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Epigenetic regulation of transcriptional activity within the syncytiotrophoblast of the human placenta.

The trophoblast is the epithelial covering of the human placental villous tree, forming the interface with the maternal circulation. It is a highly dynamic tissue, functioning in the active transport of nutrients between the maternal and foetal circulations, as well as producing and secreting hormones throughout gestation. The trophoblast protects the foetus from attack by the maternal immune system. The correct functioning of the trophoblast across gestation is vital for a healthy pregnancy outcome.

The villous trophoblast consists of two compartments: the proliferating cytotrophoblast cells (CTB); and the terminally differentiated syncytiotrophoblast (STB). STB nuclei lack proliferative capacity, instead the syncytium is sustained by continuous fusion of differentiating CTB cells , with the incorporation of new nuclei, organelles, cytoplasm and mRNAs .The nuclei within the two trophoblast compartments display contrasting morphologies, with most STB nuclei having a smaller volume, a more convoluted nuclear envelope and containing greater amounts of condensed chromatin than CTB nuclei.

It has recently been shown that a proportion of STB nuclei are transcriptionally active (Ellery et al 2009). I have employed the physical disector method to quantify this proportion. I have shown that the numerical density remains constant across gestation. The absolute numbers of transcriptionally active and inactive nuclei in the syncytium were calculated and found to increase exponentially (Fogarty et al. 2011)

This project will now focus on the mechanisms of chromatin condensation in STB nuclei. The nuclei retain a smooth nuclear profile and do not show typical features of apoptosis. Thus, we hypothesise that the increased chromatin condensation in these nuclei is due to epigenetic regulation. I will also investigate specialised regions of the syncytium, namely syncytial sprouts, which are associated with regions of proliferation, and knots, which are thought to be aggregations of aged, effete nuclei.

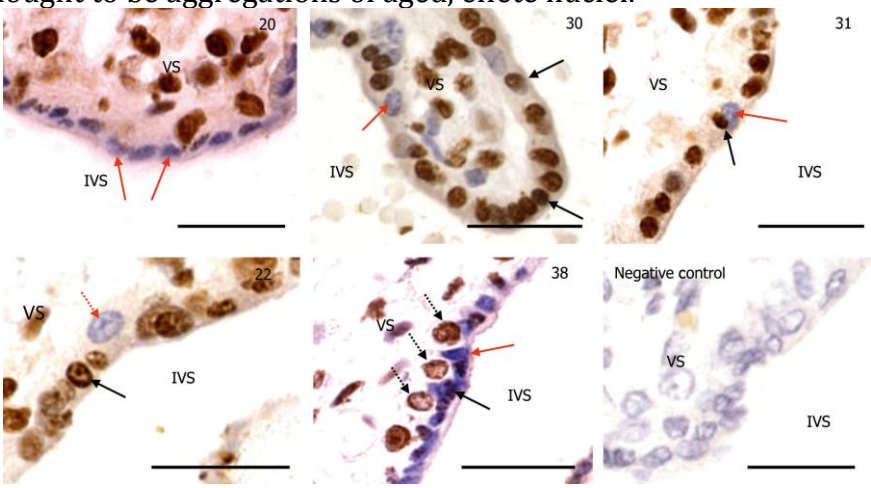

Figure: STB nuclei display different states of transcriptional activity. Immunohistochemistry for RNA Pol II was used to identify transcriptionally active nuclei. STB nuclei were identified on the basis of their relative size and location within the trophoblast. Black and red arrows indicate active and inactive nuclei, respectively. At all stages of gestation, both active and inactive STB nuclei were observed. Both transcriptional states were seen to lie adjacent to each other (A–C). Discrete stretches of inactive nuclei were also observed (not shown). Active STB nuclei seemed to correlate with the presence of an active underlying CTB nucleus, but inactive STB nuclei were seen adjacent to active CTB nuclei (D, E; dashed arrows indicate CTB nuclei).