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P57. Activation of RIG-I induces immunogenic cell death

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Background

The interaction between the immune system and cancer cells has become a focus of recent cancer therapy research. Immunogenic cell death, short ICD, was described as a cell death modality that stimulates an immune response against dead-cell antigens, in particular when they derive from cancer cells. Most malignant cells are poorly immunogenic and fail to elicit an effective antitumour immune response. Certain anti-cancer treatments, however, have been shown to induce ICD and transform cancer cells into potent inducers of an anti-cancer immune response. An important component is the induction of a specific cytotoxic T-cell response driven by DCs that have engulfed and processed tumour antigens. Recently, we have shown that the RIG-I ligand 3pRNA induces tumosr cell death *in vitro* and *in vivo*. Whether and how 3pRNA induced tumour cell death leads to a specific antitumor response is unknown. Here we analyse the immunogenicity of RIG-I induced tumour cell death *in vitro* and *in vivo*.

Material and methods

We induced tumour cell death by treating ovalbumin expressing B16 melanoma cells with 3pRNA. We co-cultured 3pRNA treated B16-OVA cells with splenic DCs and CFSE-labeled OT-I T-cells to analyse a specific T-cell activation and proliferation. Furthermore, we vaccinated 3pRNA treated B16-OVA cells subcutaneously into C57BL/6 mice to analyse their immunogenic potential *in vivo*. After vaccination, draining lymph node cells are analysed for T-cell activation and IFNg production using flow cytometry.

Results

We show that 3pRNA treatment leads to increased cytokine expression, upregulation of costimulatory molecules, cross-presentation and induction of cell death in B16-OVA melanoma cells *in vitro*. 3p-RNA treated B16-OVA cells induce proliferation and IFNg production of OT-I T-cells in co-cultures with spleen derived DCs. After subcutaneous injection of 3pRNA killed B16-OVA cells but not live B16-OVA cells into C57BL/6 mice, potent proliferation and IFNg production of antigen specific CD4 and CD8 T cells is seen in the draining lymph node. Overall, these effects were more pronounced after 3pRNA treatment than after Oxaliplatin induced cell death.

Conclusions

3pRNA treatment of tumor cells leads to a potent immunogenic phenotype with induction of antigen-specific T-cell responses both *in vitro* and *in vivo*. These findings may have implications for a new therapeutic approach in immune mediated cancer treatment.

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