MedicalXpress

MAGE genes provide insight into optimizing chemotherapy

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UT Southwestern Medical Center scientists have identified a new biomarker that could help identify patients who are more likely to respond to certain chemotherapies.

UT Southwestern researchers identified how two melanoma antigen genes (MAGE-A3 and MAGE-A6) contribute to tumor growth. Researchers found that these genes have an effect on a protein called AMPK, offering valuable insight that could help identify patients who are most likely to respond to AMPK-directed chemotherapies.

"This is an especially exciting development because there are already FDA-approved drugs, such as metformin, which activate AMPK and are being tested in clinical trials for cancer," said senior author Dr. Ryan Potts, Assistant Professor of Physiology, Biochemistry, and Pharmacology, and a member of the Harold C. Simmons Comprehensive Cancer Center. "Our study provides a new biomarker, MAGE-A3/6, which can help identify patients who are likely to respond to these treatments."

The findings are published online in the journal *Cell*.

The MAGE-A3/6 genes are found on the X chromosome in both men and women. Normally, the function of MAGE-A3/6 is restricted to the production of sperm in men. However, in some situations the genes are abnormally switched on and Dr. Potts and his team discovered that when this happens, normal cells are turned into cancerous cells.

"We found that the normally testis-restricted MAGE-A3/6 genes are aberrantly expressed in many cancers, including breast, lung, and colon cancers where they promote tumor growth. Importantly, the expression of these genes is associated with decreased survival for cancer patients. Therefore, these genes are ideal cancer-specific chemotherapy targets," said Dr. Potts, the Michael L. Rosenberg Scholar in Medical Research.

Following further investigation on how MAGE-A3/6 functions to promote cancer, Dr. Potts and his team discovered that the protein ? called AMP-activated protein kinase (AMPK) ? is inhibited by MAGE-A3/6. AMPK can detect cellular energy levels and controls energy usage in cells. If low energy levels are detected, AMPK switches off energy-consuming pathways (protein and lipid synthesis) and turns on pathways to acquire more energy (cellular breakdown). Additionally, these activities of AMPK can play a role in suppressing the growth of cancerous tumors.

The study used various molecular biological techniques in mouse and human tissues to investigate the mechanisms of interaction between MAGE-A3/6, another protein called TRIM28 and AMPK, and found that MAGE-A3/6 degrades AMPK by working with TRIM28, removing the tumor-suppressive properties and resulting in transformation of normal cells and tumor growth.

Dr. Potts' lab focuses on understanding the basic molecular, genetic, and cellular events that give rise to cancer. His lab initially defined a novel family of cancer cell-specific proteins, called MAGE proteins, which promote tumor growth, and is now focused on elucidating the biochemical, cellular, and physiological function of individual MAGE proteins.

Dr. Potts was awarded the Sara and Frank McKnight independent postdoctoral fellowship in the Department of Biochemistry at UT

Southwestern, was named an Endowed Scholar in Biomedical Research in the Department of Physiology at UT Southwestern, and received a Cancer Prevention and Research Institute of Texas (CPRIT) Scholar in Cancer Research Award.

Provided by UT Southwestern Medical Center