Evaluation of the Therapeutic Potential of Bone Marrow-Derived Myeloid Suppressor Cell (MDSC) Adoptive Transfer in Mouse Models of Autoimmunity and Allograft Rejection

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Résumé en anglais	Therapeutic use of immunoregulatory cells represents a promising approach for the treatment of uncontrolled immunity. During the last decade, myeloid-derived suppressor cells (MDSC) have emerged as novel key regulatory players in the context of tumor growth, inflammation, transplantation or autoimmunity. Recently, MDSC have been successfully generated in vitro from naive mouse bone marrow cells or healthy human PBMCs using minimal cytokine combinations. In this study, we aimed to evaluate the potential of adoptive transfer of such cells to control auto- and allo-immunity in the mouse. Culture of bone marrow cells with GM-CSF and IL-6 consistently yielded a majority of CD11b+Gr1hi/lo cells exhibiting strong inhibition of CD8+ T cell proliferation in vitro. However, adoptive transfer of these cells failed to alter antigen-specific CD8+ T cell proliferation and cytotoxicity in vivo. Furthermore, MDSC could not prevent the development of autoimmunity in a stringent model of type 1 diabetes. Rather, loading the cells prior to injection with a pancreatic neo-antigen peptide accelerated the development of the disease. Contrastingly, in a model of skin transplantation, repeated injection of MDSC or single injection of LPS-activated MDSC resulted in a significant prolongation of allograft survival. The beneficial effect of MDSC infusions on skin graft survival was paradoxically not explained by a decrease of donor-specific T cell response but associated with a systemic over-activation of T cells and antigen presenting cells, prominently in the spleen. Taken together, our results indicate that in vitro generated MDSC bear therapeutic potential but will require additional in vitro factors or adjunct immunosuppressive treatments to achieve safe and more robust immunomodulation upon adoptive transfer.

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