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Plasmacytoid dendritic cells in cancer: good or bad?

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Plasmacytoid DCs (pDCs) represent a highly specialized dendritic cell subset that play a major role in viral defense. Non-activated pDCs promote T regulatory cell-mediated immunosuppression and the presence of pDCs in tumors was negatively correlated with clinical outcome. Although freshly isolated pDCs might induce tolerance or Th2 cell development, several groups have now convincingly demonstrated that human pDCs can efficiently promote Th1 responses and produce large amounts of type I IFN, provided that they are properly activated with Toll-like receptor (TLR) ligands. Recent preclinical studies have also shown that human pDCs can stimulate anti-tumor responses *in vitro* and that administration of antigen-loaded pDCs inhibits tumor growth in mice. These findings prompted us to investigate the capacity of human pDCs to elicit immune responses *in vivo*.

Here we present the results of the first clinical trial exploiting pDCs that were activated by the preventative vaccine FSME. Fifteen distant metastatic melanoma patients received tumor peptide-loaded FSME-activated pDCs and were tested for vaccine-related toxicity and immunological responses. We demonstrated that the administered pDCs distributed over multiple lymph nodes and induced FSME-specific and tumor-specific CD8⁺ T cells responses. Moreover, patients that received the pDC-vaccine had a significantly increased overall survival compared to patients that received standard DTIC chemotherapy. These results indicate that vaccination with activated tumor peptide-loaded pDCs is feasible, safe and capable to induce anti-tumor immune responses in melanoma patients.