

Xiaoyu Gu

Dr. med.

Improved vaccine efficacy of tumor exosome compared to tumor lysate loaded dendritic cells in mice

Promotionsfach: Chirurgie

Doktorvater: Prof. Dr. med. Thilo Hackert

Exosomes are delivered by many cells and abundantly by tumor cells, they are characterized by a particular pattern of membrane proteins, and carry selected mRNA and miRNA. One of the most promising immunotherapeutic approaches in cancer is based on vaccination with dendritic cells (DC). However, the hope has been dampened, when it was found that tumor exosome (TEX) interfere with immune response induction and promote immunosuppression.

To investigate whether dendritic cell vaccination suffices to counter-regulate TEX-induced immunosuppression and whether TEX could serve as tumor antigen for DC-loading, I used the mouse myeloid leukaemia WEHI3B and the renal cell carcinoma line RENCA. The results showed that DC-vaccination significantly prolonged the survival time of WEHI3B-bearing mice, TEX loaded DC (DC-TEX) being superior to lysate-loaded DC (DC-lys), even an excess of TEX not interfering with immune response induction. The superior response to DC-TEX was accompanied by an increase in WEHI3B-specific CD4⁺ T cells, evaluated by trogocytosis and proliferation. Similar findings accounted for DC loaded with RENCA TEX. TEX was efficiently taken-up by DC and TEX uptake supported CD11c, MHCII and IL12 upregulation in DC. Importantly, TEX was partly recruited into the MHCII loading compartment such that “TEX” presentation time and recovery in T cells significantly exceeded that of tumor-lysate.

Taken together, TEX did not drive DC into a suppressive phenotype and were a superior antigen due to higher efficacy of TEX presentation that is supported by prolonged persistence, preferential processing in the MHCII-loading compartment and pronounced trogocytosis by T helper cells. Thus, TEX might provide an individual-specific antigen source for DC-loading and vaccination.

