Function of neutrophils during tumor progression unraveled

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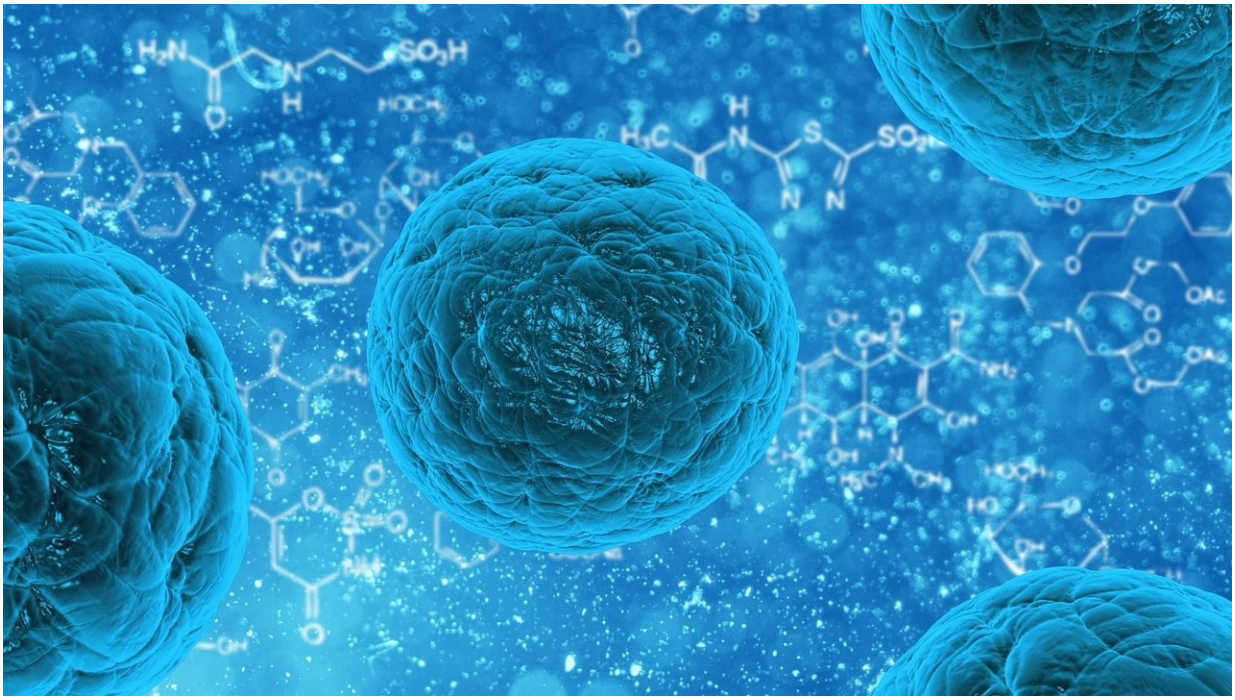

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Researchers at The Wistar Institute have characterized the function of neutrophils, a type of white blood cells, during early stages of tumor progression, showing that they migrate from the bone marrow to distant sites and facilitate tumor cell seeding and establishment of metastasis. Importantly, these neutrophils don't possess the immunosuppressive characteristics of polymorphonuclear myeloid-derived suppressor cells

(PMN-MDSC). This seminal study was published online in *Nature Immunology*.

PMN-MDSCs are pathologically activated neutrophils with the ability to suppress immune responses to cancer and to promote tumor progression by conditioning tumor cells at the primary site. The role of neutrophils in setting the stage for metastatic growth at distant sites was not clear.

"Our research shed light on the role of neutrophils in the early stages of tumor progression, when overt metastasis has not yet formed but the conditions for metastatic spread are being created," said Dmitry I. Gabrilovich, M.D., Ph.D., Christopher M. Davis Professor and program leader of the Immunology, Microenvironment and Metastasis Program at Wistar. "Our study revealed that the activation of neutrophils in cancer is a two-phase process. We focused on the first phase and described the accumulation of a previously uncharacterized population of neutrophils that lack immunosuppressive activity but display a potent ability to spontaneously migrate, whereas the later phase is associated with accumulation of neutrophils with typical features of PMN-MDSCs."

Gabrilovich and colleagues isolated neutrophils from the bone marrow of tumor bearing mice from different models of disease and at different stages of tumor development. The highly migratory population present in the early stages, which they designated as PMN-MDSC-like cells (PM-LCs), displays higher glucose uptake, increased metabolic activity and higher expression of genes associated with energy production. Further in vivo experiments demonstrated that PM-LCs promote seeding of tumor cells in distant sites and may favor metastatic dissemination.

The team validated the clinical relevance of these findings by describing the same spontaneous migratory behavior of neutrophils isolated from cancer patients.

"Our study elucidates the mechanism through which neutrophils contribute to early tumor dissemination," said Jerome Mastio, Ph.D., postdoctoral fellow in the Gabrilovich Lab and co-first author of the study. "We describe the dynamic changes that neutrophils undergo in cancer, with PM-LCs representing the first step of pathologic activation."

More information: Unique pattern of neutrophil migration and function during tumor progression, *Nature Immunology* (2018). DOI: 10.1038/s41590-018-0229-5, www.nature.com/articles/s41590-018-0229-5

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