

“A Cure for Most Cancers in Our Lifetimes”

BY HARVEY F. CHARTRAND

Dr. John C. Bell is a cancer research scientist at the Ottawa Health Research Institutes, Professor of Medicine and Biochemistry, Microbiology and Immunology, University of Ottawa and career scientist at the Ottawa Regional Cancer Centre. Dr. Bell, whose research has inspired tremendous hope in the fight against cancer, was awarded more than \$2 million to be the lead investigator in a new project with oncolytic viruses – viruses that kill cancer cells while leaving healthy cells untouched.

Ottawa Life Magazine: *How did you first stumble upon the idea of killing cancer cells with viruses? (This therapy seeks to harness the natural properties of viruses to aid in the fight against cancer.)*

Dr. John C. Bell: A number of scientific groups have been working to develop oncolytic (or cancer-killing) virus therapeutics for the last 10 years or so. We are using a virus – Vesicular Stomatitis Virus (VSV) – that has not been tried before. The way we came across it is that we were trying to understand the difference between normal tissues and cancer tissues and when we were studying these at the genetic-molecular level, we found something was missing in the cancer tissues that is present in the normal tissues. We knew that when we identified that difference, this was something we could exploit with a virus. That’s when we picked out the VSV.

OLM: *How can oncolytic viruses target cancer cells while leaving healthy cells untouched?*

JCB: There are a variety of viruses out there that have different strategies for doing this. Our particular virus exploits a gene that is missing in cancer cells. Cancer cells start out as normal cells. As they evolve and become cancerous, they throw away some genetic material to gain a growth advantage. What we found is that some of the genetic material that they throw away are genes involved in fighting virus infections. So we knew that if those genes were missing from the cancer cells

but were present in the normal tissues in the same person, we should be able to infect tumor tissues with this virus without harming normal tissues. One way to think about this is that tumors provide a fertile ground for the virus to grow in, whereas normal tissues do not allow the virus to replicate.

OLM: *It seems to me that for the first time ever, it actually appears that a cure for cancer will be discovered, maybe even in our lifetimes. Do you agree/disagree with this statement about the imminent discovery of a cure for cancer?*

JCB: I would give that a qualified ‘yes.’ The reason I won’t give an unqualified ‘yes’ is that cancer is not just one disease. It’s a multitude of different kinds of diseases with the same label. What I think will be true is that a number of different kinds of cancers will be treated with various new “biologicals” like viruses or many of the new targeted drugs that are being developed around the world. I believe these will be effective new treatments and I suppose you could even call them “cures.” But there are some forms of cancer we still haven’t been able to find treatments for, so I think it is unlikely that one “cure-all” drug will be found. I’m optimistic that there will be a cure in my lifetime for a majority of cancers.

OLM: *This promising avenue of research has tremendous potential against several forms of cancer. Which ones? Why?*

JCB: Cancer is a very complicated disease. For example, there are different forms of prostate cancer. What we found is that 75% to 80% of all the cancers that we’ve tested are infected by this virus and killed by it in the test tube. So we think many of the kinds of cancers will be treatable for individuals rather than groups of, say, prostate or breast cancer patients.

OLM: *This potential cure for certain forms of cancer sounds like it would be much less painful and debilitating than radiation therapy. Any comments?*

JCB: What we like about the virus therapy approach is that it targets only the tumor tissue and not the normal tissue. The difference between conventional therapy (chemotherapy and radiation therapy) is that chemo and radiation both tend to attack normal tissues as well. That's why it becomes so debilitating for patients. That's why quite often we don't cure the disease, because we can't go any further without damaging the normal tissues. The virus approach only attacks tumor cells, so hypothetically would be much less damaging to the patient. There should be a better chance for a successful treatment. We see that in our mice. They get a little bit sick for a couple of days but then recover and show no long-term effects of the virus therapy. Because virus therapy is so much more specific and targeted, it should be better than conventional chemo and radiation therapies.

OLM: *When do you expect to test these cancer-killing viruses on human subjects (rather than just on human cells)?*

JCB: I'm hoping that within the next year or two, we'll be definitely putting the virus into human subjects.

OLM: *Hypothetically speaking, how large an amount of the virus would have to be administered to a human patient for the treatment to be effective? Would this be a risky proposition?*

JCB: The interesting thing about the virus we use is that it is replication-competent, which means it can actually grow. When you introduce the virus into a person, that's not the final dose. Once it hits the tumor, it will actually replicate and grow within the tumor. So, hypothetically, the dosage will increase inside the patient, but in a targeted fashion. We anticipate the dosage won't be enough to make anybody sick. As for the risk factor, we're doing a lot of safety testing to ensure a high likelihood that this treatment won't be dangerous to people at all, but there is always the possibility that the virus could infect something that we are not yet aware of.

The Canadian Cancer Society and that Canadian Institutes for Health Research have been long-term supporters of the work we do. The Terry Fox Foundation just gave us \$2 million, which will fund our research for the next three years and allow us to work with other scientists across Canada (in Calgary, London, Hamilton and Montreal) to make this happen faster. We're taking a team approach so we

can get virus treatments into the clinic faster. Our own Cancer Foundation here in Ottawa continues to support me and the other scientists at the Ottawa Regional Cancer Centre.