Differentiation of rabbit embryonic stem cells into trophoblast stem cell

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Inner cell mass (ICM) and trophoctoderm (TE) arise from the first differentiation event during mammalian embryogenesis. Previously reports have shown that mouse embryonic stem (ES) cells and primate embryonic stem (ES) cells could differentiate into trophoblast under certain condition. To test whether the rabbit embryonic stem (ES) cells derived by our lab could differentiate into the trophoblast cells, we used embryoid body and monolayer system in the presence of BMP4 to differentiate rabbit embryonic stem cells into trophoblast. Our result showed that rabbit embryonic stem (ES) cells could differentiate into trophoblast stem cells. In trophoblast stem cells, mRNAs of trophoblast stem cell-specific genes (*Eomes*, *Cdx2*) were present. Most of these cells expressed cytokeratin 7, cytokeratin 18, and for prolonged culture, part of cells underwent multinucleated differentiation, expressed placental-specific genes (*Hand1*, *Gcm1*, *Tpbpa*, *CGα*, *CGβ*). We also confirmed that trophoblast stem cells expressed the notch family members (*notch1-4*) and their target gene *Hes-1*. Furthermore, we found that TGFβ could maintenance the proliferation of trophoblast stem cells derived from rabbit embryonic stem (ES) cells. These results demonstrate that notch and TGFβ signal pathway may play an important role in proliferation of trophoblast stem cells.

Keywords: rabbit embryonic stem cells (rES), trophoblast stem cells, TGFβ

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