

## Necrosis-associated factors (DAMPs) like S100A4 used to pulse dendritic cells (DCs) enhance the proliferative lymphocyte response

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Necrotic cell death with subsequent release of damage associated molecular pattern molecules (DAMPs) is a characteristic feature of advanced solid tumor. S100A4 is a DAMP family member which has been shown to be associated with clinical outcome of patients with colorectal and breast cancer.

We pulsed human monocyte-derived immature dendritic cells (iDCs) with necrotic material from colorectal tumor cell lines or with recombinant S100A4, for 3 days. Pulsed DCs were cocultured with autologous lymphocytes for 5 days and lymphocyte proliferation as well as lymphocyte metabolic activity was measured. The fraction of CD25-FoxP3-double-positive regulatory T cells within the proliferative lymphocyte pool was assessed by flow cytometry.

We could demonstrate a dose-dependent proliferative response of lymphocytes co-cultured with autologous DCs which were pulsed with S100A4 or with necrotic material (DAMPs) from lysed colorectal tumor cells, the relative proliferative index of lymphocytes was up to 2.5, compared to the lymphocyte response to non-pulsed DCs. The fraction of CD4+CD25+FoxP3+ regulatory T cells within the proliferative lymphocyte pool was influenced by S100A4.

Given that necrotic material is generally found within advanced tumor tissue, there is an urgent need to characterize specific members of DAMPs and their impact within tumor microenvironment. By describing the effect of S100A4 protein our results shed some light into the underlying mechanisms playing a crucial role in adaptive immune response to tumor.

### Biography

R. Lotfi finished his Medical School at the University of Muenster (Germany) in 1998. After 2 ½ years of Pediatrics he went to the University Hospital of Tuebingen (Germany) where he specialized in Transfusion Medicine. From 2005 to 2007 he worked as a Post-Doc in Dr. Michael T. Lotze's laboratory at the University of Pittsburgh (PA), where he focused on tumor immunology and the impact of oxidative conditions and eosinophilia within tumor microenvironment. Since 2007 he is back to Germany and is presently the head of the Department of Innovative Cellular Therapeutics in the Institute for Transfusion Medicine of the University Hospital Ulm.

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