

# Intracranial Injection of Fetal Membraneous Mesenchymal Stem Cells Improves Prognosis Following Hypoxic Ischemic Encephalopathy in Neonatal Rats Brain

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**Objectives** : Hypoxic-ischemic encephalopathy (HIE) is one of the most serious problems for immature brain. Recently, mesenchymal stem cells (MSCs) have been reported to improve functional outcome in animal cerebral ischemia models. MSCs are isolated from not only several adult tissues, also fetal appendage. Fetal membrane is an ethical free tissue from which abundant MSCs can be obtained with ease. We introduced a new strategy for a HIE model in neonatal rats using MSCs isolated from fetal membrane (fmMSCs).

**Method** : MSCs were isolated from fetal membrane in pregnant *Levis* rats enhanced by green fluorescent protein (GFP). GFP-fmMSCs are plastic-adherent, expressing CD105, CD73, CD90. They are also differentiated to osteoblasts, adipocytes and chondrocytes in the specific medium. HIE rat model was made by modified Vannccis method, ligation of the left carotid artery, consequently exposing 8% oxygen for 2-3hours.  $1 \times 10^6$  of GFP-fmMSCs suspended  $20 \mu$ l medium was directly injected into HIE rat brain at  $2 \times 2 \times 2$  mm (anterior, lateral, depth) from bregma unilaterally, 24h or immediately after hypoxia. Seven days after transplantation, rat brains were examined by immunostaining.

**Results** : Pathological findings of HIE were observed in rats 7d after HIE model procedure. We found GFP positive immunostaining cells in ischemic-hypoxic rats brain, while no GFP positive cells were detected in the ipsilateral cortex.

**Conclusion** : fmMSC successfully transplanted into HIE brain in rats. Further studies are required to investigate the effects whether fmMSC transplantation has therapeutic potential for the HIE in neonatal brain.

