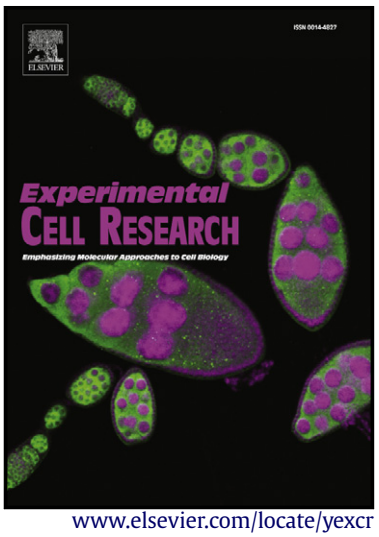

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HYALURONAN SYNTHASE 1 (HAS1) PRODUCES A CYTOKINE- AND GLUCOSE-INDUCIBLE, CD44-DEPENDENT CELL SURFACE COAT

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ABSTRACT

Hyaluronan is a ubiquitous glycosaminoglycan involved in embryonic development, inflammation and cancer. In mammals, three hyaluronan synthase isoenzymes (HAS1-3) inserted in the plasma membrane produce hyaluronan directly on cell surface. The mRNA level and enzymatic activity of HAS1 are lower than those of HAS2 and HAS3 in many cells, obscuring the importance of HAS1. Here we demonstrate using immunocytochemistry and transfection of fluorescently tagged HAS1 that its enzymatic activity depends on the ER-Golgi-plasma membrane traffic, like reported for HAS2 and HAS3. When cultured in 5 mM glucose, HAS1-transfected MCF-7 cells show very little cell surface hyaluronan, detected with a fluorescent hyaluronan binding probe. However, a large hyaluronan coat was seen in cells grown in 20 mM glucose and 1 mM glucosamine, or treated with IL-1β, TNF-α, or TGF-β. The coats were mostly removed by the presence of hyaluronan hexasaccharides, or Hermes1 antibody, indicating that they depended on the CD44 receptor, which is in a contrast to the coat produced by HAS3, remaining attached to HAS3 itself. The findings suggest that HAS1-dependent coat is induced by inflammatory agents and glycemic stress, mediated by altered presentation of either CD44 or hyaluronan, and can offer a rapid cellular response to injury and inflammation.

KEY WORDS

Hyaluronan, hyaluronan synthase, inflammation, IL-1β, glucosamine, CD44.