Cancer scientists discover new way breast cancer cells adapt to environmental stress

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An international research team led by Dr. Tak Mak, Director, The Campbell Family Institute for Breast Cancer Research at Princess Margaret Hospital (PMH), has discovered a new aspect of "metabolic transformation", the process whereby tumour cells adapt and survive under conditions that would kill normal cells.

The findings, published today in Genes and Development, show how breast cancer cells can thrive when deprived of their usual diet of glucose (sugar) and oxygen by turning to fatty acids for energy generation.

"Our results demonstrate that a protein not previously associated with breast cancer is involved in helping these cells to adapt to starvation conditions and to continue their uncontrolled growth," says Dr. Mak, principal investigator and Weekend to End Breast Cancer Chair in Breast Cancer Research at PMH. Dr. Mak is also a Professor at the University of Toronto in the Departments of Medical Biophysics and Immunology.

In the lab, researchers used an anticancer drug called rapamycin to block a molecular signalling pathway within breast cancer cells that stimulates sugar metabolism. However, instead of dying of starvation, the cells continued to multiply. The team also observed an increase in these cells of carnitine palmitoyltransferase 1C (CPT1C), a protein usually found only in the brains of healthy individuals. Moreover, cells engineered to produce high levels of CPT1C were also able to adapt their metabolism

as a survival technique.

"In other words," says Dr. Mak, "The cancer cells acted like cheaters on a diet and found a new food source in fatty acids.

"The fact that CPT1C becomes expressed under conditions of metabolic stress highlights the resilience of cancer cells. They are able to adapt to environmental challenges and find alternative sources of food in order to flourish where healthy cells would not survive."

"Our discovery that deprivation of either sugar or oxygen spurs CPT1C expression in tumour cells marks this protein as a potential target for new drug development," says Dr. Mak.

"We also demonstrated that cells that were prevented from using CPT1C to cope with a disruption in sugar metabolism became more sensitive to environmental stress. These findings represent an important stepping stone to developing targeted therapies that can block cancer cells from adapting to environmental challenges and surviving efforts to kill them."

This most recent discovery builds on Dr. Mak's impressive body of work, which has led to important breakthroughs in immunology and our understanding of cancer at the molecular level. Dr. Mak is internationally renowned for his 1984 landmark scientific paper on the cloning of the genes for the T cell receptor, a key component of the human immune system.

More information:
http://www.genesdev.org/cgi/doi/10.1101/gad.1987211

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