

# 上咽頭がんにおけるマトリックスメタロプロテアーゼ1プロモーター遺伝子多型と転移能

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# 2006 Fiscal Year Final Research Report Summary

The relationship between single nucleotide polymorphism of matrix metalloprotease-1 and metastasis of nasopharyngeal carcinoma.

Research Project

## Project/Area Number

16390487

## Research Category

Grant-in-Aid for Scientific Research (B)

## Allocation Type

Single-year Grants

## Section

一般

## Research Field

Otorhinolaryngology

## Research Institution

Kanazawa University

## Principal Investigator

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## Project Period (FY)

2004 - 2006

## Keywords

NPC / EBV / SNP / LMP1 / MMP1 / Ets-1

## Research Abstract

The Epstein-Barr Virus (EBV) latent membrane protein 1 (LMP1) has a significant role in several malignancies, including nasopharyngeal carcinoma (NPC). LMP1 is principal onco-protein, and we have shown that it also induces a set of factors that mediated invasion, angiogenesis and metastasis. Matrix metalloproteinase-1 (MMP1) is also involved in several malignancies. A single guanine insertion polymorphism (2G) in the MMP1 promoter creates an Ets binding site that causes high levels of transcription and correlates with risk for some malignancies. Here, we evaluate the impact of this 2G insertion type on NPC. We genotyped 44 Japanese and 39 Taiwanese NPC patients, as well as 58 Japanese and 23 Taiwanese healthy controls. The proportion of 2G homozygotes was higher in the NPC groups than controls (Japanese : p=

0.02, odds ratio (OR) = 2.49 ; Taiwanese : p= 0.02, OR= 3.66). An analysis of overall survival rates in the patients with NPC, and the 1G/1G genotype disclosed a favorable prognosis (5-year survival rate = 100%, P= 0.04). Multivariate analysis showed that 1G/1G has independent prognostic significance. We also examined whether LMP1 enhances MMP1 expression in epithelial cells in culture. LMP1-transfected cells with 2G/2G genotype expressed MMP1, which was abolished by activator protein-1(AP1) dominant-negative (DN) and Ets-DN. LMP1 also induced active MMP3, which can cleave latent MMP1, and AP-1 DN and Ets-DN suppressed the MMP3 expression. These results suggest that LMP1-induced MMP1 and MMP3 are closely linked and show that LMP1 activates MMP1 via an Ets binding site formed by 2G, which is a candidate marker for both risk and prognosis of NPC.

## Research Products (23 results)

All	2007	2006	2005	2004
			All	Journal Article

[Journal Article] Oncogenic role of Epstein-Barr virus-encoded small RNAs (EBERs) in nasopharyngeal carcinoma.	<b>2007</b> ▾
[Journal Article] MUC1 induced by Epstein-Barr Virus Latent Membrane Protein 1 Causes Dissociation of the Cell-Matrix Interaction and Cellular Invasiveness via STAT Signaling.	<b>2007</b> ▾
[Journal Article] Oncogenic role of Epstein-Barr virus-encoded small RNAs (EBERs) in nasopharyngeal carcinoma.	<b>2007</b> ▾
[Journal Article] EBV latent membrane protein 1 induces synthesis of Hypoxia-inducible factor 1 $\alpha$ through Siah1-mediated down-regulation of prolyl hydroxylases 1 and 3 in nasopharyngeal epithelial cells.	<b>2006</b> ▾
[Journal Article] A case report : Epstein-Barr virus-associated undifferentiated carcinoma of the tongue base.	<b>2006</b> ▾
[Journal Article] EBV latent membrane protein 1 induces synthesis of Hypoxia-inducible factor 1 $\alpha$ through Siah1-mediated down-regulation of prolyl hydroxylases 1 and 3 in nasopharyngeal epithelial cells.	<b>2006</b> ▾
[Journal Article] A case report : Epstein-Barr virus-associated undifferentiated carcinoma of the tongue base.	<b>2006</b> ▾
[Journal Article] Expression of Interleukin-8 Receptor A Predicts Poor Outcome in Patients with Nasopharyngeal Carcinoma.	<b>2005</b> ▾
[Journal Article] Epstein-Barr virus latent membrane protein1 induces the matrix metalloproteinase-1 promoter via an Ets binding site formed by a single nucleotide polymorphism : Enhanced susceptibility to nasopharyngeal carcinoma.	<b>2005</b> ▾
[Journal Article] Ribonucleotide reductase inhibitors enhance cidofovir-induced apoptosis in EBV-positive nasopharyngeal carcinoma xenografts.	<b>2005</b> ▾
[Journal Article] Epstein-Barr Virus Invasion and Metastasis.	<b>2005</b> ▾
[Journal Article] Endoscopic Nasopharyngectomy for Patients with Recurrent Nasopharyngeal Carcinoma at the Primary Site.	<b>2005</b> ▾
[Journal Article] Expression of Interleukin-8 Receptor A Predicts Poo Outcome in Patients with Nasopharyngeal Carcinoma.	<b>2005</b> ▾
[Journal Article] Epstein-Barr virus latent membrane protein1 induces the matrix metalloproteinase-1 promoter via an Ets binding site formed by a single nucleotide polymorphism : Enhanced susceptibility to nasopharyngeal carcinoma.	<b>2005</b> ▾
[Journal Article] Ribonucleotide reductase inhibitors enhance cidofovir-induced apoptosis in EBV-positive nasopharyngeal carcinoma xenografts.	<b>2005</b> ▾
[Journal Article] Epstein-Barr Virus Invasion and Metastasis.	<b>2005</b> ▾
[Journal Article] Epstein-Barr Virus (EBV) Latent Membrane Protein 1 Induces Interleukin-8 through the Nuclear Factor- $\kappa$ B Signaling Pathway in EBV Infected Nasopharyngeal Carcinoma Cell Line.	<b>2004</b> ▾
[Journal Article] Diagnostic value of serum EBV-DNA quantification and antibody to viral capsid antigen in nasopharyngeal carcinoma patients.	<b>2004</b> ▾
[Journal Article] Epstein-Barr virus latent membrane protein 1 induces synthesis of Hypoxia-inducible factor 1 $\alpha$ .	<b>2004</b> ▾
[Journal Article] Regulation of angiogenic factors by Epstein-Barr virus gne products in nasopharyngeal carcinoma.	<b>2004</b> ▾
[Journal Article] Epstein-Barr Virus (EBV) Latent Membrane Protein 1 Induces Interleukin-8 through the Nuclear Factor- $\kappa$ B Signaling Pathway in EBV-Infected Nasopharyngeal Carcinoma Cell Line.	<b>2004</b> ▾

[Journal Article] N Wakisaka, S Kondo, T Yoshizaki, S Murono, M Furukawa.

2004 ▾

[Journal Article] Regulation of angiogenic factors by Epstein-Barr virus gne products in nasopharyngeal carcinoma.

2004 ▾

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