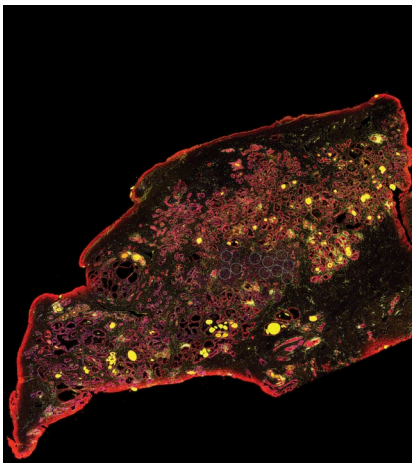
MOLECULAR CANCER RESEARCH

TABLE OF CONTENTS

TABLE OF CONTENTS

ABOUT THE COVER



Tumor-associated macrophages (TAM) are recognized for their immunosuppressive functions across cancer types. In metastatic prostate cancer, however, TAMs are not well characterized. In their study, Mei and colleagues interrogated the heterogenous subgroups of TAMs present in metastatic prostate cancer and further evaluated how these subgroups may be targeted to improve immune checkpoint inhibition therapies. Using multiplex immunohistochemistry, single-cell RNA sequencing, and NanoString GeoMx Digital Spatial Profiling (DSP), they revealed that high-grade tumors had increased levels of $CD68^+$ and $CD68^+CD163^+$ macrophages compared to low-grade tumors, with $CD68^+$ macrophages localizing more closely to tumor regions than other immune infiltrates. The cover image highlights the spatial distribution of tumor cell and immune cell regions profiled from high-grade metastatic prostate cancer using NanoString GeoMx DSP. The authors further identified four subgroups of TAMs and found that the SPP1+/TREM2+ subgroup was prominently associated with metastasis, angiogenesis, impaired antigen presentation and disease progression-free survival. SPP1+/TREM2+ macrophages were also shown to preferentially localize within the tumor, rather than peripheral normal tissue, compared to other subgroups. Interestingly, the targeting SPP1+ macrophages in combination with anti–PD-1 in mouse models significantly improved the therapeutic efficacy of ICB, highlighting the protumoral role of these TAMs in prostate cancer progression. This article can be found on page 653.

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