Cancer study is 'paradigm shift' in cause of tumor formation

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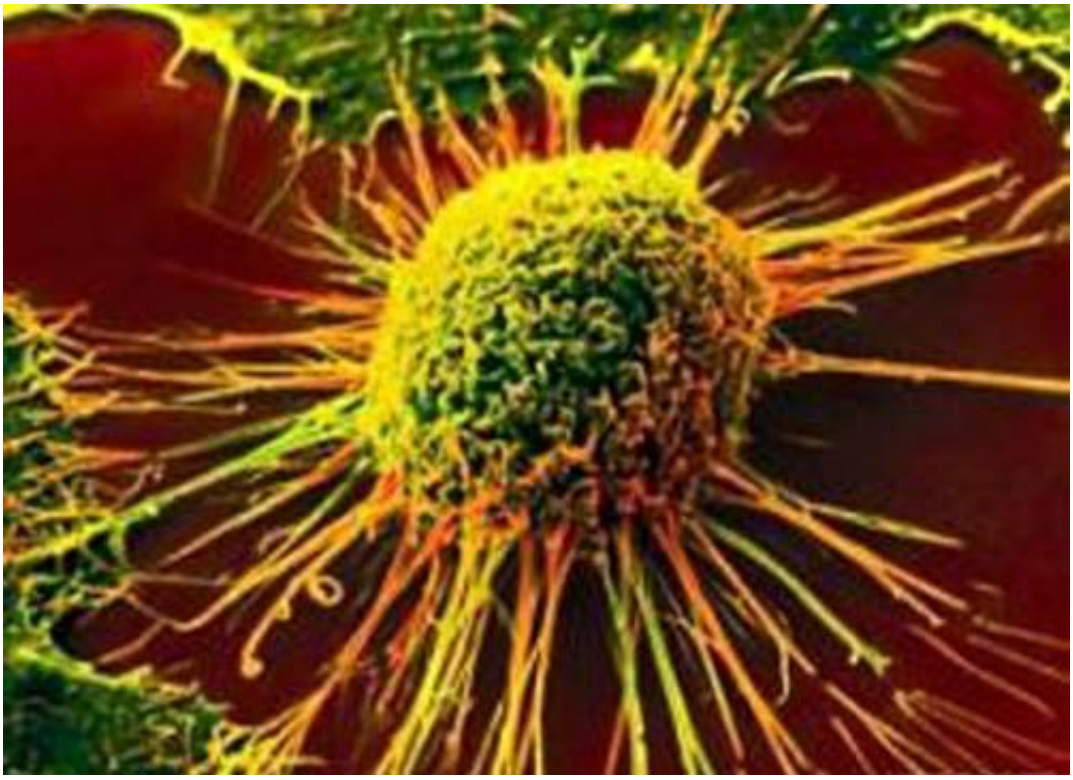

In a new study published in the American Association of Cancer Research's journal *Cancer Research*, a pair of investigators at Rutgers and Columbia universities has identified a gene that may provide a new source of potential drug targets for tumors that arise in pulmonary tuberous sclerosis complex (TSC). The discovery may change what is

known about tumor formation and help to slow or halt tumor growth, therefore having broader implications in cancer research.

TSC is a rare disorder in which benign tumors grow on vital organs, including the lung, brain, kidneys, eyes and heart. Lymphangiomyomatosis, LAM, which can arise spontaneously or as the pulmonary manifestation of Tuberous Sclerosis Complex is experienced mostly by women of childbearing age in which abnormal muscle tissue invades the lungs and airways.

Building on previous research LAM investigators Kiran Chada, D.Phil. (Oxon.) and Jeanine D'Armiento, MD, PhD, demonstrated in their study that the HMGA2 gene and its signaling pathway (the route of information which begins an action within cells), are required to produce tumors in the lung and kidneys in individuals with TSC.

"Our study of the protein coding gene HMGA2, not only shows that HMGA2 is necessary for the formation of tumors, but its absence completely eliminated tumor formations in animal models of tuberous sclerosis complex," said Dr. Chada, professor of biochemistry and molecular biology at Rutgers Robert Wood Johnson Medical School.

The researchers' study also contradicted a long-standing hypothesis that another pathway, mTOR, was essential to tumor growth in TSC and cancer. Unlike the HMGA2 pathway, which was active in 100 percent of all the tumors in TSC, the mTOR pathway was not active in the majority of animal tumors and in less than 50 percent of human tumors in the study.

"We were very surprised, but also excited regarding our investigations, which represent a radically different view on the mechanism of tumor formation in tuberous sclerosis and presents a paradigm shift in our understanding of this syndrome," said Dr. D'Armiento.

The discovery of HGMA2's essential role in tumor development in TSC may have broader implications in other disorders in which tumors appear in multiple sites within the body, including cancer. It also provides a new target for which therapies may be developed to suppress HGMA2 in individuals with TSC and other progressive tumor disorders.

More information: J. D'Armiento et al. Mesenchymal Tumorigenesis Driven by TSC2 Haploinsufficiency Requires HMGA2 and Is Independent of mTOR Pathway Activation, *Cancer Research* (2016). DOI: 10.1158/0008-5472.CAN-15-1287