News Article

Immunotherapy Research in Canada: Where Do We Stand?

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Society is moving towards a new perception of cancer. It is no longer a death sentence, but rather a "chronic illness", according to Dr. Siddhartha Mukherjee, the author of the recently published book *Biographies of Cancer*. Dr. Mukherjee claims that "we might as well focus on prolonging life, rather than eliminating death", pointing to the extremely complicated characteristics of cancers that could arise from nearly any tissue type [1]. Does this mean we are giving up on a cure for cancer? Perhaps, but ways to better control or slow the growth of cancer would be the first step to take.

"All of us are generating cancer cells every day," says Dr. Neil Berinstein, a leading cancer vaccinologist in Canada. Our immune system normally checks for and controls any newly arising cancer cells. However, one of the strategies cancer cells use to circumvent the immune system is to suppress its function. This is where immunotherapy may play an important role in the fight against cancer. Immunotherapy aims to boost the immunological response against tumor-specific antigens and reverse the immune inhibitory and evasive mechanisms employed by cancer cells. Scientists are now focusing on improving active immunotherapies such as cancer vaccines and immune adjuvants, which enhance the immune system's ability to fight the disease, versus passive immunotherapy with biologics, which depend on the direct action of the therapeutic agent (e.g. monoclonal antibodies) for an effect [2]. Also, one should note the difference between prophylactic cancer vaccines, such as human papilloma virus vaccines (e.g. Gardasil™), for the prevention of cervical cancer [3] and therapeutic cancer vaccines like Provenge, the first FDA-approved immunotherapy treatment which sensitizes the patient's antigen presenting cells against antigens on the surface of prostate cancer cells that are resistant to advanced hormone therapy [4, 5].

Current cancer treatments include chemotherapy, radio-therapy and surgical debulking. However, due to the lack of specificity of these treatment methods, one risks damaging the normal cells. Newly reported cancer therapies include photodynamic therapy (for the treatment of skin cancers), RNA nanotechnologies, nanorobotics and oncolytic viruses [1]. While these new treatments are also worthy of further investigation, the focus of this article will be to explore the current status of Canadian research in immunotherapy and cancer vaccines, some of which have already undergone Phase III clinical trials in the US and Canada.

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Canadians have made major contributions to the advancement of immunotherapy research, as exemplified by two scientists from Ontario, Drs. Pamela Ohashi and Li Zhang. Dr. Ohashi, the co-director of The Campbell Family Institute for Breast Cancer Research (CFIBCR) at the Princess Margaret Hospital (PMH), has demonstrated an improvement in the ability of immune cells to attack tumors in a combined interleukin-7-viral vaccine, which was published in *Nature Medicine* in 2009 [6]. Dr. Zhang, whose recent work was published in *Cancer Letters* in November 2010, has successfully propagated human-derived double-negative T cells *ex vivo* without losing their reactivity against multiple antigens, a discovery which has brought us much closer to developing novel patient-specific T-cell immunotherapies [7, 8].

Amidst the excitement, Health Science Inquiry interviewed Dr. Neil Berinstein in order to gain insight on the current research status of immunotherapy in Canada. Dr. Berinstein previously headed the Cancer Vaccine Program at Sanofi Pasteur, Canada's largest developer of vaccines for 10 years. As well as being the author of the recently published article "Strategies to Enhance the Therapeutic Activity of Cancer Vaccines: Using Melanoma as a Model," [9], Dr. Berinstein is also a leading Canadian scientist in the field of cancer vaccines at the Odette Cancer Centre at Sunnybrook Hospital. His current collaborations with colleagues in Japan, the United States and Europe, have contributed to the development of multi-antigen cancer vaccines and novel combination therapies.

According to Dr. Berinstein, research in the area of cancer vaccines in Canada is at "a relatively early stage". He also expressed his concern for the relative lack of enthusiasm in the therapeutic vaccine field at home in Canada compared to that in the United States, where multiple pharmaceutical and biotechnology companies actively take part in this type of research. Having rich grounds for clinical trials is a key aspect in therapeutic research. However, with weak public awareness and a relatively small cohort of scientists in Canada, Dr. Berinstein pointed out that there is definitely a room for improvement to promote immunotherapy research among Canadians. He then went on to give an example of a research program arising in Halifax, where despite being managed by a Canadian organization, the clinical trials took place in the United States due to better availability of experienced staff and patient numbers. In support of Dr. Berinstein's view, a recent report prepared for the Canadian Institute of Health Research (CIHR)'s division of Infection and Immunity written by Dr. Michelle French entitled "Vaccines of the 21st Century: Taking Canada to the Next Level" revealed the common views and suggestions from Canadian vaccinologists [10]. Thus, upon surveying

approximately 240 researchers engaged in vaccine-related research, as well as vaccine and immunization organizations in Canada, some important challenges were identified and are summarized as the table below [10].

Challenges	Recommendations
Research efforts need to be better coordinated.	Organize and facilitate vaccine research workshops and facilitate communication. Foster linkages between all stakeholders. Establish a vaccine research network.
Vaccine research and development is costly.	Create partnerships with funding organizations, industry, academic institutions and government to drive research and development.
There are still several major diseases for which there currently are no vaccines. As well, improved methods to formulate and deliver vaccines are needed.	Continue to support basic research. Also, develop and support strategic research initiatives.
The public lacks accurate knowledge about the safety and efficacy of vaccines.	Support behavioural, social and ethics research.
There is a gap between basic research and Phase I/II clinical trials.	Partner with industry to bridge the gap between basic science and clinical trials. Establish facilities and guidelines to allow researchers to take discoveries towards clinical trials. Create new funding mechanisms.
There are many clinical research questions that require public funding.	Provide additional and ongoing support for pre-clinical and post-licensure trials.

While the points raised in the report are relevant, there were limited sections dedicated to therapeutic cancer vaccine research. Thus, it seems that increasing awareness and support of this specific research field may be crucial to ensure the competitiveness of Canadian research on a global scale. Additionally, though there are movements to improve the research environment in Canada, such as CFIBCR's plan to expand their immunotherapy research program at PMH [8], Dr. Berinstein suggests that "we need more incentives from the government", a sentiment that echoes the results from the aforementioned survey by the CIHR. Investment into immunotherapy research in Canada as a means to fight and control cancer may help to retain highly trained research scientists in the country and bring long-term benefits to our health care system and patients.

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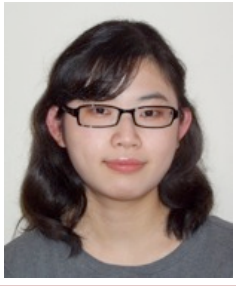

News Reporter Profile

Chan-Mi is a Ph.D. student at the Hospital for Sick Children (SickKids Hospital) in Toronto, undertaking a research project in lung inflammation. She has a M.Sc. degree from the Department of Laboratory Medicine and Pathobiology (LMP), University of Toronto, where she was involved in cancer research. She joined the HSI Team as a Newsreporter in 2010, and chose to explore immunotherapy as the topic of her article based on her interest in personalized medicine and the natural healing potential of the immune system.