Title:	Myeloid-Derived Suppressor Cells Confer Infectious Tolerance to Dampen Virus-Induced Tissue Immunoinflammation
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Abstract:	In this study, we investigated the response of myeloid-derived suppressor cells (MDSCs) during the pathogenesis of an immunoblinding disease of the cornea caused by HSV type 1 infection. We also measured the anti-inflammatory potential of in vitro–differentiated MDSCs in dampening herpetic stromal keratitis resulting from primary ocular HSV1 infection in mice. In the lymphoid organs and inflamed corneal tissues, MDSCs were phenotypically characterized as CD11b+Gr1lo-int cells. Sorted CD11b+Gr1lo-int cells, but not CD11b+Gr1hi cells, suppressed the proliferation and cytokine production by stimulated CD4+ T cells. In vitro–generated MDSCs inhibited the activity of stimulated CD4+ T cells in a predominantly contact-dependent manner. An adoptive transfer of in vitro–generated MDSCs before or after ocular HSV1 infection controlled herpetic stromal keratitis lesions. The transferred MDSCs were primarily recovered from the lymphoid organs of recipients. Surprisingly, MDSCs recipients expanded their endogenous Foxp3+ regulatory T cells (Tregs). We further demonstrated the MDSCs mediated stabilization of Foxp3 expression in already differentiated Tregs and their ability to cause an efficient de novo conversion of Foxp3+ Tregs from stimulated Foxp3−CD4+ T cells. These effects occurred independent of TGF-β signaling. Therefore, the therapeutic potential of MDSCs could be harnessed as a multipronged strategy to confer an infectious tolerance to the host by activating endogenous regulatory mechanisms.
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