



Title	Aberrant Expression of Disintegrin-metalloprotease Proteins in the Formation and Progression of the Uterine Cervical Cancer
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Citation	大阪大学, 2011, 博士論文
Version Type	
URL	https://hdl.handle.net/11094/58221
rights	
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博士の専攻分野の名称 博士(医学)

学位記番号 第24361号

学位授与年月日 平成23年3月25日

学位授与の要件 学位規則第4条第1項該当

医学系研究科病態制御医学専攻

学位論文名 Aberrant Expression of Disintegrin-metalloprotease Proteins in the Formation and Progression of the Uterine Cervical Cancer
(子宮頸部癌の発生・進展におけるディスインテグリン・メタロプロテーゼ分子の発現異常)

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論文審査の結果の要旨

Objective: Dysregulated expressions of disintegrin - metalloprotease proteins (ADAM and ADAMTS) have been reported in many types of cancers, and are believed to play important roles in cancer formation and metastasis. However, little is known about the expression of ADAMs and ADAMTS in the development of human cervical cancer.

Methods: Reverse transcriptase polymerase chain reaction, and immunoblotting were performed to assess the expression of several members of disintegrin-metalloproteases, and tissue inhibitor of metalloproteinases (TIMPs) in squamous-type cervical cancer cells, and oncogenically modified keratinocytes (immortalized human cervical keratinocytes transduced with Human papilloma virus-16 E6/E7 proteins with or without oncogenes). Immunohistochemistry of ADAM-9, ADAM-10 and TIMP-3 was performed on 31 primary human cervical tissue specimens of preinvasive, and invasive cervical carcinoma.

Results: mRNA levels of ADAM-9, ADAM-10, ADAM-12, TIMP-2 and TIMP-3 were upregulated as cervical cells progress from dysplastic to malignant lesions compared to normal cervical cells. These results were corroborated at the protein level by western blot analysis and immunohistochemistry.

Conclusion: The expression of disintegrin-metalloprotease and their endogenous regulators were dysregulated during cervical carcinogenesis. The aberrant expressions of ADAMs might contribute to the pathogenesis of cervical cancer formation and progression.

論文内容の要旨

[目的]

Dysregulated expressions of disintegrin - metalloprotease proteins (ADAM and ADAMTS) have been reported in many types of cancers, and are believed to play important roles in cancer formation and metastasis. However, little is known about the expression of ADAMs and ADAMTS in the development of human cervical cancer.

[方法ならびに成績]

Reverse transcriptase polymerase chain reaction, and immunoblotting were performed to assess the expression of several members of disintegrin-metalloproteases, and tissue inhibitor of metalloproteinases (TIMPs) in squamous-type cervical cancer cells, and oncogenically modified keratinocytes (immortalized human cervical keratinocytes transduced with Human papilloma virus-16 E6/E7 proteins with or without oncogenes). Immunohistochemistry of ADAM-9, ADAM-10 and TIMP-3 was performed on 31 primary human cervical tissue specimens of preinvasive, and invasive cervical carcinoma. mRNA levels of ADAM-9, ADAM-10, ADAM-12, TIMP-2 and TIMP-3 were upregulated as cervical cells progress from dysplastic to malignant lesions compared to normal cervical cells. These results were corroborated at the protein level by western blot analysis and immunohistochemistry.

[総括]

The expression of disintegrin-metalloprotease and their endogenous regulators were dysregulated during cervical carcinogenesis. The aberrant expressions of ADAMs might contribute to the pathogenesis of cervical cancer formation and progression.