38P - The comparative transcriptomic analysis of monocytes of colorectal cancer patients and healthy donors

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Background. Tumor microenvironment affects key activities of cancer cells and contributes to the tumor response to chemotherapy. Tumor-associated macrophages (TAMs) are a major component of innate immunity supporting primary tumor growth and metastasis. Studies in animal models and patients with colorectal cancer (CRC) recently demonstrated that TAMs suppress growth of primary tumor and metastasis. Circulating monocytes are recruited to tumor and constitute the main plastic resource of TAMs. However, the role of programming of circulating monocytes in the functional polarization and activation of pro- and anti-tumor functions of TAMs is poorly understood.

Material and method

Peripheral blood monocytes of 22 CRC patients and 13 healthy donors were isolated by FACS. RNA was isolated and cDNA libraries were prepared. The whole-transcriptome profile of monocytes was determined by NGS. Bioinformatics analysis included standard technics, we used the Hallmark gene sets, Reactome, KEGG and GO databases for the presentation of NGS results. The study was carried out according to Declaration of Helsinki and was approved by the local committee of Medical Ethics.

Results and discussion

We compared the transcriptome of monocytes from healthy donors and CRC patients. Using NES parameter> 1.5, we found the following transcriptional programs are activated in the monocytes of patients: LPS-mediated response, cell differentiation, regulation of cyclin-dependent kinases, iron transport, IL-4-dependent response, INFgamma-dependent response, angiogenesis, cell adhesion, leukocyte migration, chemotaxis, collagen formation. Transcriptional programs that are responsible for the histone acetylation, chromatin rearrangement and protein modification were suppressed in monocytes of CRC patients. The transcriptional profile of monocytes of patients with rectal cancer and colon cancer, when independently compared with monocytes of healthy donors, revealed similar groups of differentially expressed genes.

Conclusion

We identified new differential patterns of monocyte programming in CRC patients in comparison with healthy donors. Our data will allow us clarify transcriptional and epigenetic mechanisms of anti-tumor TAM programming in CRC.

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Irina Larionova has no conflicts of interest to declare.

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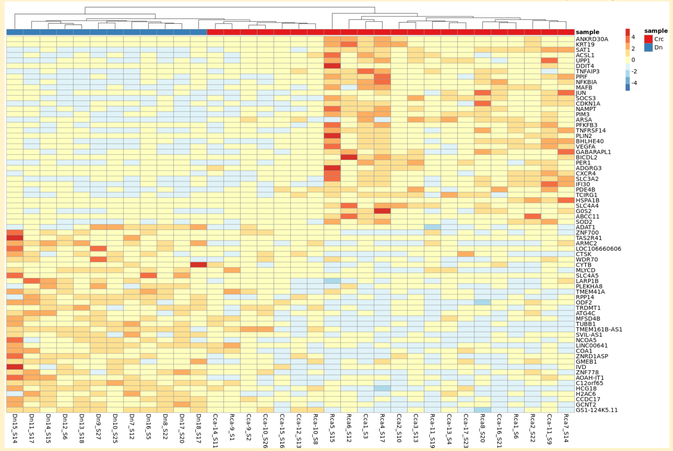
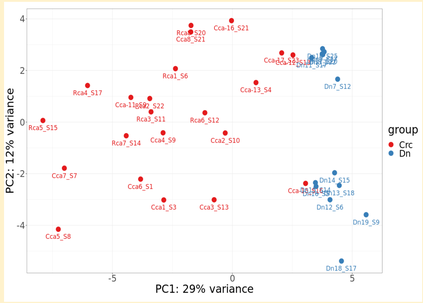
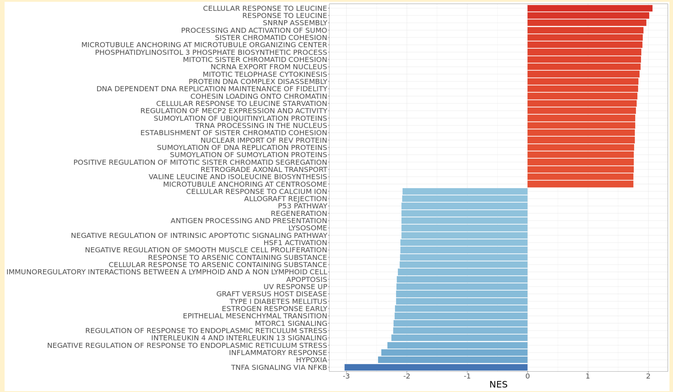


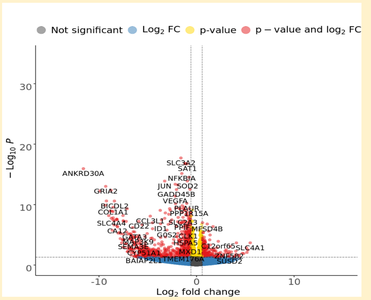
Heatmap displaying top DEG activated and inhibited in monocytes of CRC patients. Crc - monocytes from CRC patients; Dn - monocytes from healthy donors. FDR <0.1



PCA analysis of monocyte samples from healthy donors (Dn) versus monocytes from CRC patients (Crc)



Histograms of enrichment of activated and inhibited genes by functional pathways. The NES parameter reflects the degree of enrichment of the functional pathway. NES> 0 - functional pathways activated in Dn; NES <0 - functional pathways activated in Crc.



Volcano diagram showing the distribution of genes by their significance and the magnitude of the differences. LFC> 0 - genes with increased expression in Dn; LFC <0 - genes with increased expression in Crc