**Cancer therapy with tumor cell lysate pulsed monocyte-derived dendritic cells in patients with metastastic colon cancer: Improvement by danger signals**

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**Background:** The prognosis of colon cancers with hematogenous spread remains poor at 12–20 months. We report the use of a dendritic cell based immunotherapy to improve patient survival, especially with cell culture conditions mimicking infection.

**Methods:** After isolating monocytes from the blood of 39 patients with metastasized colon cancer, dendritic cells were generated ex vivo in the presence of recombinant cytokines (IL-4; GM-CSF) and autologous serum. The DC loaded with tumor cell lysate were administered to the patients intradermally. Culture conditions were tested for upregulation of costimulatory molecules, downregulation of IL-10 and upregulation of IL-12 secretion by ELISPOT and fluorescence cytometry.

**Results:** DC vaccination induced a clinical response in 9 (23%) patients with a median overall survival after onset of DC-therapy of 12 months (11–44 months for responders and 1–20 months for non-responders) and 23 months after diagnosis of metastases (16–63 months for responders and 1–23 months for non-responders). These data show that a dendritic cell based immunotherapy may prolong the patients overall survival. However, complete remissions are rare. This can be due to weak stimulation of CTL response due to insufficient antigen presentation, lack of costimulatory molecules as well as secretion of IL-10 rather than IL-12 by the DC’s. Here we could show that Toll-like receptors (TLR) ligands like Poly-I:C or lipopeptides as so called danger signals in combination with interferons can induce an upregulation of costimulatory molecules accompanied by inhibition of IL-10 and induction of IL-12 secretion in vitro. By using these culture conditions we induced a clinical complete remission of liver metastases after failure of standard therapy in one patient (overall survival after onset of DC-therapy 13 months, after diagnosis 24 months).

**Conclusions:** According to Matzinger’s hypothesis an effective immune response occurs only by responding to a danger signal associated with infection or stress. Thus, cellculture condition should be used with TLR ligands mimicking a bacterial or viral infection. In general, a dendritic cell based immunotherapy can be successful in advanced stages of colon cancer patients.