Abstract

In vitro studies in our laboratory have indicated that heparan sulfate proteoglycans (HSPGs) play an important role in murine embryo implantation. In order to investigate the potential function of HSPGs in human implantation, two human cell lines (RL95 and JAR) were used to model uterine epithelium and embryonal trophectoderm, respectively. A heterologous cell-cell adhesion assay was developed to determine if binding of JAR cells to RL95 cells was heparan sulfate-dependent. Labeled, single cell suspensions of JAR cells attached to confluent monolayers of RL95 cells in a dose- and time-dependent manner. Heparin-like glycosaminoglycans and JAR cell proteoglycans competitively inhibited JAR cell adhesion to RL95 cells by 50% or more. A panel of chemically modified heparins were used to demonstrate that O-sulfation and amino group substitution were critical for inhibition of cell-cell adhesion. Treatment with chlorate, an inhibitor of ATP-sulfurylase, resulted in a 56% reduction in cell-cell binding compared to untreated controls. Heparinase and chondroitinase ABC markedly inhibited JAR-RL95 binding, while chondroitinase AC had no significant effect. These observations indicated that HSPGs as well as dermatan sulfate-containing proteoglycans participated in cell-cell binding. Collectively, these results indicate that initial binding interactions between JAR and RL95 cells is mediated by cell surface glycosaminoglycans (GAGs) with heparin-like properties (i.e., heparan sulfate and dermatan sulfate). These observations are consistent with an important role for HS and heparin-like GAGs as well as their corresponding binding sites in early stages of human trophoblast-uterine epithelial cell binding.