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Characterizing a human embryonic stem cell model of placental development

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When human embryonic stem cells (hESC) are treated with BMP4, they differentiate into trophoblast cells, the major cell type of the placenta. There are three main types of trophoblasts: syncytio-, cyto-, and extravillous trophoblasts. Here we studied syncytiotrophoblast formation using immunostaining and microarrays to follow changes in expression of genes known to be expressed in placental syncytiotrophoblast and regulated by BMP4 in hESC over time. We also examined the effect of oxygen atmosphere on the differentiation process by comparing cells cultured under high (H) oxygen (20%) and low (L) oxygen (4%) conditions. We narrowed our focus to the protein products of two genes: GATA2, and CGA. GATA 2 is a transcription factor important for syncytiotrophoblast differentiation, while hCGα (the product of CGA) is a product of syncytiotrophoblast and a subunit of the pregnancy hormone hCG. Our aim of this project was to determine by immunofluorescence when and where BMP-treated hESC express these two proteins. A time course was performed with two sets of hESC (line H1) cells exposed to BMP4 for one, three and six days under either N or L conditions. At day 1, neither GATA2 nor hCGα were expressed, but by day 3 small regions of GATA2-positive cells were evident, some of which were also hCGα-positive. By day 6, staining for both proteins was widespread, but the hCGα was always present in a subset of GATA2-positive cells. More GATA2/hCGα staining was seen under N as compared to L. Microarray analysis showed up-regulation of additional syncytiotrophoblast-associated genes and were consistent with the immunostaining data. We conclude that HES cells treated with BMP express syncytiotrophoblast markers, and that high oxygen accelerates differentiation of hESC.