A novel soluble variant of human CEACAM1 appears due to molecular turn-over processes in contact-inhibited differentiated epithelial and endothelial cells

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Carcinoembroyic antigen-related cell adhesion molecule 1 (CEACAM1) is a highly glycosylated cell adhesion receptor molecule. It is expressed on hematopoietic cells, epithelia and angiogenicly activated endothelia. CEACAM1 plays an important role in cell morphogenesis, tumorigenesis, insulin metabolism, T-cell regulation and neovascularisation. It is a member of the immunoglobulin superfamily and consists of one N-terminal V-like Ig domain, followed by three C2-like Ig domains (N-A1-B1-A2) and shows a molecular weight of 120-160 kDa. In human urine we found a variant of CEACAM1 with a molecular weight of 72 kDa. Epitope mapping based on sandwich-ELISA and western blotting using mono-specific antibodies for the N-domain (#18/20), the A2 domain (8G5), the linker between the B1-A2 domains (4D1C2) and the cytoplasmic part (CC1-cyt) revealed that this novel CEACAM1 form was lacking the N-domain and at least part of the A2 domain.Analyzing the putative origin of the truncated CEACAM1 revealed that cells expressing CEACAM1 endogenously (A549, T102/3) and those transfected with CEACAM1 (Hela-CEACAM1) contained the native as well as the truncated form of CEACAM1. Interestingly, studies using cortex endothelial cell line (AS-M.5) revealed a truncated CEACAM1 variant with a significantly higher molecular weight of 95 kDa. Further studies showed that the truncated CEACAM1 appeared not due to differences in deglycosylation or apoptosis. Furthermore, studies utilizing A549 epithelia cells, a cell type loosing its entire endogenous CEACAM1 expression by entering the proliferative stage, revealed that truncated CEACAM1 becomes not generated when full length CEACAM1 expression is down-regulated in epithelial cells entering cell proliferation. However, studies revealed that when cells were kept in the contact inhibition state a significant accumulation of truncated CEACAM1 appeared in the cell lysates and in the supernatant. The present data suggest that truncated CEACAM1 found in urine is generated during molecular turnover processes in epithelial and endothelial cells. Thus, this study leads to a better understanding of CEACAM1 turnover processes and the mechanism involved in the production of functionally, an inactive CEACAM1 form since this truncated CEACAM1 lacks the ligand binding N-domain and the signal transducing cytoplasmic domain. Similar turnover processes and mechanism involved may be applicable to other adhesion receptors such as cadherins, selectins, and integrins.

In summary, we demonstrate here for the first time a novel truncated form of CEACAM1 in human urine, which might serve as new diagnostic tool for inflammation or cancer.