Characterization of Myeloid–Derived Suppressor Cell Subpopulations in Localized Colorectal Adenocarcinoma Patients

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Introduction: The growth of colorectal adenocarcinoma (CRC), one of the most prevalent malignancies in humans, is accompanied by chronic inflammation, a process known to be partially mediated by the release of immature potent immune suppressive cells to the bloodstream, and their accumulation within the tumor microenvironment. Such myeloid-derived suppressor cells (MDSCs) were previously shown to correlate with tumor stage and overall survival. However, this was shown only for advanced colorectal adenocarcinoma, and only peripheral blood was examined, without attention to the immunosuppressive role that MDSC may play within the tumor microenvironment. Aim: To characterize different MDSC subpopulations in peripheral blood and tumor tissue taken during diagnostic colonoscopy from patients with localized CRC.

Methods: Blood samples and tumor tissue specimens were taken from CRC patients (n = 10) and healthy controls (n = 5) during diagnostic colonoscopy. MDSC were analyzed by 7-stain flow cytometry (CD45, CD33, HLA-DR, CD14, CD66b, CD16, CD11b). MDSC subsets were classified as monocytic (MoMDSC) (CD14+/CD33+/HLA-DRlow) and granulocytic (GrMDSC) (CD14-/CD33dim/HLA-DR-) MDSC. The last subset was found to be further divided according to CD11b/CD16 expression. The ability to suppress allogeneic lymphocyte stimulation was measured by Carboxyfluorescein succinimidyl ester (CFSE) assay.

Results: While localized CRC were not able to increase MDSCs level in peripheral blood relative to control (in contrast with metastatic CRC), tumor specimens did show increased level of MDSCs recruitment relative to normal mucosa. CD16-/CD11b–, but not CD11b+/CD16+ cells were able to decrease lymphocytic response to CD3/CD28 stimulation in dye–based proliferation assay. Examination of circulating MDSC subpopulations revealed differences between CRC patients and healthy controls i.e. CRC patient had a 3-fold increase in circulating MoMDSC levels while a concomitant 2-fold decrease in circulating CD16+/CD11b+ GrMDSCs was detected.

Conclusion: The MDSC subpopulations differ between peripheral blood of healthy individuals and CRC patients and between peripheral blood and tumor tissue in cancer patients. To the best of our knowledge, this is the first time MDSC are studied in such profound detail in CRC. These results lay the basis for future research to study the role of MDSC subpopulations in CRC progression and as possible prognostic markers for localized CRC.