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Therapeutic potential of primitive mesenchymal stem cells to treat degenerative diseases

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Perinatal tissues are non-invasive, abundant and rather primitive sources of mesenchymal stem cells (MSCs) in comparison to MSCs isolated from adult tissues. They have received increasing attention since they do not pose ethical or moral concerns. We have developed a robust, reproducible and high yielding method for isolation of highly proliferative MSCs from umbilical cord/placenta tissue. MSCs isolated from all other sources stop growing after a few passages. However, irrespective of the source, all MSCs exhibit fibroblastoid morphology, express $CD29^+$, $CD44^+$, $CD73^+$, $CD90^+$ and $CD105^+$ and differentiate into adipogenic, chondrogenic and osteogenic lineages and some into neural lineage as well. However, the cord/placenta MSCs display higher colony forming efficiency and express even some pluripotent genes. They can also be maintained for self-renewal and potency for extended period of time; therefore, we call them primitive MSCs. We have investigated the therapeutic potential of these primitive MSCs to treat degenerative diseases including degenerative disc disease (DDD) and retinal degenerative disease (RDD) using animal models. When MSCs and their chondrogenic derivatives were injected into the IVDs of a rabbit model of DDD, they significantly improved the histology, cellularity, extracellular matrix protein and water and glycosaminoglycan contents. The IVDs receiving chondroprogenitor or nucleus pulposus (NP) like cells derived from MSCs exhibited higher expression of NP specific markers. The transplanted cells were functionally active in rabbit IVDs as they expressed human genes and proteins, SOX9, ACAN, COL2, FOXF1, KRT19, PAX6, CA12 and COMP implicated in NP biosynthesis. These studies suggested involvement of TGFβ1 pathway in regulating NP regeneration in rabbit IVD. Likewise, primitive MSCs and their neural derivatives have shown efficacy to improve vision in rd12 mice, a model of RDD. Latest findings of these translational studies as well as challenges and new opportunities will be discussed in the presentation.

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