Immune-profiling reveals DNAM-1 downregulation in tumor-infiltrating lymphocytes of RCC patients

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Comprehensive analysis of the immune landscape in RCC patients revealed that intratumoral NK cells, as well as T cells, have profoundly altered phenotypes compared with circulating lymphocytes, with downregulation of the activation receptor DNAM-1 possibly representing a tumor escape mechanism.

Moreover, low expression of DNAM-1 and PD-1 on intratumoral and circulating NK cells, respectively, were identified as potential biomarkers of disease progression.

**Introduction**

Natural killer (NK) cells infiltrate renal cell carcinoma (RCC) tumors and may play a key role in modulating tumor progression. Although high NK cell frequencies have been correlated with improved patient survival, both NK cells, as well as T cells, have been found to be suppressed in the tumor microenvironment.

In this study, we investigated immune cell and soluble factor profiles in blood and tumor biopsies of 14 patients with primary RCC. Using the multivariate analysis tool Orthogonal Projections to Latent Structures (OPLS), we correlated these with disease parameters, and we identified extensive alterations in immune landscapes of tumors compared with blood.

**Workflow**

Collection of blood and tumor samples  

**Multi-color flow cytometry of immune cell markers**  

**Multiplex analysis of soluble factors**  

Analysis of immune phenotypes and secreted factors  

**Multivariate statistical data analysis**  

- Relationship to clinical data  
  - Fuhrman grade  
  - primary tumor stage  
- Multidimensional paired analysis  
  - blood pre and post surgery  
  - blood vs tumor

**Results**

High DNAM-1 on intratumoral CD56bright NK cells is associated with lower Fuhrman grade

High PD-1 on circulating NK and T cells is associated with lower primary tumor (pT) stage

The immune landscape is profoundly altered in RCC tumors

RCC cells induce DNAM-1 downregulation and PD-1 upregulation in vitro

**Ongoing research**

Currently, we investigate the mechanism of the RCC-induced DNAM-1 downregulation and its functional consequences.