Professor G. Burton and Dr A.C. Ferguson-Smith
University of Cambridge

Student: N. Fogarty

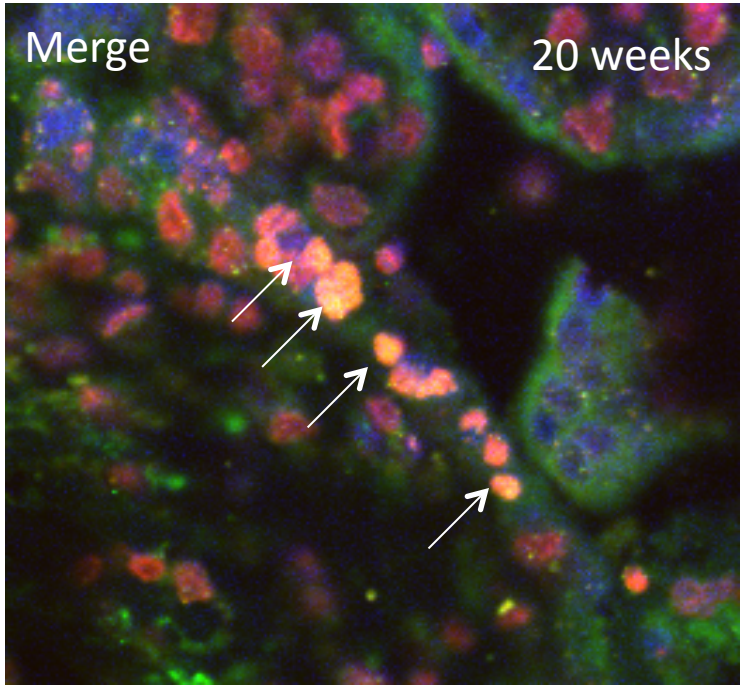
Epigenetic regulation of transcriptional activity within the syncytiotrophoblast of the human placenta.

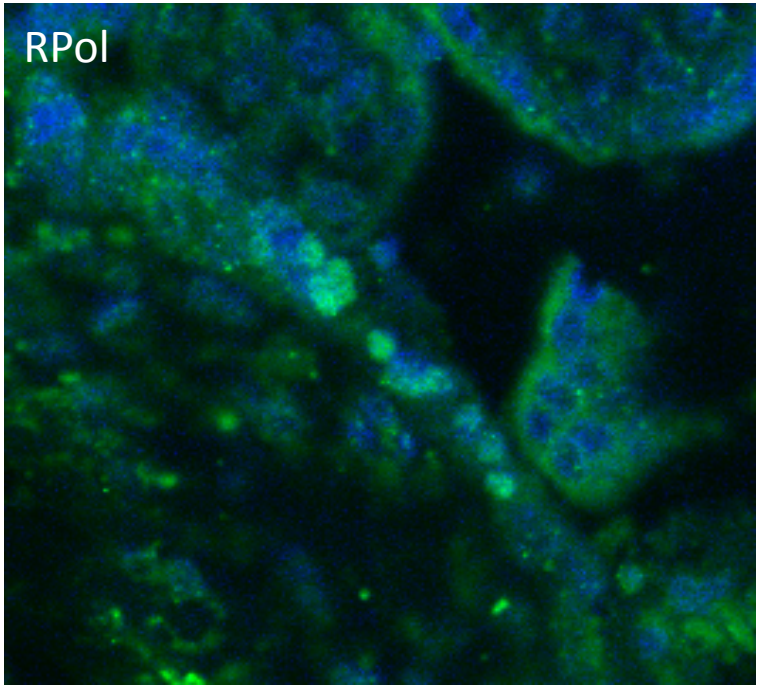
The syncytiotrophoblast forms the epithelial covering of the human placental villous tree, and is of critical importance to a successful pregnancy. It plays key roles in the active transport of nutrients between mother and fetus, hormone synthesis, metabolic regulation and immunological protection. Syncytiotrophoblast is a terminally differentiated, multi-nucleated tissue that is generated by the continual fusion of underlying cytotrophoblast progenitor cells. As a consequence, the syncytial nuclei may vary in age by many months.

The nuclei display contrasting patterns of chromatin condensation. Many, particularly in early pregnancy, are euchromatic whereas later in pregnancy nuclei with large aggregates of dense heterochromatin are seen, often closely packed together. In view of these appearances it might be expected that the nuclei show different levels of transcriptional activity. Surprisingly, however, *in vitro* studies have shown no incorporation of ^{3}H-uracil into any syncytial nuclei, suggesting they are all transcriptionally inactive.

This study has adopted a different approach, using immunohistochemistry to test for markers of active transcription, including RNA polymerases I and II, the transcription factor phospho-CREB, and the nucleolar transcription factor UBF. Nuclei staining positive for these markers were identified within the syncytiotrophoblast, often demonstrating co-localisation (Figure 1). Quantitative studies performed during the first year of this project in collaboration with Professor Terry Mayhew (University of Nottingham) on samples across gestational age have revealed that the proportion of Pol II nuclei remains constant. As a result, the total number of Pol II nuclei increases exponentially.

Our data therefore indicate that a proportion of syncytiotrophoblast nuclei are transcriptionally active, a finding that has major consequences for our understanding of the cell biology of this intriguing and important tissue. Future studies are aimed at investigating epigenetic changes that may account for the unique contrasting patterns of chromatin condensation seen within these nuclei.





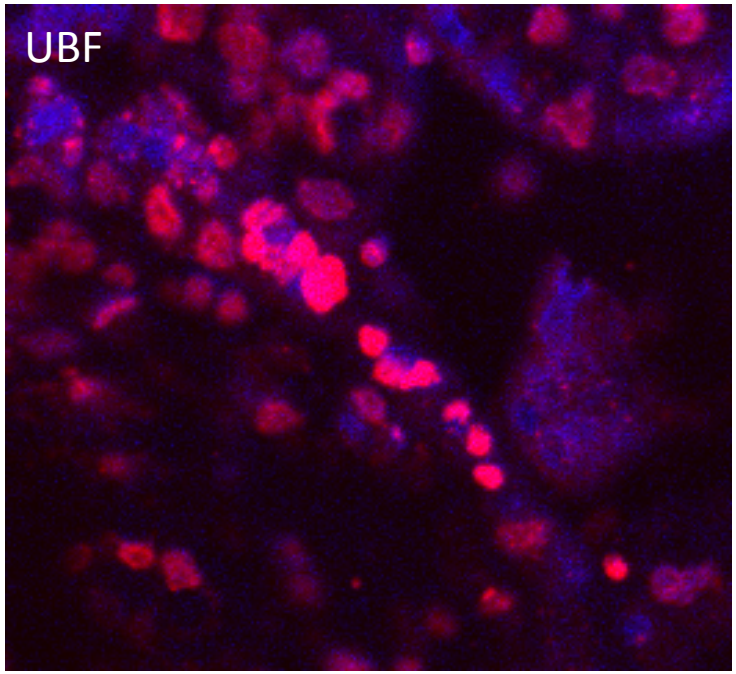


Figure 1. Transcriptional activity in syncytiotrophoblast nuclei. Immunofluorescence shows co-localisation (arrowed) of UBF (red) and RNA Polymerase II (green) in a proportion of STB nuclei. 20 weeks gestational age.