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Identification of tumor antigen-specific T cells in the peripheral blood of colorectal cancer patients

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ABSTRACT:
Interactions between the immune system and the tumor are now recognized as key determinants of clinical outcome in colorectal cancer (CRC). Immune landscapes have been extensively studied within resected primary tumors and immune markers, such as T cells, have been found to be associated with CRC patients' survival. Little is known about the immune profile of cells in peripheral blood. We hypothesize that the functional status of T cells, characterized by their response to CRC tumor-associated antigens (TAAs), can be monitored in the peripheral blood of patients and that they have prognostic relevance in CRC.

In vitro T cell responses to pools of overlapping peptides representing the TAAs MUC-1, hTERT, NY-ESO-1 and CEA were assessed by analyzing IFN-gamma and TNF-alpha production by $CD8^+$ T cells using flow cytometry, in 5 stage II-III CRC patients just prior to surgical resection and 3 healthy age- and sex-matched controls.

T cells responding to MUC-1, hTERT, NY-ESO-1 and CEA were present in 3, 3, 1 and 5 CRC patients, respectively, whereas only one response to TAAs (MUC-1) was found in one healthy control. When TAA responses were pooled together, 83.3% of responders were patients (n=5) and 100% of non-responders were healthy controls (n=2).

The presence of circulating T cells responding to CEA in all 5 patients, but also to MUC-1 and hTERT in 3 patients suggests that these TAAs may be good targets for immunotherapy in CRC. Our findings also provide a rationale to investigate the prognostic value of CEA-, MUC-1- and hTERT-specific T cells in the peripheral blood of CRC patients and to consider vaccination with these antigens to boost or induce responses to control residual tumor post-surgery.