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Could Viruses Take Cancer Immunotherapy to the Next Level?

ACGT-Funded Research Shows Resistant Breast Cancer in Mice Cured 60-90 Percent with Combination of Two Immunotherapies: Oncolytic Viruses and Checkpoint Inhibitors

OTTAWA, Canada, January 3, 2018 — The **Alliance for Cancer Gene Therapy (ACGT)**, a non-profit based in Stamford, Connecticut, dedicated to funding breakthrough cancer [gene therapy](#) treatments, has had its funding pay off with a promising study on breast cancer coming out of **The Ottawa Hospital** and the **University of Ottawa** in Ottawa, Canada. The study suggests that a combinations of two immunotherapies — [oncolytic viruses](#) and [checkpoint inhibitors](#) — could be much more successful than traditional treatments in fighting breast cancer and possibly other cancers. The study, which used mouse models, was published in [Science Translational Medicine](#) and was conducted by ACGT grantee, **Dr. John Bell**, and his research lab in conjunction with **Dr. Marie-Claude Bourgeois-Daigneault**, lead author of the study and postdoctoral fellow in Dr. Bell's research group.

Cancer immunotherapy has proven to be a powerful tool in fighting cancer and has revolutionized treatment for cancers such as melanoma and leukemia. Unfortunately though, other forms of cancer, and especially solid tumor cancers, have remained resistant.

ACGT has a track record of funding innovative, breakthrough cancer treatments and was one of the initial funders for laboratory research and clinical trials of immunotherapy in support of Dr. Carl June's work at the University of Pennsylvania, where his team has been successfully treating relapsed pediatric leukemia with gene therapy. ACGT started funding cancer cell and gene therapies in the early 2000's when it was still deemed 'risky' science. Since then, ACGT has administered a total of 55 grants, including 19 clinical translation grants and 36 young investigator grants totaling more than \$28 million. Dr. John Bell received a clinical translation grant from ACGT in 2013 for his work with oncolytic viruses and their applications in treating other cancers like brain cancer.

For the study out of Ottawa and Dr. John Bell's lab, Dr. Marie-Claude Bourgeois-Daigneault stated, "It was absolutely amazing to see that we could cure cancer in most of our mice, even in models that are normally very resistant to immunotherapy. We believe that the same mechanisms are at work in human cancers, but further research is needed to test this kind of therapy in humans."

In the current study, the researchers focused on "triple negative" breast cancer, which is the most aggressive and difficult-to-treat kind of breast cancer.

The researchers studied three mouse models of triple negative breast cancer, and found that all were resistant to a checkpoint inhibitor which is commonly used to treat other kinds of cancer. They also found that while an oncolytic virus called Maraba could replicate inside these cancers and help

the mouse's immune system recognize and attack the cancer, the virus alone had minimal impact on overall survival.

The researchers then tested the virus and checkpoint inhibitor together in models that mimic the metastatic spread of breast cancer after surgery, which is very common in patients. They found that this combination cured 60 to 90 percent of the mice, compared to zero for the checkpoint inhibitor alone and 20 to 30 percent for the virus alone. In these models, the virus was given before the surgery and the checkpoint inhibitor was given after.

"Our immune system is constantly trying to recognize and kill cancer cells, but the cancer cells are always trying to hide from it," explained Dr. Bell, senior scientist at The Ottawa Hospital and professor at the University of Ottawa. "When you infect a cancer cell with a virus, it raises a big red flag, which helps the immune system recognize and attack the cancer. But in some kinds of cancer this still isn't enough. We found that when you add a checkpoint inhibitor after the virus, this releases all the alarms and the immune system sends in the full army against the cancer."

A recently-published clinical trial confirmed that oncolytic viruses and checkpoint inhibitors have potential for treating melanoma, but this is the first study to show the potential in breast cancer. It is also the first study to test viruses and checkpoint inhibitors in a surgery and metastasis model, which is particularly relevant for patients.

Ongoing clinical trials are testing oncolytic viruses (including Maraba) in combination with checkpoint inhibitors in people with cancer. People who are interested in these trials at The Ottawa Hospital can read these [frequently asked questions](#).

"ACGT has long believed that the cure for cancer lies in the genes," said Margaret Cianci, executive director of the Alliance for Cancer Gene Therapy. "Using tools like viruses and checkpoint inhibitors to activate the immune system and create a cellular response against cancer is incredibly promising. We always have big hopes for our scientific grants and to see results like these is very exciting."

About Alliance for Cancer Gene Therapy (ACGT)

Established in 2001, ACGT is the nation's only non-profit dedicated exclusively to cell and gene therapy treatments for all types of cancer. One hundred percent of contributions go directly to research. Founded by Barbara Netter and her late husband Edward, ACGT was created to conduct and accelerate critically needed innovative research. ACGT is located at 96 Cummings Point Road, Stamford, Connecticut 06902; 203-358-5055. To learn more, visit acgtfoundation.org or join the ACGT community on [Facebook](#), [Twitter](#) and [YouTube](#) at @acgtfoundation.

About The Ottawa Hospital

The Ottawa Hospital is one of Canada's largest learning and research hospitals with more than 1,100 beds, approximately 12,000 staff and an annual budget of \$1.2 billion. The focus on research and learning helps the Ottawa Hospital develop new and innovative ways to treat patients and improve care. As a multi-campus hospital, affiliated with the University of Ottawa, the Ottawa Hospital delivers specialized care to the Eastern Ontario region, but its techniques and research discoveries are adopted around the world. The Ottawa Hospital engages the community at all levels to support its vision for better patient care. See ohri.ca for more information about research at The Ottawa Hospital.

About the University of Ottawa

The University of Ottawa is home to 50,000+ students, faculty and staff, who live, work and study in both French and English. The campus is a crossroads of cultures and ideas, where bold minds come

together to inspire game-changing ideas. The University is one of Canada's top 10 research universities — with professors and researchers exploring new approaches to today's challenges. The University is one of a handful of Canadian universities ranked among the top 200 in the world and attracts exceptional thinkers and welcomes diverse perspectives from across the globe. uottawa.ca.

Acknowledgements and additional information

- Dr. Bell's research is supported by [generous donors to The Ottawa Hospital](#). This study was also supported by the Alliance for Cancer Gene Therapy, the Canadian Institute for Health Research, the Terry Fox Research Institute, the Canadian Cancer Society Research Institute, the Ontario Institute for Cancer Research, the Ottawa Regional Cancer Foundation and BioCanRx.
- Maraba virus therapy was jointly pioneered by Dr. John Bell (The Ottawa Hospital, University of Ottawa), Dr. David Stojdl (Children's Hospital of Eastern Ontario, University of Ottawa) and Dr. Brian Lichty (McMaster University). Drs. Bell, Stojdl and Lichty founded a company called Turnstone Biologics which is advancing the development of the virus. Turnstone did not fund the research described here.
- Dr. Bell is also the Scientific Director of BioCanRx, Co-leader of the Immuno-oncology Translational Research Initiative at the Ontario Institute for Cancer Research and founder of the Canadian Oncolytic Virus Consortium.
- The research described here was published in Science Translational Medicine on January 3, 2018. The publication is titled "Neo-Adjuvant Oncolytic Virotherapy Before Surgery Sensitizes Triple-Negative Breast Cancer to Immune Checkpoint Therapy". The authors are: Marie-Claude Bourgeois-Daigneault, Dominic Guy Roy, Amelia Sadie Aitken, Nader El Sayes, Nikolas Tim Martin, Oliver Varette, Theresa Falls, Lauren Elizabeth St-Germain, Adrian Pelin, Brian Dennis Lichty, David Francis Stojdl, Guy Ungerechts, Jean-Simon Diallo and John Cameron Bell. The paper is featured on the cover of the journal, together with a similar study on brain cancer from a different group.

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