Cloning, expression, characterization and role in autocrine cell growth of cell surface retention sequence binding protein-1

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摘要.

Abstract

Cell surface retention sequence binding protein-1 (CRSBP-1) is a cell surface binding protein for the cell surface retention sequence (CRS) motif of the v-sis gene product (platelet-derived growth factor-BB). It has been shown to be responsible for cell surface retention of the v-sis gene product in v-sis-transformed cells (fibroblasts) and has been hypothesized to play a role in autocrine growth and transformation of these cells. Here we demonstrate that the CRSBP-1 cDNA cloned from bovine liver libraries encodes a 322-residue type I membrane protein containing a 23-residue signal peptide, a 215-residue cell surface domain, a 21-residue transmembrane domain, and a 63-residue cytoplasmic domain. CRSBP-1 expressed in transfected cells is an ~120-kDa disulfide-linked homodimeric glycoprotein and exhibits dual ligand (CRS-containing growth regulators (v-sis gene product and insulin-like growth factor binding protein-3, IGFBP-3) and hyaluronic acid) binding activity. CRSBP-1 overexpression (by stable transfection of cells with CRSBP-1 cDNA) enhances autocrine loop signaling, cell growth, and tumorigenicity (in mice) of v-sis-transformed cells. CRSBP-1 expression also enhances autocrine cell growth mediated by IGFBP-3 in human lung carcinoma cells (H1299 cells), which express very little, if any, endogenous CRSBP-1 and exhibits a mitogenic response to exogenous IGFBP-3, stably transfected with IGFBP-3 cDNA. However, CRSBP-1 overexpression does not affect growth of normal and transformed cells that do not produce these CRS-containing growth regulators. These results suggest that CRSBP-1 plays a role in autocrine regulation of cell growth mediated by growth regulators containing CRS.