Elevated KAI1 Protein Expression Identified in Malignant Melanoma

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Dear Editor:

KAI1, also known as CD82, is a member of the TM4SF protein family. KAI1 was first discovered during a study on T-cell activation. While recent studies have proposed that TM4SF affects the behavior of cancer cell growth, the exact mechanism has not been described. KAI1/CD82 is found in high levels in the spleen, lung, liver, placenta, kidney and prostate, in moderate levels in the pancreas, skeletal muscle, and thymus, and in low levels in the brain, heart, ovary, stomach, and uterus. However, It was not reported that KAI1/CD82 protein was expressed in normal skin tissue.

Although there have been many studies on the role in the regulation of cell growth, cell-to-cell adhesion and motility, KAI1 and the TM4 family function remains unclear. An association between KAI1/CD82 and cancer progression was discovered during a study conducted to identify metastasis suppressor genes.

KAI1 expression is reduced in a large number of cancers. Dong et al.¹ reported reduced RNA expression of KAI1 during prostate cancer metastasis by northern blot analysis. Transfecting metastatic prostate cancer cells into nude mice resulted in suppression of lung metastasis by KAI1. Tests using reverse transcriptase-polymerase chain reaction and immunohistochemistry have reported reduced levels of CD82 mRNA and protein in thyroid cancer². A

study by Hinoda et al.³ used immunohistochemical tests to assess the association between KAI1 and the progression of gastric cancer. Northern blot analysis conducted by Guo et al.⁴ showed similar levels of KAI1 mRNA expression in both normal and cancerous esophagus and similar levels in tissue samples with or without metastasis. Therefore, metastasis in esophageal and gastric cancer is independent of KAI1⁴. However, a recent study has revealed increased expression of KAI1 protein in chromophobe renal cell carcinoma⁵. In light of this, we explored the expression of KAI1 in skin cancers in order to determine whether it downregulates or upregulates the expression of

Fig. 1. (A) KAI1/CD82 protein was expressed on malignant melanoma by western blot analysis. (B) The score of relative KAI1/CD82 protein expression. Normal: normal skin, MM: malignant melanoma, SCC: squamous cell carcinoma, BCC: basal cell carcinoma.

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Fig. 2. Representative immunohistochemistry staining for KAI1/CD82 protein expression in paraffin-embedded malignant melanoma (A: strongly positive immunostaining, $\times 200$), squamous cell carcinoma (B: very weakly positive immunostaining, $\times 200$), basal cell carcinoma (C: very weakly positive immunostaining, $\times 200$) and normal skin (D: no immunostaining, $\times 100$).

skin tumors. The Institutional Review Board of Seoul Soonchunhyang University Hospital reviewed and approved this research protocol, which involved the use of tissue samples.

We experimentally assessed whether loss of KAI1 protein expression in metastatic cancer is a common event in malignant skin cancers or if it occurs only in some tumor types. Based on the aforementioned finding, we chose basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma (MM) and used western blot analysis in order to determine if KAI1 expression suppresses all cancer types or certain cancer types.

We evaluated the expression of KAI1 protein in MM, SCC and BCC using western blot and immunohistochemistry. In this study, KAI1, which is a marker of metastatic potentiality in breast cancer, was measured in BCC, SCC and MM using western blot and the immunohistologic method. The results show that KAI1 was hardly expressed in 6 cases of BCC. In 6 cases of SCC, KAI1 was hardly

expressed. Loss of KAI1 protein expression including SCC, BCC in our study corresponded to previous studies results⁶⁻⁸. In the 6 cases of MM, the expression of KAI1 was strongly positive (Fig. 1A). The amount of expression in western blotting is displayed graphically (Fig. 1B). The expression patterns of KAI1 protein in MM were similar with those by Yusenko and Kovacs⁵. However, different patterns were shown in other types of cancer including prostate, gastric, colon, cervix, breast, bladder, lung, pancreas, liver, and thyroid cancers. An immunohistochemical study showed that the staining pattern of KAI1 in normal human skin tissues mirrored those of western blot analysis (Fig. 2).

To the best of our knowledge, KAI1 expression in cutaneous BCCs, SCCs and MMs has not yet been studied. KAI1 protein expression has been known to be associated with a higher grade of malignant skin tissue. However, the exact function and mechanism of KAI1 during tumor genesis have not been confirmed. While KAI1 is suppres-

sed in specific types of cancer, KAI1 is over expressed in MM. Interestingly, KAI1 was not expressed in cutaneous BCCs, SCCs and normal tissues. More work is needed to characterize the pathway through which KAI1 is over-expressed in MM skin tumor.

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REFERENCES

1. Dong JT, Isaacs WB, Barrett JC, Isaacs JT. Genomic organization of the human KAI1 metastasis-suppressor gene. *Genomics* 1997;41:25-32.
2. Chen Z, Mustafa T, Trojanowicz B, Brauckhoff M, Gimm O, Schmutzler C, et al. CD82, and CD63 in thyroid cancer. *Int J Mol Med* 2004;14:517-527.
3. Hinoda Y, Adachi Y, Takaoka A, Mitsuchi H, Satoh Y, Itoh F, et al. Decreased expression of the metastasis suppressor gene KAI1 in gastric cancer. *Cancer Lett* 1998;129:229-234.
4. Guo XZ, Friess H, Maurer C, Berberat P, Tang WH, Zimmermann A, et al. KAI1 is unchanged in metastatic and nonmetastatic esophageal and gastric cancers. *Cancer Res* 1998;58:753-758.
5. Yusenko MV, Kovacs G. Identifying CD82 (KAI1) as a marker for human chromophobe renal cell carcinoma. *Histopathology* 2009;55:687-695.
6. Geradts J, Maynard R, Birrer MJ, Hendricks D, Abbondanzo SL, Fong KM, et al. Frequent loss of KAI1 expression in squamous and lymphoid neoplasms. An immunohistochemical study of archival tissues. *Am J Pathol* 1999;154:1665-1671.
7. Farhadi RD, Smee R, Ow K, Yang JL, Russell PJ, Crouch R, et al. Down-regulation of KAI1/CD82 protein expression in oral cancer correlates with reduced disease free survival and overall patient survival. *Cancer Lett* 2004;213:91-98.
8. Okochi H, Kato M, Nashiro K, Yoshie O, Miyazono K, Furue M. Expression of tetra-spans transmembrane family (CD9, CD37, CD53, CD63, CD81 and CD82) in normal and neoplastic human keratinocytes: an association of CD9 with alpha 3 beta 1 integrin. *Br J Dermatol* 1997;137:856-863.

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Lichenoid Drug Eruption after Low-Dose Imatinib Mesylate Treatment

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Dear Editor:

Imatinib mesylate, a selective antitumor tyrosine kinase inhibitor, has been approved as the first-line therapy for gastrointestinal stromal cell tumor and chronic myeloid leukemia. Lichenoid drug eruption (LDE) is known to

cause uncommon adverse cutaneous reactions of imatinib mesylate, usually appearing with 400 mg or more of imatinib mesylate per day^{1,2}. Here, we present a case of severe LDE after low-dose imatinib mesylate treatment for gastrointestinal stromal cell tumor.

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