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Study reveals new insight into tumor progression

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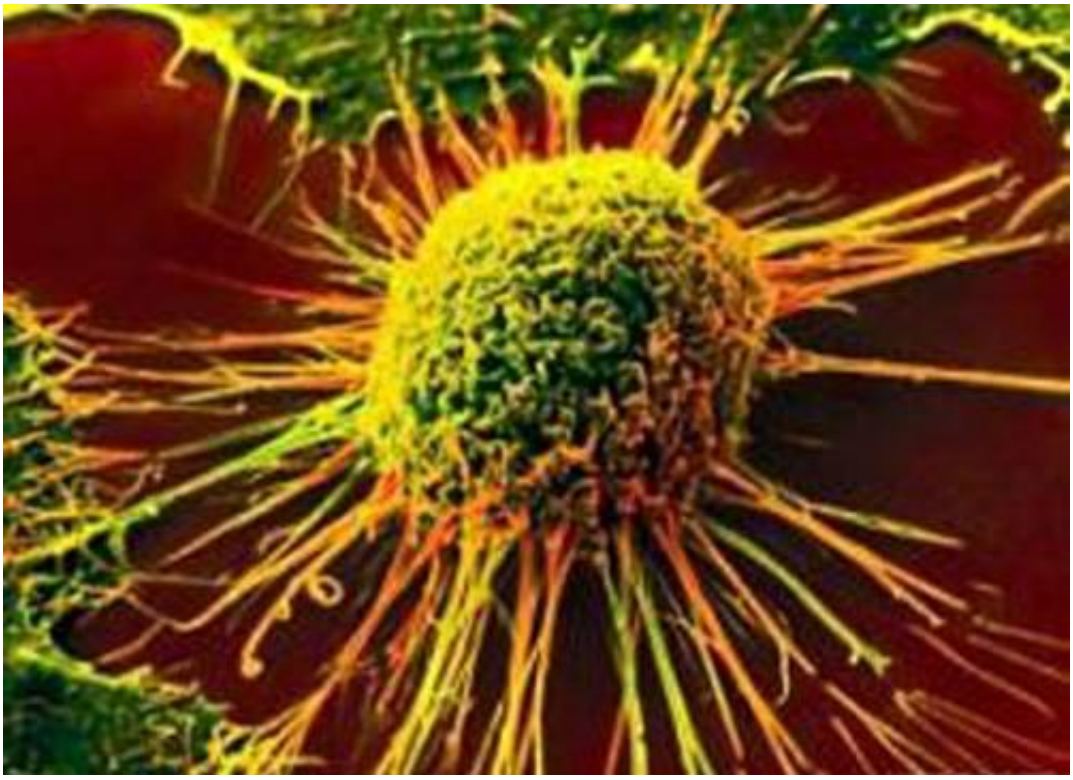

Scientists know that activation of growth factor receptors like epidermal growth factor receptors (EGFR) promote tumor progression in many types of cancer.

Scientists at The University of Texas MD Anderson Cancer Center have

shown that EGFR may be shut down with the help of a cytokine known as MIF (macrophage migration inhibitory factor). It's a finding they believe could signal a new way to look at treating tumors.

Their study results, which focused on brain, breast, and prostate cancer, are published in the Aug. 17, 2015 issue of *Nature Cell Biology*.

Exactly how EGFR activation is regulated in the tumor microenvironment has not been understood, nor do human cells have an external antagonist that regulates EGFR. The tumor microenvironment is the cellular landscape in which a tumor exists, including surrounding blood vessels, immune cells, fibroblasts and other cells and structures. It's increasingly being recognized as a key factor in disease progression.

MIF appears to be vital to regulation of EGFR activation in tumor cells' extracellular or external environment.

"MIF can be secreted from both tumor and immune cells," said Zhimin Lu, M.D., Ph.D., professor of Neuro-Oncology. "Importantly, secreted MIF is modified by an attached sugar group which allows MIF to gain a specific new function compared to its non-modified form."

Lu's team discovered that the modified MIF binds to EGFR. This inhibits EGFR by blocking the epidermal growth factor to bind to EGFR in cancer cells.

"Cancer cells secret MMP13, an enzyme involved in many phases of cancer progression," said Lu. "MMP13 degrades extracellular MIF impacting EGFR in such a way that it promotes EGFR activation, tumor cell invasion, and finally, forms brain tumors."

The team's findings demonstrate an important mechanism underlying amplified EGFR activation in tumors. This is mediated by

downregulation of its antagonist, MIF, in the tumor microenvironment.

Lu said that understanding the synergies between EGFR and MIF provide an "instrumental insight" into tumor progression and could open up new approaches to treating cancer by intervening in this self-regulating loop.

More information: Secreted and O-GlcNAcylated MIF binds to the human EGF receptor and inhibits its activation, DOI: 10.1038/ncb3222

Provided by University of Texas M. D. Anderson Cancer Center