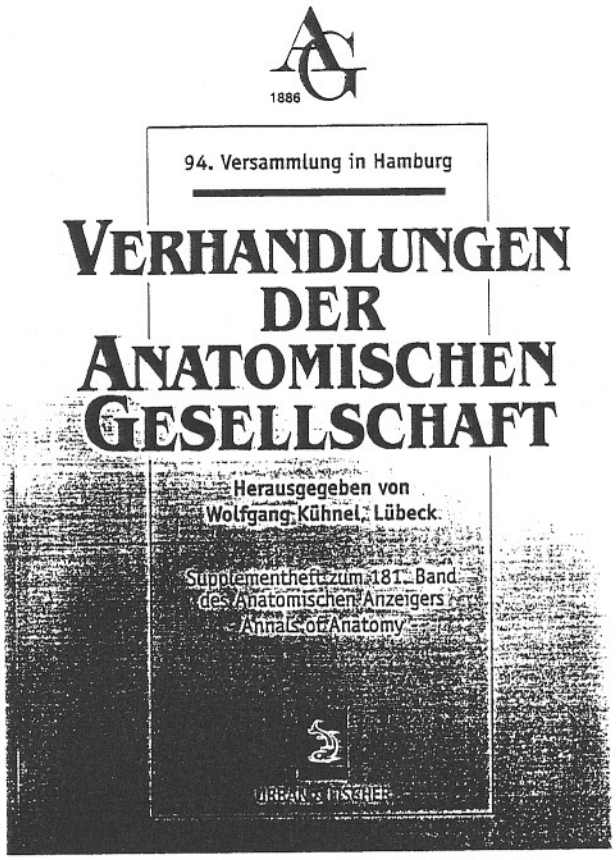

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Staurosporine, a protein kinase C inhibitor, causes down-regulation of the epithelial phenotype in human endometrial HEC-1-A cells and induces adhesiveness for trophoblast

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The uterine epithelium displays a polarized organization with apical, lateral, and basal plasma membrane domains. Although non-adhesive for trophoblast throughout most of the menstrual cycle, uterine epithelial cells allow attachment of blastocysts to their apical pole during embryo implantation. A mechanism to achieve apical adhesiveness for trophoblast is recently discussed postulating that uterine epithelial cells modulate their apico-basal polarity. Here, we report that, when human uterine epithelial HEC-1-A cells (HEC) are treated with the protein kinase C inhibitor staurosporine, cell polarity is down-regulated. Simultaneously, this alteration of the epithelial phenotype is accompanied by a large increase in the adhesiveness of the free plasma membrane domain of HEC for trophoblast-type JAR cells as shown by the centrifugal force-based adhesion assay. Staurosporine-induced alterations involved remodeling of the apical membrane, i.e. loss of surface microvilli and the formation of cytoplasmic processes containing actin filaments. The distribution of adhesion molecules (α6-, β1-, β4-integrin subunits) became extended from a distinctive localization at baso-lateral borders in untreated HEC to apical sites in treated cells. In addition, the actin cytoskeleton was restructured: While the stress fiber system normally associated with the basal cell pole disappeared, apically localized actin filaments became prominent. Moreover, treatment of HEC with staurosporine caused a loss of the tight junctional barrier function, although tight junction proteins (occludin; ZO-1) remained localized at the lateral membrane in treated cells, as did adherens junction (E-cadherin) and desmosome proteins (desmoplakin I). In contrast to the described changes in the actin pattern, staurosporine did not affect the pattern of cytokeratin type intermediate filaments. Overall, these results demonstrate that (i) the apico-basal polarity of uterine epithelial HEC cells can be down-regulated and (ii) the apical adhesiveness for trophoblast can be up-regulated by treatment with staurosporine, and suggest that a protein kinase C mediated signaling pathway might be a link between modulation of the epithelial phenotype and induction of apical adhesiveness in these cells.