Endometriosis is a non-malignant disorder defined as the presence of endometrial tissue outside the uterus, with lesions typically found on the peritoneal lining in close association with mesothelial cells. Its aetiology is uncertain but it is believed that TGFβ plays a key role. Inhibitor of DNA binding (ID) proteins are transcriptional targets of TGFβ. Overexpression of ID1 has been implicated during tumor angiogenesis by promoting proliferation of endothelial progenitors through regulation of vascular endothelial growth factor (VEGF.) Our aim was to determine the regulation of IDs by TGFβ in the peritoneum and the downstream effect of ID on VEGF expression.

TGFβ1 was measured in peritoneal fluid by ELISA (n=18). Expression of IDs and VEGF was examined in peritoneal biopsies (n=8) from women with/without endometriosis (LREC 11/AL/0376), in primary human peritoneal mesothelial cells (PMC) (n=6) and an immortalised mesothelial cell line (MeT5A) (n=3). ID target genes were confirmed by siRNA knockdown in MeT5A cells (n=3).

Concentrations of TGFβ1 were increased in the peritoneum of women with endometriosis (p<0.05). ID1-4 and VEGF were immunolocalised to mesothelial cells in tissue sections. Treatment of mesothelial cells with TGFβ1 increased ID1 (p<0.05) but decreased ID2 (p<0.05) transcript abundance. TGFβ1 increased VEGF expression (p<0.05); and its regulation by IDs was confirmed by siRNA knockdown in MeT5A cells (p<0.05).

Our data highlights a role for ID proteins in the pathophysiology of endometriosis as a downstream effector of TGFβ1 dependent regulation of VEGF. Targeting this pathway may lead to new therapeutic agents capable of inhibiting endometriosis development.