PROGESTIN-INDUCED PROPROTEIN CONVERTASE 6 IS NECESSARY FOR DECIDUALISATION OF HUMAN ENDOMETRIAL STROMAL CELLS *IN VITRO*

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Decidualisation of human endometrium is an essential preparative event for successful establishment of pregnancy, and involves dramatic morphological and functional differentiation of the human endometrial stromal cells (ESCs). Proprotein convertase 6 (PC6) plays an important role in the processes of stromal cell decidualisation and embryo implantation in the mouse. PC6 is a member of the proprotein convertase family responsible for processing precursor proteins to their bioactive forms by selective proteolysis. In the present study we investigated the regulation of PC6 mRNA and protein expression in ESCs during decidualisation *in vitro*, and established a function for PC6 in decidualisation using morpholino antisense oligonucleotides (MOs). PC6 mRNA levels in ESCs during decidualisation were determined using quantitative real-time RT-PCR. 17β-oestradiol (E) plus medroxy-progesterone acetate (P) caused a significant increase in PC6 mRNA during decidualisation, whereas E alone did not increase PC6 mRNA expression. Consistent with the results of real-time PCR, much stronger PC6 immunostaining was observed in the cytoplasm of E plus P-treated ESCs (decidualised) compared to the E-treated ESCs (non-decidualised) on Day 12 of culture. This strong staining for PC6 was abolished by cotreatment with ZK 98299, a progesterone receptor antagonist. To investigate whether the induction of PC6 was necessary for decidualisation *in vitro*, MOs were used to block PC6 synthesis in cultured ESCs. PRL production, a typical marker for decidualisation, was significantly attenuated in decidualing ESCs following treatment with PC6 MOs in comparison to controls. These results suggest that PC6 plays a key role for decidualisation in human ESCs.

10.1071/SRB04Ab228