell research focuses on defining the required cell type for the right task in regenerative therapy. Thus, the foremost objective for successful cell replacement treatments is to understand which cell type e.g. stem cells or early progenitor cells versus mature and functional derivatives of these stem/progenitors are more suitable to achieve the desired long-term treatment benefit and ultimately tissue repair/regeneration. Several stem cell sources including embryonic, umbilical cord blood-derived, adult or tissue-residing and induced pluripotent stem cells have been evaluated in several settings displaying both advantages and disadvantages depending on the cell type end experimental setting used. Research in the last decade indicated that another fetal stem cell source, the amniotic fluid-derived stem cell (AFS) is gaining importance and yields promising results for regenerative applications. This research field is rapidly expanding since the discovery of fetal cells in amniotic fluid more than 50 years ago and that amniotic fluid is not just a liquid protective barrier for the developing fetus but is also a reservoir of many important substances ensuring fetal well being and maturation during gestation. Alongside these discoveries the focus shifted to the cells floating in amniotic fluid. Amniotic fluid contains a heterogeneous mixture of cells originating from the fetus or the fetal membrane which have been described to be composed of already committed and differentiated amniocytes and of cells displaying stem cell potential similar to mesenchymal stem cells. However, the feasibility and efficacy of these amniotic fluid-derived stem cells (AFS) in regenerative medicine applications is hampered by the outcome discrepancies amongst reports. This might be due to the observation that the potency of AFS is based on the employed isolation and enrichment approach. The review by Mara Cananzi and Paolo De Coppi (p. 77) summarizes general information about the isolation, characterization and potency of AFS with the focus on AFS selected by the expression of the cell surface marker CD117. These CD117-positive AFS exhibit the most promising stem cell capacity of all reported AF-derived cells so far and have been employed in several preclinical studies ranging from various tissue compartments and disease models. The outcome of these studies supported the notion that AFS are indeed a suitable cellular source for tissue repair processes by improving the endogenous tissue repair through secretion of soluble factors or by providing progeny capable to actively participate in tissue repair.

However, AFS cannot only be considered for in vivo tissue repair processes but also to supply progeny for the in vitro engineering of tissue replacement parts. The review by Shaun Kunisaki (p. 99) gives an insightful overview on the treatment options for congenital anomalies with the emphasis on AFS for the in vitro tissue engineering of replacement parts. The main advantage of AFS is that they can be applied in an autologous setting. Amniotic fluid can be collected during amniocentesis and AF-derived cells can be isolated and expanded alongside gestation. The advances in generating replacement parts from AFS allow the repair of congenital anomalies either still in utero or directly after birth with living grafts. It is assumed that theses grafts possess the intrinsic capacity to grow with the child thus reducing the need of repeated surgery to maintain the repair effect during postnatal development.

In general, amniocentesis is performed if a genetic defect of the unborn child is suspected. Thus the obtained AFS reflect the health status of the unborn child and can be used to investigate factors controlling cell fate. The review by Margit Rosner, Katharina Schipany, Bharanidharan Shanmugasundaram, Gert Lubec, Oliver Brandau and Markus Hengstschläger (p. 96) summarizes the data available on AFS to investigate cellular behavior and the role of signaling pathways. The authors focus on the mTOR pathway, which is known to be involved in many cellular processes including cell fate specification. They introduce the notion that AFS from different donors could be used to mimic disease modeling or for deciphering relevant signaling pathways for stem cell homeostasis by applying a gene manipulation approach. Results from these efforts should advance our understanding of stem cell definition and differentiation potential in vitro and in vivo. Taken together these reviews highlight the broad versatility of AF-derived stem cells to address basic scientific principles and their potential for advancing the understanding of tissue regeneration.

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