Cancer Immunity (6 February 2006) Vol. 6 Suppl. 1, p. 3

CANCER
IMMUNITY
Meeting Abstract

The DNA damage pathway regulates innate immune system ligands of the NKG2D receptor

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Abstract

Natural killer (NK) cell receptors regulate the capacity of NK cells and T cell subsets to attack tumor cells. Recognition of transformed or infected cells by NK cells can occur as a result of upregulation of ligands for stimulatory receptors and/or downregulation of ligands for inhibitory receptors. The NKG2D receptor has been implicated in the recognition of transformed or infected cells as a result of upregulation by the latter cells of one or more of several host-encoded cell surface ligands for NKG2D. A key question is: what are the molecular mechanisms that enable cells to perceive infection and transformation, resulting in upregulation of ligands that target the cells for destruction. Evidence will be presented that NKG2D ligands in normal cells and tumor cells are regulated by the DNA damage response, which is frequently activated in advanced tumors and precancerous lesions. The findings provide a new and revealing mechanism for how tumor cells can be recognized by the innate immune system, and consequently can activate adaptive immune responses. They may also bear on the mechanisms of action and future design of chemotherapeutic drugs, which activate the DNA damage response.