

## Re: The Terminology Issue for Myeloid-Derived Suppressor Cells

### In Response:

In the literature, including our own (1), diverse terms (such as Gr-1<sup>+</sup>CD11b<sup>+</sup> myeloid cells, Gr-1<sup>+</sup> myeloid cells, Gr-1<sup>+</sup>CD11b<sup>+</sup> immature myeloid cells, CD11b<sup>+</sup>Gr1<sup>+</sup>CD31<sup>+</sup>myeloid progenitor, immature myeloid cells, myeloid suppressor cells, etc.) are used to describe murine Gr1<sup>+</sup>CD11b<sup>+</sup> cells of myeloid lineage, which represent an important immunosuppressive factor in cancer and some other pathologies (reviewed in refs. 2, 3). However, none fully encompasses the characteristics of this cell type. We believe that the term “myeloid-derived suppressor cells” (MDSCs), proposed by Gabrilovich et al., better conveys the properties of this important cell type by

(a) indicating that MDSCs belong to the myeloid lineage. Myeloid cells accumulated in tumor-bearing hosts represent a heterogeneous population comprising immature macrophages, granulocytes, dendritic cells, and other myeloid cells at earlier stages of differentiation. In mice, MDSCs express both Gr1 and CD11b, typical markers of the myeloid lineage but lack or exhibit reduced expression of markers of mature myeloid cells. Human MDSCs are CD34<sup>+</sup>CD33<sup>+</sup>CD13<sup>+</sup>, consistent with a human myeloid lineage.

(b) implying their heterogeneity of phenotype and functional plasticity. MDSCs are rather heterogeneous and plastic in phenotype and functional potency. Normal myeloid cells isolated from mouse bone marrow do not produce significant immunosuppression, but can be recruited and evolve into MDSCs in response to a variety of tumor-derived cytokines and/or direct contact with tumor cells. The precise nature of the suppressor cell population depends on the tumor and tumor-derived factors of the host.

(c) describing the immunosuppressive nature of these cells. The accumulation of MDSCs in cancer or even secondary lymphoid organs is an important factor in tumor non-responsiveness. MDSCs inhibit not only activation of T cells by anti-CD3 and superantigen but also antigen-specific CD4<sup>+</sup> and CD8<sup>+</sup> T cells. There is remarkable diversity and complexity of immunosuppressive mechanisms used by MDSCs, including the inhibition of antigen-specific T-cell function via CD80 or B7-H1 expression, nitric oxide production, or L-arginine metabolism.

(d) distinguishing MDSCs from lymphoid-derived immunosuppressive or immunoregulatory cells, including natural killer T cells, CD4<sup>+</sup>CD25<sup>+</sup> T regulatory (Treg) cells, T helper type 3 cells, and Treg type 1 cells.

(e) being applicable in both mice and humans. Whereas Tregs express common surface markers (CD4 and CD25) between these species, MDSCs unfortunately do not; mouse MDSCs express Gr1 and CD11b molecules, whereas their human counterparts are determined using expression of CD34 and CD33.

(f) avoiding confusion between mesenchymal stem cells and the commonly used term myeloid suppressor cells (both MSCs).

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### References

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