

McGill researchers identify key genetic factors which can lead to cancer

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(PhysOrg.com) -- Researchers at McGill University have discovered a previously unknown series of interactions between genes that control whether cells become cancerous. The discovery may lead to a new generation of targeted therapies tuned to individual patients, the researchers said. Their results are published today in the journal *Cancer Cell*.

The researchers studied genetically engineered mice lacking the ability to produce the [genes](#) 4E-BP1 and 4E-BP2. As these genes were believed to play an important role in inhibiting cancer, the researchers expected the 4E-BP "knockout" mice (so called because the genes encoding these proteins are deleted) to exhibit highly accelerated cancer growth.

To their surprise, it simply didn't happen.

"We didn't understand what was going on," said Dr. Emmanuel Petroulakis, a post-doctoral researcher at the Sonenberg Laboratory at McGill's Faculty of Medicine and the study's first author. "We tried other experiments to try to promote the cells from these mice to become malignant, and they failed. We were shocked."

Dr. Petroulakis and study corresponding author Dr. Nahum Sonenberg - winner of the 2008 Gairdner Prize for his discoveries in the areas of protein synthesis in [human cells](#) - decided that totally unknown genetic pathways must be involved, and crossed their mice with a strain lacking another gene, p53, already known to be a master "tumour suppressor."

"Then we got what we expected," explained Dr. Petroulakis. "More than we expected. Mice with both the 4E-BP's and p53 knocked out showed enhanced tumour growth, more than we'd see just knocking out p53 alone. This proves that the 4E-BPs are indeed tumour suppressors, but only in the context of this master tumour suppressor. That's a whole new effect, a totally new concept in the literature."

The significance of the discovery may be profound, Petroulakis continued, and may explain why some cancer therapies work well in some patients and not at all in others.

"p53 is one of the most commonly mutated genes," he said. "So if it's essentially absent or non-functional in about 50 percent of patients, therapies that target the 4E-BP activity such as what is called mTOR inhibitor drugs in those patients won't work. Now we know that we've got to understand the p53 status of a tumour first, before beginning treatment with these inhibitors."

"Things are moving towards personalized medicine," he added. "Using these techniques, if we understand the other molecular signatures operating at the same time, we can better design therapies tailored towards individual patients."

"This is another fine example how basic research, which intends to provide answers to fundamental questions about molecular mechanisms of cell proliferation, leads to unexpected findings that advance our ability to understand and cure human disease" says Dr. Sonenberg.

Provided by McGill University ([news](#) : [web](#))

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