

Roles of membrane type matrix metalloproteinase in breast tumor metastasis

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1997 Fiscal Year Final Research Report Summary

ROLES OF MEMBRANE TYPE MATRIX METALLOPROTEINASE IN BREAST TUMOR METASTASIS

Research Project

Project/Area Number

07044240

Research Category

Grant-in-Aid for international Scientific Research

Allocation Type

Single-year Grants

Section

Joint Research

Research Field

Experimental pathology

Research Institution

UNIVERSITY OF TOKYO (1997)
Kanazawa University (1995-1996)

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Project Period (FY)

1995 - 1997

Keywords

CANCER / INVASON AND METASTASIS / BREAST CARCINOMA / MATRIX METALLOPROTEINASE

Research Abstract

Gelatinase A (GelA) is believed to be important for cancer cell invasion and metastasis. Gelatinase A is produced as an inactive proenzyme (proGelA) and activated by a cell surface activator on cancer cells. We identified membrane-type 1 matrix metalloproteinase as a possible cell surface activator in 1994 and have extended the study to elucidate its relevance to cancer including breast carcinomas. During the three years we obtained the following results supported by the grant.


1. MT1-MMP expression was demonstrated in various types of human cancers such as breast, gastric, colon, head and neck, and nasopharyngeal carcinomas.
2. Expression of MT1-MMP in carcinomas correlated well to the activation of GelA in the tissue suggesting that MT1-MMP is surely the GelA activator in cancers.
3. Immunohistochemistry localized both MT1-MMP and gelatinase A to the cancer cells and also surrounding stromal fibroblasts.
4. However carcinoma cells did not express GelA but it was expressed in the surrounding fibroblasts.
5. MT1-MMP was shown to bind proGelA by using TIMP-2 as an adapter. Thus Three molecular complex is thought to be formed on cancer cell surface. ProGelA in the complex is thought to be activated by the neighboring free MT1-MMP.

Research Products (12 results)

All Other

All Publications (12 results)

- [Publications] 佐藤 博 他4名: "Assignment of Human Genes for Membrane-Type-1,-2 and -3 Matrix Metalloproteinases to 14q12.2,16q12.2-21 and 8q21,Respectively by in Situ Hybridization." Genomics. 39. 412-413 (1997) ▼
- [Publications] Pulyaeva, H 他6名: "MT1-MMP correlates with MMP-2 activation potential seen after epithelial to mesenchymal transition in human breast carcinoma cells." Clinical Experimental Metastasis. 15. 111-120 (1997) ▼
- [Publications] Gilles, C.他4名: "Collagen type I induced MT1-MMP expression and MMP-2 activation:Implication in the metastatic progression of breast carcinoma." Laboratory Investigation. 76. 651-660 (1997) ▼
- [Publications] 中原 寛 他5名: "Transmembrane domain mediated membrane type 1-matrix metalloproteinase docking to invadopodia is required for cell invasion." Proceedings of National Academy of Science. 94. 7959-7964 (1997) ▼
- [Publications] Uria, J, A. 他4名: "Regulation of collagenase-3 expression in human breast carcinomas is mediated by stromal-epithelial cell interactions." Cancer Research. 57. 4882-4888 (1997) ▼
- [Publications] Yu, M. 他6名: "Tyrosin phosphorylation mediates ConA-induced membrane type-1 matrix metalloproteinase expression and matrix metalloproteinase-2 activation in MDA-MB-231 human breast carcinoma cells." Cancer Research. 57. 5028-5032 (1997) ▼
- [Publications] Sato, H., Tanaka, M., Takino, T., Inoue, M.& Seiki, M.: "Assignment of the Human Genes for Membrane-Type-1, -2 and -3 Matrix Metalloproteinases to 14q12.2,16q12.2-21 and 8q21, Respectively by in Situ Hybridization." Genomics. 39. 412-413 (1997) ▼
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- [Publications] Nakahara, H., Thompson, E.W.Sato, H., Seiki, M.Yeh, Y.& Chen W.T.: "Transmembrane domain mediated mambrane type 1-matrix metalloproteinase docking to invadopodia is required for cell invasion." Proc.Natl.Acad.Sci.U.S.A.94. 7959-7964 (1997) ▼
- [Publications] Uria, J.A., Stahle-Backdahl, M., Seiki, M.Fueyo, A.& Lopez-Otin, C.: "Regulation of collagenase-3 expression in human breast carcinomas is mediated by stromal-epithelial cell interactions." Cancer Res.57. 4882-4888 (1997) ▼

[Publications] Yu.M., Bowden, E.T., Sitlani, H., Sato, H., Seiki, M., Mueller, S.C.& Thompson, E.W.: "Tyrosin phosphorylation mediates ConA-induced membrane type-1 matrix metalloproteinase expression and matrix metalloproteinase-2 activation in MDA-MB-231 human breast carcinoma cells." Cancer Res.57. 5028-5032 (1997) 

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