Discovery may help fight late-stage ovarian cancer

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A potential breakthrough in treating late-stage ovarian cancer has come from University of Guelph researchers who have discovered a peptide that shrinks advanced tumours and improves survival rates for this deadly but often undetected disease.

"We're extremely excited about this," said Jim Petrik, a professor in U of G's Department of Biomedical Sciences who conducted the research with PhD student Nicole Campbell. "It has the potential, particularly in ovarian cancer, to have a significant impact."

Their findings will appear in *Molecular Cancer Therapeutics*, published by the American Association for Cancer Research.

Ovarian cancer is the most lethal gynecological cancer. Its symptoms, which include nausea, bloating and abdominal pain, are vague and can be attributed to a number of ailments.

Often the disease remains undetected until it's well advanced, when the odds of survival are poor. "It's called the silent killer because it really does sneak up on you," Petrik said.

He and Campbell discovered that ABT-898, a peptide derived from the thrombospondin molecule, shrinks established late-stage tumours in mouse models of ovarian cancer. In addition to regressing tumours, ABT-898 essentially prunes dysfunctional blood vessels in the tumour while leaving healthy vessels intact.

Petrik explains that chemotherapy treatment relies on blood vessels to transport tumour-fighting drugs. But abnormal blood vessels inside tumours make drug delivery inefficient.

"This new treatment enhances the ability to deliver chemotherapy drugs inside of the tumour where they need to go. So in combination with chemotherapy, it has fantastic potential."

Besides shrinking tumours, ABT-898 improves survival rates because cancer cells do not have time to adapt to the treatment.

"This is crucial. Women tend to succumb to ovarian cancer because the inefficient delivery of chemotherapy drugs allows the cells to build up resistance and they no longer respond to treatment," Petrik said.

More efficient drug delivery also means doctors can administer lower amounts, alleviating many of the side effects of chemotherapy. As well, said Petrik, "this is a naturally occurring protein that we are exploiting; we are not making anything synthetic."

He hopes the research will lead to human trials and, ultimately, to the development of targeted cancer therapies.

Petrik has studied ovarian cancer for more than a decade, especially regulation of growth factors and formation of blood vessels in the ovary. A U of G faculty member since 2001, he teaches physiology and anatomy at the Ontario Veterinary College.

This latest discovery was possible because Petrik's laboratory had developed a model in which cancer cells are injected directly into healthy mouse ovaries. Ovarian cancer spontaneously occurs in about two months, allowing U of G researchers to follow tumour progression.

Most researchers rely on artificially cultured clumps of cells and immunocompromised mice that poorly mimic disease progression in normal animals.

"It provides us with a tool to ask questions like this and look at interventions such as this in a way that is far more relevant to the human disease," Petrik said.

Provided by University of Guelph