The role of ADAM28 in cancer cell proliferation and progression

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ADAMs (a disintegrin and metalloproteinases) are new gene family of proteins with sequence similarity to the reprolysin family of snake venoms and share the metalloproteinase domain with matrix metalloproteinases (MMPs). Recent studies suggest that ADAMs are related to both cancer development and progression [1]. We have previously demonstrated that ADAM28 is selectively overexpressed by carcinoma cells in human invasive breast carcinomas and involved in breast carcinoma cell proliferation through cleavage of insulin-like growth factor binding protein-3 (IGFBP-3) [2]. More recently, we have established an experimental mouse model to monitor cancer cell metastasis by in vivo bioluminescence imaging. In this method, transplanted cells expressing luciferase and green fluorescent protein (GFP) can be readily detected within the tissues of live animals after administration of luciferin. We found that injection of ADAM28-expressing carcinoma cells, which express luciferase and GFP, via tail vein show metastasis in the lungs and minute metastasis foci are readily detected by immunostaining of GFP. In mice receiving the ADAM28 siRNA atellocollagen complex, this metastasis was inhibited by 80-90%, suggesting that ADAM28 plays a key role in cancer cell metastasis. To explore functions of ADAM28 in cancer cell invasion and metastasis, we screened interacting proteins for ADAM28 by yeast two-hybrid system, and identified von Willebrand factor (vWF) and connective tissue growth factor (CTGF) as candidate proteins. In this symposium, we will also discuss ADAM28-induced cancer cell invasion and metastasis by cleavage of vWF and/or CTGF.

[References]