

p63 inhibits extravillous trophoblast migration and maintains cells in a cytotrophoblast stem cell-like state.

Journal: Am J Pathol

Publication Year: 2014

Authors: Yingchun Li, Matteo Moretto-Zita, Sandra Leon-Garcia, Mana M Parast

PubMed link: 25307348

Funding Grants: Molecular Mechanisms of Trophoblast Stem Cell Specification and Self-Renewal

Public Summary:

We had previously identified p63 as a protein found in placental stem cells and showed that it is required for differentiation of pluripotent stem cells into placental cells. In this paper, we probed its role further in placental cells, by changing its expression in these cells. We found that p63 plays a role both in promoting proliferation of, and inhibiting differentiation in, these placental cells.

Scientific Abstract:

Proper differentiation of placental epithelial cells, called trophoblast, is required for implantation. Early during placentation, trophoblast cell columns help anchor the developing embryo in the uterine wall. Although proximally continuous with villous cytotrophoblast (CTB) distally, these cells differentiate into invasive extravillous trophoblast. We previously reported that p63, a p53 family member, is highly expressed in proliferative villous CTB and required for induction of the trophoblast lineage in human pluripotent stem cells. We now further explore its function in human trophoblast by using both primary CTB from the early placenta and established trophoblast cell lines. We show that p63 is expressed in epidermal growth factor receptor-positive CTB and that its expression decreases with differentiation into HLA-G(+) extravillous trophoblast. In trophoblast cell lines, p63 is expressed in JEG3 cells but absent from HTR8 cells. Overexpression of p63 in both cell lines enhances cell proliferation and significantly reduces cell migration; conversely, down-regulation of p63 in JEG3 cells reduces cell proliferation and restores cell migration. Analysis of epithelial-to-mesenchymal transition, cell adhesion, and matrix degradation pathways shows that p63 blocks epithelial-to-mesenchymal transition, promotes a CTB-specific cell adhesion profile, and inhibits expression of matrix metalloproteinases. Taken together, these data show that p63 maintains the proliferative CTB state, at least partially through regulation of epithelial-to-mesenchymal transition, cell adhesion, and matrix degradation pathways.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/p63-inhibits-extravillous-trophoblast-migration-and-maintains-cells>