

# 遺伝子導入・欠損マウスによる細胞外マトリックス代謝の解析

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# 1997 Fiscal Year Final Research Report Summary

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## Analyzes on ECM metabolism in transgenic and knockout mice

Research Project

### Project/Area Number

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08044262

### Research Category

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Grant-in-Aid for international Scientific Research

### Allocation Type

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Single-year Grants

### Section

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Joint Research .

### Research Field

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Experimental pathology

### Research Institution

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School of Medicine, Keio University (1997)  
Kanazawa University (1996)

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### Project Period (FY)

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1996 - 1997

### Keywords

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## Research Abstract

Among the matrix metalloproteinase (MMP) gene family members, MMP-2 (gelatinase A) is believed to be involved in cancer invasion and metastasis and joint destruction, and thus its function in vivo is important. Membrane-type MMPs (MT-MMPs) were recently cloned as activators of proMMP-2 and the degradation mechanism of extracellular matrix by the MT-MMPs/MMP-2 system is one of the key projects in the field of MMP research. In the present studies, we have demonstrated that proMMP-2 activation is mediated by MT1-MMP in the human invasive breast carcinomas and human thyroid carcinomas. In the human osteoarthritic and rheumatoid arthritic cartilages, MT1-MMP also played a major role in the activation of proMMP-2, showing a positive correlation with cartilage destruction. We also revealed that MT1-MMP is an extracellular matrix-degrading proteinase capable of digesting interstitial collagens and aggrecan as well as an activator of proMMP-2. MT3-MMP had a similar activity against these substrates except for type I collagen. Transgenic mice expressing MT1-MMP specifically in the cartilages are being made and analyses of their phenotypes are now under way. These mice will be back crossed with MMP-2 knockout mice which had been made by a Japanese group and their phenotypes will be examined.

## Research Products (23 results)

All	Other
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All	Publications (23 results)
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- [Publications] Imai K.: "Membrane-type matrix metalloproteinase 1 is a gelatinolytic enzyme and secreted in a complex with tissue inhibitor of metalloproteinases 2." *Cancer Res.* 56. 2707-2710, (1996) ▼
- [Publications] Ohuchi E.: "Membrane-type 1-matrix metalloproteinase digests interstitial collagens and other extracellular matrix macromolecules." *J.Biol.Chem.*272. 2446-2451, (1997) ▼
- [Publications] Tsunozuka Y.: "Expression of membrane-type matrix metalloproteinase 1(MT1-MMP)in tumor cells enhances pulmonary metastasis in an experimental metastasis assay." *Cancer Res.*56. 5678-5683, (1997) ▼
- [Publications] Imai K.: "Degradation of decorin by matrix metalloproteinases.Identification of the cleavage sites,kinetic analyses and transforming growth factor-b1 release." *Biochem.J.*322. 809-814, (1997) ▼
- [Publications] Ueno H.: "Expression and tissue localization of membrane-type 1,2 and 3 matrix metalloproteinases in human invasive breast carcinomas." *Cancer Res.*57. 2055-2060, (1997) ▼
- [Publications] Imai K.: "Expression of membrane-type 1 matrix metalloproteinase and activation of progelatinase A in human osteoarthritic cartilage." *Am.J.Pathol.*151. 245-256 (1997) ▼
- [Publications] Nagase H. and Okada Y.: "Proteinases and matrix degradation.Textbook of Rheumatology." W.B.Saunders Company.Philadelphia, 1904 (1997) ▼
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- [Publications] Matsuki H., Fujimoto N., Iwata K., Knauper V., Okada Y.and Hayakawa T.: "A one-step sandwich enzyme immunoassay for human matrix metalloproteinase 8 (neutrophil collagenase) using monoclonal antibodies" *Clin.Chim.Acta.* 244. 129-143 (1996) ▼
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- [Publications] Ito.M., Masuda K., It Y., Akizawa T., Yoshioka M., K.Imai, Okada Y., Sato H.and Seiki M.: "Purification and refolding of recombinant human proMMP-7 (pro-matrilysin) expressed in *Echelicia coli* and its characterization" *J.Biochem.*119. 667-673 (1996) ▼
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- [Publications] Imai K., Ohuchi E., Aoki T., Nomura H., Fujii Y., Sato H., Seiki M.and Okada Y.: "Membrane-type matrix metalloproteinase 1 is a gelatinolytic enzyme and secreted in a complex with tissue inhibitor of metalloproteinases 2" *Cancer Res.* 56. 2707-2710 (1996) ▼

[Publications] Sato H., Takino T., Kinoshita T., Imai K., Okaa Y., Stetler-Stevenson W/G.and Seiki M.: "Cell surface binding and activation of gelatinase A induced by expression of membrane-type matrix metalloproteinase-1 (MT-MMP-1)" FEBS Lett. 385. 238-240 (1996) ▼

[Publications] Ohuchi E., Imai K., Fujii Y., Sato H., Seiki M.and Okada Y.: "Membrane-type 1-matrix metalloproteinase digests interstitial collagens and other extracellular matrix macromolecules." J.Biol.Chem.272. 2446-2451 (1997) ▼

[Publications] Tsunetzuka Y., Kinoh H., Takino T., Watanabe Y., Okada Y., Shinagawa A., Sato H.and Seiki M.: "Expression of membrane-type matrix metalloproteinase 1 (MT1-MMP) in tumor cells enhances pulmonary metastasis in an experimental metastasis assay." Cancer Res. 56. 5678-5683 (1997) ▼

[Publications] Imai K., Hiramatsu A., Fukushima D., Pierschbacher M.D.and Okada Y.: "Degradation of decorin by matrix metalloproteinases. Identification of the cleavage sites, kinetic analyzes and transforming growth factor-b1 release" Biochem.J.322. 809-814 (1997) ▼

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[Publications] Imai K., Ohta S., Matsumoto T., Fujimoto N., Sato H., Seiki M.and Okada Y.: "Expression of membrane-type 1 matrix metalloproteinase and activation of progelatinase A in human osteoarthritic cartilage" Am.J.Pathol.151. 245-256 (1997) ▼

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