

Cleavage of Syndecan-1 by Membrane-Type Matrix Metalloproteinase-1 Stimulates Cell Migration.

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The transmembrane heparan sulfate proteoglycan syndecan-1 was identified from a human placenta cDNA library by the expression cloning method as a gene product which interacts with membrane-type matrix metalloproteinase-1 (MT1-MMP). Co-expression of MT1-MMP with syndecan-1 in HEK293T cells promoted syndecan-1 shedding, and concentration of cell-associated syndecan-1 was reduced. Treatment of cells with MMP inhibitor BB-94 or tissue inhibitor of MMP (TIMP)-2 but not TIMP-1 interfered with the syndecan-1 shedding promoted by MT1-MMP expression. In contrast, syndecan-1 shedding induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) treatment was inhibited by BB-94 but not by either TIMP-1 or TIMP-2. Shedding of syndecan-1 was also induced by MT3-MMP, but not by other MT-MMPs. Recombinant syndecan-1 core protein was shown to be cleaved by recombinant MT1-MMP or MT3-MMP at G⁸²-L⁸³ and G²⁴⁵-L²⁴⁶ peptide bonds. HT1080 fibrosarcoma cells stably transfected with the syndecan-1 cDNA (HT1080/SDC), which express endogenous MT1-MMP spontaneously, shed syndecan-1. Migration of HT1080/SDC cells on collagen-coated dishes was significantly slow compared with that of control HT1080 cells. Treatment of HT1080/SDC cells with BB-94 or TIMP-2 induced accumulation of syndecan-1 on cell surface, concomitant with further retardation of cell migration. These results suggest that the shedding of syndecan-1 promoted by MT1-MMP stimulates cell migration.

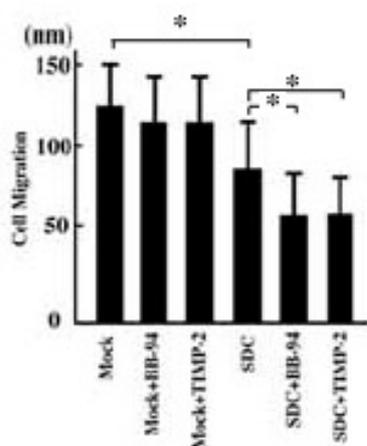


Fig. 1 Mock-transfected HT1080 (Mock lanes) or HT1080/syndecan-1 (SDC lanes) cells were subjected to wound-induced migration assay on collagen-coated dishes in medium containing 0.1 μ M BB-94 or 2 μ g/ml TIMP-2 protein. Note that migration of syndecan-1-expressing cells was severely inhibited by MMP inhibitors. *, $P < 0.01$.

Reference: Endo, K., Takino, T., Miyamori, H., Kinsen, H., Yoshizaki, T., Furukawa, M. and Sato, H. (2003) Cleavage of Syndecan-1 by Membrane-Type Matrix Metalloproteinase-1 Stimulates Cell Migration. *J. Biol. Chem.* 278, 40764-40770.