

MTA3 regulates differentiation of human cytotrophoblast stem cells.

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Authors:	Mariko Horii, Matteo Moretto-Zita, Katharine K Nelson, Yingchun Li, Mana M Parast
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Public Summary:

We identified MTA3 as a protein expressed in placental stem cells. By changing its expression, we found that MTA3 plays a role in regulating the differentiation of these stem cells into functional placental cells.

Scientific Abstract:

INTRODUCTION: Early placental development depends on the correct balance of cytotrophoblast (CTB) proliferation and differentiation, into either syncytiotrophoblast (STB) involved in nutrient/gas exchange, or invasive extravillous trophoblast (EVT) involved in establishment of blood flow to the placenta. Metastasis associated protein-3 (MTA3) is a transcriptional co-repressor known to regulate cell migration. In addition, MTA3 is reportedly decreased in preeclampsia. We set out to investigate the role of MTA3 in human trophoblast differentiation. **METHODS:** We co-stained first and third trimester placental sections with antibodies to MTA3 and other trophoblast markers. We also evaluated MTA3 expression following in vitro differentiation of primary isolated CTB. In order to evaluate the role of MTA3 in trophoblast differentiation, we used lentiviral constructs to overexpress and knock down its expression. Trophoblast differentiation was assessed by a combination of marker expression and functional assays, including hCG ELISA and cell migration. **RESULTS:** MTA3 was abundantly expressed in CTB and proximal cell column EVT in the human placenta and decreased with further differentiation into STB and mature EVT. MTA3 knockdown in JEG3 resulted in a 2-3 fold decrease in STB markers, CGB and GCM1, as well as in hCG secretion. In terms of EVT differentiation, MTA3 knockdown led to a 1.5-2 fold increase in HLA-G and cell migration, but decreased the mature EVT marker ITGA1. **DISCUSSION:** Taken together, our data suggest a role for MTA3 in terminal trophoblast differentiation into both hCG-secreting STB and mature EVT.

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