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Titel des Beitrags: Tumor-associated E-cadherin mutations affect binding to the killer cell lectin-like receptor G1 in humans.

Abstract: The killer cell lectin-like receptor G1 (KLRG1) is expressed by NK cells and memory T cells in man and mice. Cadherins were recently identified as ligands for mouse KLRG1 but ligands for human KLRG1 have not yet been defined. In this study, we first demonstrate that human E-cadherin is a ligand for human KLRG1. This finding is remarkable because human and mouse KLRG1 show only an intermediate degree of homology (57% aa identity). In addition, we show that E-cadherin, expressed on K562 target cells, inhibited polyclonal human NK cells. Inhibition of NK cell function was observed consistently in three independent functional assays but the extent of inhibition was modest and required high expression of E-cadherin on target cells. E-cadherin function is often inactivated during development of human carcinomas and splice-site mutations resulting in in-frame loss of exon 8 or 9 occur frequently in diffuse type gastric carcinomas. Our experiments further revealed that interaction of human KLRG1 to E-cadherin was susceptible to these tumor-associated mutations and that KLRG1(+) NK cells were triggered more easily by K562 target cells carrying these mutations in comparison to target cells expressing wild-type E-cadherin. These results also indicate that the E-cadherin binding sites important for homophilic interaction are also involved in KLRG1 binding. Taken together, these data demonstrate that the main adhesion
molecule of epithelial tissue, E-cadherin, is involved in regulation of NK cells in both humans and mice.