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Monocytes and macrophages may promote human cancer growth

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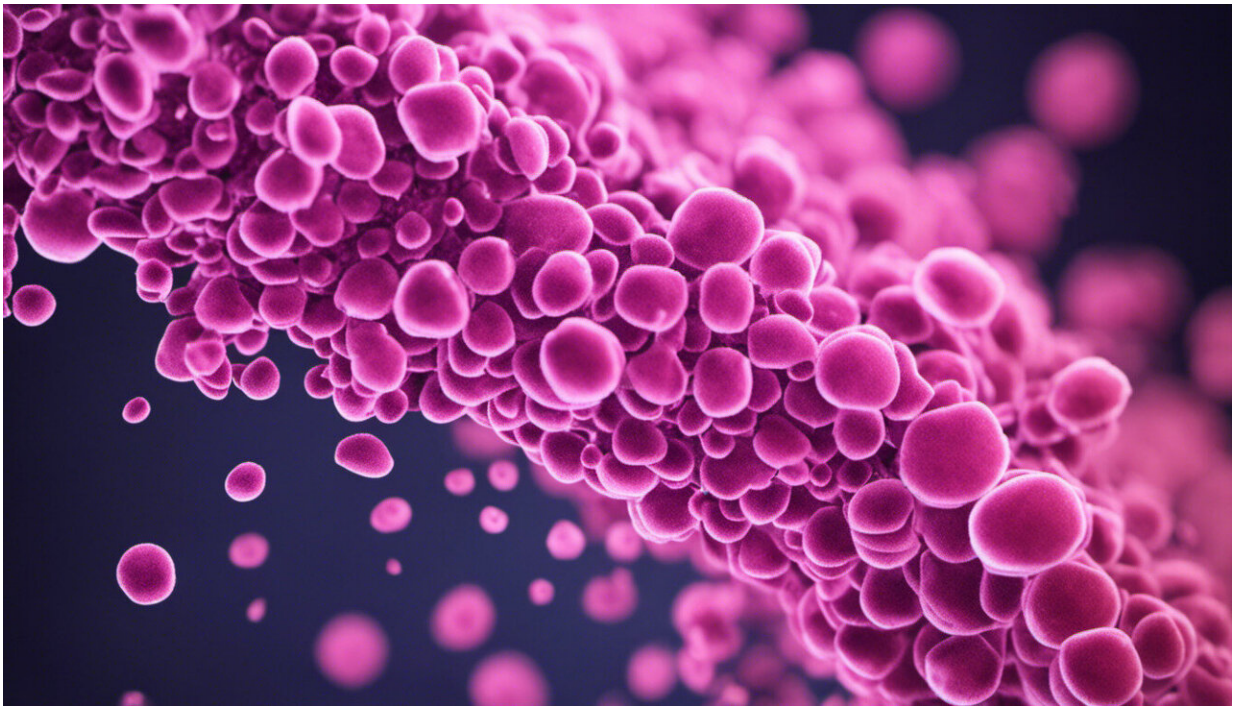

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White blood cells such as monocytes and macrophages are known mediators of inflammation, and according to new findings by researchers at A*STAR, also play a key role in promoting human cancer.

The study is one of the first to comprehensively characterize monocytes

and macrophages found in cancer patients, and provide a mechanistic link between these cells and tumor promotion.

"There is a lot of evidence in mice that macrophages are tumor-promoting, but the information in human cancer had been scarce until now," says Subhra K. Biswas from the A*STAR Singapore Immunology Network, who led the research.

The study describes the phenotype and 'crosstalk' of monocytes and macrophages with tumor cells in a human cancer and discusses the mechanisms that guide the communication. "These white blood cells show functional plasticity in cancer and display different strategies to promote tumor growth at different stages," explains Biswas.

Through experiments conducted on both xenografts in mice and renal cancer patients, the team found that monocytes and macrophages display a tumor-enabling profile, which encourages the growth of new blood vessels, a process known as angiogenesis, and cancer invasion of normal tissue. The researchers also identified the molecular mechanism responsible for steering these cells toward a 'pro-tumor' identity, or phenotype.

"Induction of this tumor-promoting phenotype required an interleukin-1-receptor-(IL-1R)-dependent mechanism," explains Biswas. IL-1R is a cytokine receptor which binds to the interleukin-1 cytokine. The IL-1R pathway in monocytes and macrophages is essential for their tumor-promoting role. The researchers further demonstrated that inhibiting the pathway prevented the white blood cells from becoming pro-tumor, and hence decreased cancer growth.

Although Biswas' team studied renal cancer, the findings may also be broadly applicable to other tumor types since epidemiological studies show that a high density of tumor-infiltrating macrophages is linked to

poor outcomes in most human cancers. The next step is to characterize human monocyte–macrophage phenotypes in other cancers to discover common and divergent features among the different types of cancer.

"Our study supports the idea of targeting these white blood cell types or their related molecules to regulate cancer progression," Biswas says. "It will be necessary, however, to clarify the functional plasticity of these cells during human cancer before determining the stage at which inhibiting these cells could be effective in humans," he adds. This is something the group plans to focus on moving forward.

More information: "Molecular profiling reveals a tumor-promoting phenotype of monocytes and macrophages in human cancer progression." *Immunity* 41, 815–829 (2014). dx.doi.org/10.1016/j.immuni.2014.09.014

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