MedicalXpress

Viral 'magic bullet' targets cancer cells with help of new compound

September 16 2008

Researchers at McGill University and the affiliated Lady Davis Research Institute of the Jewish General Hospital – along with colleagues at the University of Ottawa and the Ottawa Health Research Institute (OHRI)–report a significant breakthrough in the use of viruses to target and destroy cancer cells, a field known as oncolytic virotherapy. Their results were published in the September early edition of the *Proceedings of the National Academy of Sciences* (PNAS).

The research team, led by Dr. John Hiscott of McGill's Faculty of Medicine and the Lady Davis Institute, along with Dr. John C. Bell and colleagues at the University of Ottawa and OHRI, have discovered that a family of compounds called histone deacetylase inhibitors (HDIs) may be the missing link that turns oncolytic viruses into a potent new weapon against cancer. Their research program is supported by the Canadian Oncolytic Virus Consortium, which is funded by the National Cancer Institute of Canada (NCIC) and the Terry Fox Foundation.

"One of the greatest challenges in cancer therapy is to target and kill cancer cells that are resistant to conventional therapy," said Dr. Hiscott. "The strategy that we developed is to use a harmless, non-human virus that specifically enters, replicates and kills cancer cells, but not normal cells." However, Dr. Hiscott explained, many primary cancers have proven resistant to a pure virotherapy approach. "One way to overcome this obstacle is to treat the tumor with other molecules that augment the ability of these viruses to target and kill the cancer cells."

Dr. Nanh Nguyen and Dr. Hesham Abdelbary, senior researchers and lead authors in the Hiscott and Bell labs, focused on HDIs, which inhibit specific enzymes involved in modulating the structure of chromosomes in cancer cells. They tested the combination HDI/virotherapy approach in cell culture experiments in the lab, in animal models of cancer, and also in human tissues from breast, prostate and colon cancer immediately after excision from patients.

"Treatment with these compounds dramatically increases the susceptibility of these cancers to killing by the oncolytic virus," Dr. Hiscott said. "The combination dramatically and unexpectedly stimulates the ability of the viruses to target and kill cancer cells."

The researchers utilize a tiny, bullet-shaped insect rhabdovirus known as VSV, chosen specifically for its inability to infect normal human cells. "VSV has been studied by virologists for several decades, and its replication is well understood at the molecular level," Dr. Hiscott said. "It is not a human pathogen, so most individuals do not have antibodies directed against it, which means there is a window of opportunity to successfully treat patients before they mount an immune response."

Dr. Hiscott and his colleagues are enthusiastic that this new approach may lead to the rapid implementation of new experimental therapies for breast, prostate, colon and other primary cancers that are currently resistant to virotherapy.

"Virotherapy is potentially valuable by adding a new biotherapeutic approach to cancer treatment," he said. "Because human trials with similar viruses and with HDIs have already been approved, there is the possibility that the results of these studies might be applied rapidly. We might see human trials within a year or two. These experiments are vital to determine if this 'viral bullet' is actually a 'magic bullet' that hits the intended target."

Source: McGill University