Using math to kill cancer cells

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Here's a good reason to pay attention in math class. *Nature Communications* has published a paper from Ottawa researchers today, outlining how advanced mathematical modelling can be used in the fight against cancer. The technique predicts how different treatments and genetic modifications might allow cancer-killing, oncolytic viruses to overcome the natural defences that cancer cells use to stave off viral infection.

"Oncolytic viruses are special in that they specifically target cancer cells ," explains Dr. Bell, a senior scientist at the Ottawa Hospital Research Institute and professor at the University of Ottawa's Faculty of Medicine. "Unfortunately, cancer is a very complicated and diverse disease, and some viruses work well in some circumstances and not well in others. As a result, there has been a lot of effort in trying to modify the viruses to make them safe, so they don't target healthy tissue and yet are more efficient in eliminating cancer cells."

Dr. Bell and co-author Dr. Mads Kaern, an assistant professor in the University of Ottawa's Faculty of Medicine and Canada Research Chair at the University's Ottawa Institute of Systems Biology, led a team that has used mathematical modelling to devise strategies for making cancer cells exquisitely sensitive to virus infection—killing them without affecting normal, healthy cells.

"By using these mathematical models to predict how viral modifications would actually impact cancer cells and normal cells, we are able to accelerate the pace of research," says Dr. Kaern, who is also cross-

appointed to the University's Department of Physics. "It allows us to quickly identify the most promising approaches to be tested in the lab, something that is usually done through expensive and time-consuming trial and error."

Drs. Bell and Kaern have established a mathematical model that described an infection cycle, including the way a virus replicated, spread and activated cellular defense mechanisms. From there, they used knowledge about key physiological differences between normal cells and cancer cells to identify how modifying the genome of the virus might counter the anti-viral defenses of cancer cells. Model simulations were remarkably accurate, with the identified viral modifications efficiently eradicating cancer in a mouse model of the disease.

"What is remarkable is how well we could actually predict the experimental outcome based on computational analysis," says Dr. Bell. "This work creates a useful framework for developing similar types of mathematical models in the fight against cancer."

The research, funded by an innovation grant from the Canadian Cancer Society, is only the beginning, explains Dr. Kaern. "We worked with a specific kind of cancer cell. We will now expand that to look at other cancer cell types and see to what degree the predictions we made in one special case can be generalized to others, and to identify strategies to target other types of cancer cells."

The findings may also help researchers better understand the interaction between these cancer cells and the virus. While one magic cure-all will likely never happen due to cancer's complexity, the researchers have developed a framework where they can learn more about the disease in the cases where the simulations don't match.

"From my perspective, that's the most interesting part," concluded Dr.

Kaern. "The most fascinating thing is to challenge existing knowledge represented in a mathematical model and try to understand why these models sometimes fail. It's a very exciting opportunity to be a part of this, and I am glad that our efforts in training students in computational cell biology have resulted in such a significant advancement."

More information: The full article, "Model-based Rational Design of an Oncolytic Virus with Improved Therapeutic Potential," was published June 14, 2013, in *Nature Communications*.

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