KININOGEN ACTIVITY IS CONTROLLED BY INTERACTION WITH CELLS

Motta G. and Tersariol I.L.S.

Departamento de Bioquímica UNIFESP/EPM, São Paulo, Brasil.

Kininogens are cystatins and their main function has been described as precursors of bradykinin. Nevertheless, high molecular weight kininogen (HK) presents antithrombin, antiadhesive, profibrinolytic activities and plays role in angiogenesis. We analyzed HK interaction with cells using endothelial cells from rabbit aorta (RAECs) and two different Chinese hamster ovary cell lines, wild type (CHO-K1) and mutant (CHO-745), which is deficient in proteoglycans synthesis. RAECs bound HK and only a peptide derived from domain 5 completely blocked this binding. HK colocalized with cathepsin B and heparan sulfate on cell surface and with Lyso Tracker inside cells. Intact HK (140 kDa) bound was partially hydrolyzed after 3 h and a fragment (82 kDa) detected increased over time up to 9 h. This hydrolysis was inhibited by E-64 and cathepsinB-inhibitor. HK assembled to both CHO-K1 (37°C B_{max} = 4.5 x 10^6 sites/cell and K_{dapp} = 6.1 nM; 4°C B_{max} = 0.36 x 10^6 sites/cell and K_{dapp} = 1.8 nM) and CHO-745 (37°C B_{max} = 2.6 x 10^6 sites/cell and K_{dapp} 1.4 nM; 4°C B_{max} = 1.5 x 10^6 sites/cell and K_{dapp} = 7.1 nM) and its hydrolysis started within one hour interaction in both cell lines. Our data suggest that HK processing by cells is a mechanism which involves endocytosis and hydrolysis mediated by cysteine peptidases and glycosaminoglycans which controls HK activity. Supported by FAPESP and CNPq.
Key words: kininogens, cell interaction, processing