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T-cell suppression is associated with circulating and tumor infiltrating CD33+11b+HLA-DR- myeloid suppressor cells in gastric cancer: A possible relation to microRNA-494 and TGF-β tumor expression

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Statement of the Problem: Because of heterogeneity of gastric cancer (GC), searching for more accurate predictors of GC prognosis has become a growing interest. Infiltration of immune cells in tumors is associated with prognosis; among them are the immunosuppressive myeloid derived cells (MDSCs). Their accumulation constitutes an important mechanism of tumor immune evasion. Hence, their characterization is essential for diagnosis and therapeutics of cancer. Increased expression of microRNA-494 was noticed in MDSCs from tumor-bearing mice suggesting another new therapeutic objective for cancer treatment. It was also discovered that tumor-derived transforming growth factor beta (TGF-β) was responsible for the up-regulation of microRNA-494 in MDSCs. The purpose of this study is to address the suppressive effect of MDSCs on T-cells in GC and its possible association with micro-RNA-494 and TGF-β expression in tumor tissue.

Methodology & Theoretical Orientation: A case control study on 40 GC patients and corresponding controls where done. Tissue samples and peripheral blood were used for isolation of CD33+11b+HLADR- MDSCs cells using flowcytometry. MDSCs were co-cultured with isolated T-cells to assess proliferation and cytokine production. Real-time PCR and enzyme linked immunosorbent assay were used to evaluate tumor expression of miRNA-494 and TGF-β respectively.

Findings: MDSCs percentages were significantly elevated in GC patients than controls and significantly increased in tumor specimens than paraneoplastic tissue. This increased expression is accompanied with elevation of TGF-β production in tumor than surroundings. MiRNA-494 was also extensively expressed in tumor samples. Addition of MDSCs from cancer patients markedly suppressed the proliferation of autologous T-cells and cytokine production; however, no inhibitory effect was observed for MDSCs from healthy donors.

Conclusion & Significance: The result indicates that tumor-derived MDSCs but not MDSCs from healthy donors have the immunosuppressive effect on T-cells. Infiltration of MDSCs in tumors is associated with the prognosis of GC.

Biography

Mai Moaaz is an Assistant Professor of Immunology. She has a passion in the field of tumor immunology and an expertise in tumor tissue culture system and experimenting new modalities for cancer immunotherapy. Her tissue culture system provides the ex vivo tissue architecture that is necessary to maintain or reconstitute an environment closely resembling that of the tumor tissue to reflect the complex tissue architecture of an individual tumor. She is conducting current studies on tumors as an approach to cancer immunotherapy.

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