**The role of stanniocalcin-1 in spiral artery remodelling**

**Arwa Mazen, Sandra Ashton, Judith Cartwright, Guy Whitley**

In early pregnancy extravillous trophoblasts invade into and remodel the maternal spiral arteries (SA) replacing both the endothelial cells (EC) and vascular smooth muscle cells (VSMC). However the mechanism has not been completely elucidated. Using a 3D vascular spheroid model we have shown that trophoblast conditioned medium (TCM) stimulates the expression of a number of genes including stanniocalcin-1 (STC-1). STC-1 is a widely expressed glycoprotein implicated in tumour angiogenesis however its role in SA remodelling has not been investigated.

**Objectives:** To investigate the regulation and function of STC-1 in spiral artery remodelling.

**Methods:** The trophoblast cell line SGHPL-4 was grown in 3D culture and after 72h the TCM harvested. An angiogenic protein array was used to determine the components of the TCM. The human umbilical vein endothelial cell line SGHEC-7 was stimulated with TCM and the secretion of STC-1 determined by ELISA. Identification of pathways activated by TCM and responsible for the increased secretion of STC-1 were investigated using pharmacological inhibitors. The expression of STC-1 in first trimester decidual tissue was determined by immunohistochemistry. The effect of recombinant STC-1 on VSMC migration was determined by time-lapse microscopy.

**Results:** STC-1 is expressed in EC of first trimester spiral arteries undergoing vascular remodelling. Both TCM and PMA (an activator of protein kinase C (PKC), stimulated the secretion of STC-1 however the PKC inhibitor Gö6983 did not affect TCM stimulated STC-1 secretion by endothelial cells. Although it was possible to identify a number of growth factors and cytokines present in TCM none were able to replicate the effect of TCM on STC-1 secretion. Recombinant STC-1 stimulates the migration of VSMCs.

**Conclusion:** TCM stimulates the secretion of STC-1 by endothelial cells and this can then stimulate VSMC to migrate and so may play a role in SA remodelling seen in early pregnancy.