The paradoxical role of an immune receptor, DNAM-1, in tumor development

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Immune cells recognize and kill tumor cells before they grow into a lump of tumors, resulting in suppression of tumor development. On the other hand, it has recently been known that inflammation resulted from immune responses is involved in tumorigenesis. Thus, immune responses play a paradoxical role in tumor development.

DNAM-1 (CD226) is a signal transducing adhesion molecule expressed on the majority of NK cells, T cells and macrophages. Upon binding of DNAM-1 with CD155, a DNAM-1 ligand, expressed on tumor cells, $CD8^+$ T cells and NK cells are activated and kill tumor targets in vitro. We observed that CD155-expressing tumor cells inoculated into DNAM-1-diffeicent mice grew more rapidly than those inoculated into wild-type (WT) mice. We also observed that blockade of the interaction of DNAM-1 on $CD8^+$ T cells or NK cells with CD155 on tumor cells by soluble CD155 promoted development of tumor cells in vivo. These results indicated that DNAM-1 is involved in tumor immunity in vivo. Moreover, we observed that DNAM-1-deficient mice showed development of CD155-expressing fibrosarcoma and papilloma induced by chemical carcinogens methylcholanthrene and 7, 12-dimethylbenz [a] anthracene (DMBA), respectively, significantly more rapidly than did WT mice. These results indicate that DNAM-1 plays an important role in immune surveillance against tumor development.

On the contrary to these results, we have recently found that addition of 12-O-tetradecanoylphorbol-13-acetate (TPA) to DMBA suppressed, rather than augmented, development of papillomas in DNAM-1-deficient mice, compared with WT mice. Because TPA accelerates inflammation, DNAM-1 may be involved in inflammation-related tumor development.

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EDUCATIONS/TRAINING

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POSITIONS AND HONORS

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2003-present:	Councilor, Japanese Society for Immunology
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RECENT PUBLICATIONS

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