

Breast cancer researchers find new drug target companion prognostic test for hormone therapy resistance

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A team of international cancer researchers led by Dr. Mathieu Lupien at the Princess Margaret Cancer Centre, University Health Network, has identified the signalling pathway that is over-activated in estrogen receptor (ER)-positive breast cancer cells that are resistant to hormone therapies such as tamoxifen, aromatase inhibitors or fulvestrant.

Resistance to hormone therapy is reported in almost half of ER-positive [breast cancer patients](#) and no cure is currently available. The fact that the pathway, called Notch, is a [drug target](#) creates hope for a new therapy.

The findings, published online today in *PNAS*, the *Proceedings of the National Academy of Sciences* of the United States of America, "provide a new [therapeutic target](#) against hormone therapy-resistant breast cancers and a companion test to identify tumours that would become resistant" says Dr. Lupien, a scientist at the Ontario Cancer Institute, the research arm of the cancer centre, and an Assistant Professor in the Department of Medical Biophysics, University of Toronto. He specializes in epigenetics of hormone-dependent cancers – the study of non-genetic determinants of cellular identity that can also be altered to initiate or modify disease.

"In studying the epigenetics of hormone therapy resistance, we discovered that [breast cancer cells](#) behave like a chameleon. Indeed, as the chameleon changes its skin colour to camouflage itself and evade

predators," says Dr. Lupien, "breast cancer cells change the appearance of their DNA through epigenetics to evade, in this case, hormone therapy." In so doing, hormone therapy-resistant breast cancer cells highlight regions of their DNA related to the [Notch pathway](#).

At the molecular level, the research team characterized the epigenetic appearances of the DNA of drug-resistant and drug-responsive breast cancer cells. The team discovered that the [Notch signaling pathway](#) plays the predominant role in drug-resistant breast cancer cells even if cells remain positive for ER.

"This is a highly promising discovery that could rapidly translate in the clinic. Drugs against the Notch pathway are available." says Dr. Lupien. The key will be to test the efficacy of these drugs against hormone therapy resistance in breast cancer.

Provided by University Health Network

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