The Terminology Issue for Myeloid-Derived Suppressor Cells

To the Editor:

The recent study by Yang et al. (1) described antigen-specific immunosuppression by Gr-1$^+$CD11b$^+$ myeloid cells, which was mediated by the expression of CD80. This report continued a series of recent articles published in *Cancer Research*, which provided strong evidence in support of a critical role of these cells in tumor progression (1–6). Recent years have witnessed increasing interest in immunosuppressive cells of myeloid origin. During the last 18 months alone, more than 50 articles have appeared in peer-reviewed journals on this subject. Accumulation of these cells has been reported under pathologic conditions, including bacterial and parasitic infections, acute and chronic inflammation, and traumatic stress. However, most of the attention has been focused on the role of these cells in cancer. Immunosuppressive myeloid cells accumulate in large numbers in tumor-bearing mice, in practically all tested experimental models, as well as in patients with breast, lung, prostate, kidney, head and neck, and other types of cancer. These cells are produced in response to a variety of tumor-derived cytokines and are a heterogeneous mixture of myeloid cells at different stages of differentiation. The precise nature of the suppressor cell population (i.e., precursors of granulocytes, macrophages, dendritic cells, or early myeloid progenitors) depends on the tumor and tumor-derived factors of the hosts. Despite this heterogeneity, immunosuppressive myeloid cells share some common characteristics: lack or reduced expression of markers of mature myeloid cells, expression of both Gr-1 and CD11b molecules in mice, inability to differentiate into mature myeloid cells in the presence of tumor-derived factors, high levels of reactive oxygen species, and activation of arginase I and other molecules. Most importantly, these cells possess a high potential to suppress immune responses *in vitro* and *in vivo*. Immunosuppressive myeloid cells are now considered by many as a critical mechanism of tumor escape as well as an important immunosuppressive factor for other pathologic conditions.

Because these cells play a key role in regulation of immunity, we feel it necessary to address one issue that causes confusion in this field. These cells lack a clear, unified name. In the literature, these cells have been called "immature myeloid cells" or "myeloid suppressor cells" (MSC). Although both of these names reflect the biology of cells, neither term is entirely accurate. The name "immature myeloid cells" implies that these cells are normal myeloid precursors. However, this may not be the case. Recent studies have shown clear differences in the biology of normal immature myeloid cells and the cells that accumulate in tumor-bearing hosts. In addition, this term does not reflect the most important feature of these cells: their ability to suppress immune responses. The name "MSC" implies that these cells include populations of mature myeloid cells, such as macrophages or dendritic cells, capable of displaying some immunosuppressive features under certain circumstances. However, this name is also not accurate, being too generic and potentially misleading because these cells are not mature myeloid cells. In addition, the abbreviation "MSC" is commonly used for the characterization of mesenchymal stem cells. We believe that the lack of an accurate name for these cells creates confusion and hampers attempts to develop a cohesive picture of the mechanisms of immunosuppression in cancer and other pathologic conditions.

Therefore, we suggest that these cells be called "myeloid-derived suppressor cells". We believe that this term more closely reflects the origin and function of these cells and hope that it will stimulate further scientific discussions and progress not only in immunology but also in cancer biology where undoubtedly the same or similar cell populations play a major functional role.

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