CCN5 INHIBITS THE PROLIFERATION AND MOTILITY OF HUMAN MYOMETRIAL AND LEIOMYOMA SMOOTH MUSCLE CELLS

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Uterine fibroids are a significant problem in women's health. The only treatment option currently available with minimal recurrence risk and reduction of symptoms is hysterectomy. Because leiomyomas are benign tumors of smooth muscle cells, one approach to developing therapeutic rationales is to elucidate the mechanisms that regulate uterine smooth muscle cell proliferation and to search for molecules that can inhibit uterine smooth muscle cell mitogenesis. Two candidate molecules are the glycosaminoglycan heparin and CCN5, a heparin-induced gene and member of the CCN family. We have previously shown that heparin is capable of inhibiting both vascular and uterine smooth muscle cell proliferation and motility. In addition, we have demonstrated that overexpression of CCN5 using an adenoviral construct inhibits vascular smooth muscle cell proliferation and motility, but does not affect adhesion and apoptosis. Here, we demonstrate that the proliferation and motility of both human myometrial and leiomyoma smooth muscle cells are inhibited by overexpression of CCN5. When compared to cells infected with GFP control adenovirus, the proliferation of CCN5-infected cells is inhibited by up to 60%, depending on the MOI. Using a scratch wound assay, our results indicate that AdCCN5 at MOI as low as 10 results in a 33% reduction in migration compared to AdGFP-infected cells. Experiments are currently in progress to determine whether CCN5 influences cell death in uterine smooth muscle cells. We also are examining the role of heparin in induction of CCN5 expression and whether myometrial and leiomyoma smooth muscle cells express similar levels of CCN5.