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Titel des Beitrags: The heat shock protein HSP70 promotes mouse NK cell activity against tumors that express inducible NKG2D ligands.

Abstract: The stress-inducible heat shock protein (HSP) 70 is known to function as an endogenous danger signal that can increase the immunogenicity of tumors and induce CTL responses. We show in this study that HSP70 also activates mouse NK cells that recognize stress-inducible NKG2D ligands on tumor cells. Tumor size and the rate of metastases derived from HSP70-overexpressing human melanoma cells were found to be reduced in T and B cell-deficient SCID mice, but not in SCID/beige mice that lack additionally functional NK cells. In the SCID mice with HSP70-overexpressing tumors, NK cells were activated so that they killed ex vivo tumor cells that expressed NKG2D ligands. In the tumors, the MHC class I chain-related (MIC) A and B molecules were found to be expressed. Interestingly, a counter selection was observed against the expression of MICA/B in HSP70-overexpressing tumors compared with control tumors in SCID, but not in SCID/beige mice, suggesting a functional relevance of MICA/B expression. The melanoma cells were found to release exosomes. HSP70-positive exosomes from the HSP70-overexpressing cells, in contrast to HSP70-negative exosomes from the control cells, were able to activate mouse NK cells in vitro to kill YAC-1 cells, which express NKG2D.
ligands constitutively, or the human melanoma cells, in which MICA/B expression was induced. Thus, HSP70 and inducible NKG2D ligands synergistically promote the activation of mouse NK cells resulting in a reduced tumor growth and suppression of metastatic disease.