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Parvovirus H1-induced tumor cell death enhances human immune response via crosspresentation of dendritic cells

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Introduction

Certain autonomous parvoviruses and their derivates are currently under evaluation as antitumor vectors since they preferentially replicate and kill *in vitro*-transformed cells and may reduce the incidence of spontaneous and implanted tumors in animals. However, their oncolytic properties are not yet fully understood and seem to involve more than tumor cell killing. H1-mediated tumor cell lysates may trigger antigen presenting cells to augment host immune responses. Therefore, we analysed maturation, activation and crosspresentation of dendritic cells (DC) after phagocytosis of H1-induced tumor cell lysates using the known human SK29-Mel melanoma cell model.

Methods

For detection of cell death Annexin V/Propidiumjodide assay in FACscan analysis was used. To analyse phagocytosis by DC PKH-2 stained immature DC were cocultured with PKH-26 stained H1-, UV- induced or freeze thaw cycled (and combinations of these) melanoma cells and quantified via FACscan and fluorescence microscopy. Comparably, FACscan was used for the analysis of DC maturation and activation. DC were labeled with CD45-FITC, CD14-, CD80-, CD83-, CD86-PE and 7-AAD. Cross-presentation of tumor cell antigens to CTL via DC were detected by IFNγ-release with a HLA-A2 negative subclone of SK29Mel-1.

Results

We first established that the HLA-A2 positive (SK29-Mel-1) and an HLA-A2 negative (SK29Mel-1.22) melanoma cell lines were equally susceptible to H1-induced cell killing. Secondly, we found that monocyt-derived, immature DC pagocytosed H1-mediated lysates better than mechanically destroyed cells. These DC were more perceptive to late than to early H1 infected cell lysates. DC cocultured with late apoptotic H1-induced SK29Mel cells presented typical markers of maturation and activation. Furthermore SK29Mel-1.22 activated DC confirmed crosspresentation to autologoues CTL.

Conclusion

We revealed to the first time that parvovirus-induced tumor cell killing stimulates DC and CTL. The immune system may rapidly detect and respond to H1-infected tumors, thus making the clinical perspectives of parvoviral vectors even more promising