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Review

Extracellular matrix and the myeloid - in - myeloma compartment: balancing tolerogenic and immunogenic inflammation in the myeloma niche

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Abstract

The last 10–15 years have witnessed a revolution in treating multiple myeloma, an incurable cancer of Ab - producing plasma cells. Advances in myeloma therapy were ushered in by novel agents that remodel the myeloma immune microenvironment. The first generation of novel agents included immunomodulatory drugs (thalidomide analogs) and proteasome inhibitors that target crucial pathways that regulate immunity and inflammation, such as NF - κ B. This paradigm continued with the recent regulatory approval of mAbs (elotuzumab, daratumumab) that impact both tumor cells and associated immune cells. Moreover, recent clinical data support checkpoint inhibition immunotherapy in myeloma. With the success of these agents has come the growing realization that the myeloid infiltrate in myeloma lesions—what we collectively call the myeloid - in - myeloma compartment—variably sustains or deters tumor cells by shaping the inflammatory milieu of the myeloma niche and by promoting or antagonizing immune - modulating therapies. The myeloid - in - myeloma compartment includes myeloma - associated macrophages and granulocytes, dendritic cells, and myeloid - derived - suppressor cells. These cell types reflect variable states of differentiation and activation of tumor - infiltrating cells derived from resident myeloid progenitors in the bone marrow—the canonical myeloma niche—or myeloid cells that seed both canonical and extramedullary, noncanonical niches. Myeloma - infiltrating myeloid cells engage in crosstalk with extracellular matrix components, stromal cells, and tumor cells. This complex regulation determines the composition, activation state, and maturation of the myeloid - in - myeloma compartment as well as the balance between immunogenic and tolerogenic inflammation in the niche. Redressing this balance may be a crucial determinant for the success of antimyeloma immunotherapies.

Deming and Fotis Asimakopoulos, Versican-Derived Matrikines Regulate Batf3–Dendritic Cell Differentiation and Promote T Cell Infiltration in Colorectal Cancer, *The Journal of Immunology*, **199**, 5, (1933)
Crossref

Dimakatso Alice Senthebane, Arielle Rowe, Nicholas Ekow Thomford, Hendrina Shipanga, Daniella Munro, Mohammad A. M. Al Mazeedi, Hashim A. M. Almazyadi, Karlien Kallmeyer, Collet Dandara, Michael S. Pepper, M. Iqbal Parker and Kevin Dzobo, The Role of Tumor Microenvironment in Chemoresistance: To Survive, Keep Your Enemies Closer, *International Journal of Molecular Sciences*, 10.3390/ijms18071586, **18**, 7, (1586), (2017).
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