Low Oxygen Recruits Inflammatory Cells to Tumors, Stimulating Growth

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(PhysOrg.com) -- The inner regions of tumors have a low-oxygen content and often contain inflammatory cells called macrophages, which researchers suspect promote tumor growth. Now, University of Pennsylvania School of Medicine researchers show that this is the case: Tumor cells in this low-oxygen area actively recruit macrophages and blocking their recruitment reduces tumor growth and aggressiveness in mouse models. The results suggest new targets for cancer drug development.

“We know that hypoxia affects many aspects of tumor progression, but this is another novel way that it clearly does, by recruiting inflammatory cells,” says Celeste Simon, PhD, professor of Cell and Developmental Biology, who presented the results in a symposium on Wednesday, April 21st, at the American Association of Cancer Research annual meeting.

“It is clear that macrophages accumulate in hypoxic, or low oxygen, regions of patient tumor samples,” continues Simon, who is also a Howard Hughes Medical Institute investigator. “And it has been inferred that the factors that respond to low oxygen would actually have a positive effect on tumor growth.”

The team deleted a hypoxia inducible gene from macrophage cells in mice and then analyzed what happened in colon and liver cancer models. The macrophages that lacked the hypoxia inducible factor did not accumulate in tumors in both cancer models. As a result, the tumors in the genetically deficient mice were smaller, had fewer blood vessels, and

did not progress to a higher stage of disease.

Teasing apart this mechanism, the researchers found that the hypoxic tumor cells secrete chemicals that normally bind to receptors on the surface of macrophages. Without the hypoxia inducible gene, the macrophages expressed less of the receptor and so did not respond to the tumor growth signals.

With that information in hand, Simon surmises the team has uncovered a possible new drug target for cancer therapy. “If you can come up with a well tolerated anti-inflammatory drug, that could work out very well,” she said.

Provided by University of Pennsylvania School of Medicine