P003 Heparan sulfate influence the ripening of the human uterus

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During pregnancy, the smooth muscle of the uterus must be relaxed to allow the growth of the fetus and the cervix must be stiff and closed to retain the fetus. Some weeks before labor, the uterus transforms to a contractile organ and the cervix becomes soft to be able to dilate. This active remodeling of the tissue is accomplished by fibroblasts. It is shown that injections of low molecular weight heparins (LMWH) to patients with coagulation disorders results in a 40% shorter delivery time. Prerequisite for this effect is the recruitment of fibroblasts with inflammatory properties in the cervix. Thus fibroblasts established from non pregnant donors secrete minute amount of interleukins and metalloproteinases whereas fibroblasts from post partal donors are efficient producers of interleukin 6 and 8 and metalloproteinases. The role of interleukin 8 and 6 is to recruit and activate neutrophils, which are responsible for the final remodeling at partus. Since injections of LMWH induce a more efficient delivery, heparan sulfate of various structures were tested for stimulatory activity on cervical fibroblasts. Non pregnant fibroblasts did not respond however post partal versions responded strongly by increasing IL-6 and IL-8 secretion. To check if the anticoagulant motif of heparan sulfate and heparin is required for activity, heparin was treated by periodate/alkali to cleave of the anticoagulant pentasaccharide. The resulting compound did affect the cervical fibroblasts in a dose dependent manner.