

Abstract

Background: Cancer is a complex disease involving interactions of the immune system and tumor cells. Recent results highlighted the important role of T cells in controlling the early stage of metastatic invasion and survival. To gain deeper insights into tumor progression and tumor recurrence mechanisms in human colorectal cancer (CRC), we have applied integrative analyses. Experiments were performed for genome-wide expression profiles from 105 patients, quantitative real time qPCR of 81 immune genes from 153 patients, and 14 immunohistochemical markers from 107 patients.

Results: A set of genes specifically expressed in immune cell subpopulations in healthy volunteers was compared with the gene expression in CRC patients. Clusters of immune genes were related to patients with a similar cancer stage (tumor progression) or with a similar risk to relapse (tumor recurrence). qPCR and tissue microarray (TMA) analyses showed a strong intratumoral correlation of T and B cells. The prolonged co-localization at the tumor site of T and B cells could be favorized by a mechanism involving CXCL13 and CXCR5. Further, during tumor progression the densities of specific immune cell subpopulations were affected. The density of T cell subpopulations significantly decreased in the center of the tumor (CT) and in the invasive margin (IM). By integrating the correlation and survival analysis from qPCR and TMA data it could be shown that B and T lymphocytes are organized within a core network and that they are the most prominent immune cells associated with the absence of tumor recurrence.

Conclusion: This integrative analysis underlines the coordinated actions of the adaptive immune cells (T and B cells) and their importance in strengthening the protection against tumor recurrence.

Keywords: Colorectal Cancer, Immunology, Integrative analysis