SELECTIN-BLOCKING ACTIVITY OF A FUCOSYLATED CHONDROITIN SULFATE GLYCOSAMINOGLYCAN FROM SEA-CUCUMBER: EFFECT ON TUMOR METASTASIS AND NEUTROPHIL RECRUITMENT*

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As a consequence of its anti-selectin activity, heparin attenuates metastasis and inflammation. Here we show that fucosylated chondroitin sulfate (FucCS), composed of a chondroitin sulfate backbone substituted at the 3-position of the β-D-glucuronic acid residues with 2,4 disulfated α-L-fucopyranosyl branches, is a potent inhibitor of P- and L-selectin binding to immobilized sialyl Lewis^x and LS180 carcinoma cell attachment to immobilized P- and L-selectins. Inhibition occurs in a concentration-dependent manner. FucCS was 4-8 folds more potent than heparin in the inhibition of the P- and L-selectin-sialyl Lewis^x interactions. FucCS also inhibited lung colonization by adenocarcinoma MC-38 cells in an experimental metastasis model as well as neutrophil recruitment in two models of inflammation. Inhibition occurred at a dose that produces no significant change in plasma aPTT. Removal of the sulfated fucose branches on the FucCS, abolished the inhibitory effect *in vitro* and *in vivo*. Overall, the results suggest that invertebrate FucCS may be a potential alternative to heparin for blocking metastasis and inflammatory reactions without the undesirable side effects of anticoagulant heparin.