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Novel regulatory mechanism for cell division found

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A protein kinase or enzyme known as PKM2 has proven to control cell division, potentially providing a molecular basis for tumor diagnosis and treatment.

A study, led by Zhimin Lu, M.D., Ph.D., professor of neuro-oncology at The University of Texas MD Anderson Cancer Center, showcased the non-metabolic abilities of PKM2 (pyruvate kinase M2) in promoting tumor cell proliferation when cells produce more of the enzyme.

The study results were published in today's issue of *Nature Communications*.

Dr. Lu's group previously demonstrated that PKM2 controls gene expression by binding to transcriptional factors and phosphorylating histone, proteins that have the unique ability to turn genes on and off. Phosphorylation is a process by which a phosphate group is added to a protein.

"PKM2 is expressed at high levels during tumor progression and is important for cell growth. However there's been little information about whether it directly controls cell division." said Lu. "Our findings underscored its function in tumor formation during the final stages of cell division known as cytokinesis."

Understanding how cytokinesis goes awry is important since abnormal cell division impacts tumor cell growth and spread. Lu's team looked at

the role of PKM2 in brain tumor development in mice. After analyzing the protein-coding gene, MLC2 (myosin light chain 2), Lu's group revealed how phosphorylation of MLC2 by PKM2 in brain tumors occurs. Phosphorylation of MLC2 controls a process which allows separation of a dividing parental cell into two 'daughter' cells.

"The results revealed that PKM2-regulated MLC2 phosphorylation and the related cytokinesis are instrumental in brain tumor development and are found to precisely control cell division," said Lu. "More importantly, our research shows that PKM2-regulated cytokinesis occurs in malignant tumors with bad outcome, such as glioblastoma, pancreatic cancer, and melanoma."

Tumor cells, in which certain protein-coding genes (EGFR, K-Ras and B-Raf) are activated, develop new patterns of "molecular signatures" for regulating cell proliferation. These changes enable the tumor cells to coordinate their metabolism and cycle progression through PKM2.

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