

THE ROLE OF METALLOPROTEINASES (MMPs) IN TUMOR DEVELOPMENT

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Introduction: MMPs are a family of proteinases that regulate cell behavior by remodeling stromal and cell surface proteins, thereby influencing cell survival, genomic stability, and differentiation. MMPs are key players in the neoplastic cells' development and dissemination.

Material and methods: In order to achieve the proposed goal, the publications from the specialized journals of the PubMed, Medline and Hinari electronic libraries have been examined.

Keywords: Metalloproteases, ADAM, ADAMTS, cancer, matrix metalloproteases.

Purpose: To summarize the evidence derived from international studies on expression and involvement of metalloproteinases in the tumor growth, invasion, migration and angiogenesis to identify potential therapeutic strategies.

Results: A positive correlation between tumor progression and the expression of multiple MMPs in tumor tissues has been demonstrated. There are many reports showing that members of the ADAM family are overexpressed in human cancers. Protumor activities have also been reported for ADAMTS-1 in mammary carcinomas, ADAMTS-12 in breast cancer cells, ADAMTS-4 and ADAMTS-5 in glioblastoma. Other ADAMTS metalloproteases showing tumor-associated effects are ADAMTS-2, ADAMTS-14 and ADAMTS-18.

Conclusions: Altered expression of MMPs, ADAMs and ADAMTSs has been found in diverse tumor types. However, the exact role of these proteinases in the initiation or progression of the disease is generally still poorly elucidated. Specific inhibitors of ADAM could be potential remedies in anti-cancer therapy.

Expression of ADAM metalloproteinases in human cancers and their possible functions

ADAM	Expression in cancer	Functions in cancer
ADAM8	Lung, kidney, brain	Promotion of migration
ADAM9	Breast, pancreas, stomach, skin, liver, lung	Promotion of cell adhesion and invasion, binding to integrins
ADAM10	Oral cavity, stomach, ovary	Promotion of cell growth and migration
ADAM12	Brain, breast, liver,	HB-EGF shedding, promotion of cell growth
ADAM15	Breast, prostate, stomach, lung	Promotion of cell growth
ADAM17	Breast, ovary, kidney, colon, prostate	TGF- β shedding, promotion of cell growth
ADAM19	Brain, kidney	No study
ADAM28	Lung, breast, kidney	IGFBP-3 cleavage, promotion of cell growth

Implication of ADAM molecules in different processes contributing to cancer development. ADAMs are composed of distinct domains endowing the proteins with multiple functions.

