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Abstract

Guided differentiation of ES cell into mesenchymal stem cell

Mesenchymal stem cells (MSCs) are defined by their ability both to undergo sustained proliferation in vitro and to give rise to multiple mesenchymal cell lineages including bone, cartilage, and fat cells. Although MSCs are a demonstrated reality with applications in regenerative medicine, not much is known about their in vivo characteristics, such as their developmental derivation. In this study, we sought to define the developmental pathway of MSCs. Using ES cell differentiation culture, we found that Sox1+ neuroepithelial cells generate MSCs at the highest efficiency. In our system, the ES cell-derived day 9 PDGFR+ precursors induced by RA morphologically exhibit the mesenchymal phenotype and undergo the self-renew in vitro with maintaining the potential to give rise to multiple lineages including bone, cartilage, and fat cells. Interestingly, the PDGFR+ cells are derived not from mesoderm cells but from neuroepithelium cells in our ES cell culture. This unexpected result suggests that the neuroepithelium is a candidate of embryonic origin of MSCs. To confirm this result in actual embryo, we are proceeding to search for the origin of MSCs in vivo using genetically fate-tracking method. In E9.5 embryos, we could induce MSCs from Sox1+ cells but not from PDGFR+ mesoderm. While this type of MSC is found also in neonatal bone marrow at low frequency, most MSCs in postnatal bone marrow are derived from other origins, which are also enriched in the PDGFR+ population. Thus, we show that MSCs are generated from multiple sources, with those derived from neuroepithelium constituting the earliest wave.

Biography

1987	M.D. Kumamoto University of School of Medicine, Kumamoto, Japan
1993	PhD., Internal Medicine, Kumamoto University School of Medicine
1995-1997	Research associate, Osaka University, Osaka, Japan
1998-2000	Postdoc. Howard Hughes Medical Institute, UCLA, USA
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