

Cancer Control at a Crossroads:

The Case for Translational Research



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Table of Contents

Executive Summary

Cancer Control at a Crossroads	1
What is the History of Cancer?	1
What Causes Cancer?	2
Can we Prevent Cancer?	4
Are we making Progress in the Diagnosis and Treatment of Cancer?	5
Translational Research	7
What is Translational Research?	7
What are Some Examples of Translational Research Projects?	8
What are the Barriers to Translational Research	10
What Examples Exist of Successful Translational Research Initiatives?	10
What does the Canadian Cancer Research Alliance (CCRA) Recommend?	12
Cancer Cohort	13
Translational Research	13

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EXECUTIVE SUMMARY

Although cancer has existed for thousands of years, progress in prevention and cure has been slow, characterized by incremental advances driven by scientific milestones such as the discovery of anaesthesia, radiation and the early chemotherapy agents. However, in the last two decades we have seen an exponential increase in our understanding of the biological and molecular processes involved in cancer, leading to aggressive and innovative new approaches to prevention, diagnosis and treatment. Over the same time period, clinical research has progressed in a more linear fashion, creating an imbalance between the wealth of knowledge accumulating from discovery research and its application in patient care. Increasingly, this imbalance is now being addressed through the field of translational research.

Cancer is caused by an accumulation of genetic mutations that eventually lead to changes in basic cell functions, such as signalling pathways. These mutations can be caused by many factors, some that are within our control such as tobacco use and sun exposure and some that are not, such as inherited predispositions to certain gene mutations (e.g., BRCA1 and BRCA2), unknown environmental factors and the natural aging process.

For many cancers, available treatments are not curative primarily because of a lack of specificity. However, our improved understanding of cancer has opened the door to more specific targeted therapies directed to well-characterized tumour markers. These new therapies are anticipated to cause less damage to normal tissues, reducing the often severe adverse side-effects experienced as a result of conventional therapies. For the first time, the possibility of individualized therapy tailored to a unique set of molecular markers on an individual cancer is within our grasp. Such therapy is likely to be not only more effective but also more discriminatory, saving patients from unnecessary treatments that would be ineffective against their particular tumour.

EXECUTIVE SUMMARY - CONTINUED

At the same time, advances in imaging and radiotherapy have improved our ability to detect cancer at its earliest and most treatable stages and have made it possible to monitor, treat and eradicate small tumours with greatly improved specificity and a corresponding reduction in collateral damage.

Many other countries are now responding to the urgent need for translational research by creating networks designed to bring together the parties needed to fast-track the movement of new interventions, technologies and treatments into the clinic. Canada must also respond by creating environments conducive to translational research that will capitalize on the new discoveries, many of them made by Canadian researchers, which will eventually lead to improved cancer control. Based on our considerable existing strengths in both biomedical and clinical research, we must move to create opportunities that will foster meaningful and sustainable collaborations between researchers in non-clinical environments, clinicians and other health care professionals involved in the cancer care continuum from prevention to palliation.

It is anticipated that a Canadian translational research initiative would address important clinical problems in cancer prevention, diagnosis, treatment or supportive care, with an emphasis on providing measurable improvements in patient care within five years. Through a virtual network of translational research centres, biomedical and clinical researchers will work in collaboration with other health care professionals in cancer centres across the country, facilitating improved linkages between provincial cancer agencies and national, provincial and private sector partners. In addition, a new generation of clinical scientists will be recruited and trained to bridge the divide between basic and clinical research and expedite the uptake of new technologies, treatments and interventions into clinical practice.



CANCER CONTROL AT A CROSSROADS

What is the History of Cancer?

Cancer is not exclusively a modern disease, in fact tumours have been found in dinosaur bones dating back 150 million years. The earliest description of cancer (although the actual word 'cancer,' credited to Hippocrates, was not used until around 400 BC), was an account of eight cases of "tumours" or "ulcers" of the breast in Egypt in 1600 BC, well over 3000 years ago. These tumours were treated by cauterization with a tool called a "fire drill" which leaves much to the imagination! The writings of the time record that: "there is no cure" – a perception that continues to fuel the fear many people still have of the disease today.

The introduction of anaesthesia in 1846 heralded a new era in surgery, during which it was discovered that radical surgery accompanied by removal of local lymph nodes could sometimes cure cancer. In the late 1800s, Paget suggested that tumour cells could spread through the bloodstream and lodge in other organs, although they seemed to be only able to grow at specific sites. As a result, the limitations of surgery became clear and the need for systemic therapies was recognised. In 1878, Thomas Beatson discovered that the breasts of rabbits stopped producing milk after he removed the ovaries and made the connection between estrogen and breast cancer, even before the hormone itself was discovered. These discoveries laid the foundation for modern hormone therapy in breast and prostate cancer. In 1896, the discovery of x-rays not only provided a new tool for cancer diagnosis and treatment but also pointed to radiation as one of the causes of cancer. In 1945, during the search for weapons in the Second World War, nitrogen mustard was discovered and later found to be an effective killer of certain lymphomas, paving the way for today's growing arsenal of chemotherapy agents. The first cure of metastatic cancer using these drugs came in 1956 when methotrexate was used to treat choriocarcinoma. Today, more than 60 chemotherapy drugs are in widespread use.

What Causes Cancer?

Cancer occurs when normal cells that are still capable of proliferation suffer damage to their DNA that is not repaired. This damage can lead to changes or mutations which accrue over time until some cells enter a phase of uncontrolled growth and in some cases acquire the ability to travel through the body to other distant sites, where they continue to grow and establish their own blood supply (angiogenesis), producing metastases. These metastatic tumours interfere with the function of normal organs and tissues and, if untreated, eventually kill the patient. This uncontrolled growth is usually triggered through two kinds of pathways:

- ❧ *genetic alterations leading to the activation of oncogenes that can promote excessive cell division, cell survival in the absence of survival signals, and genetic instability; and*
- ❧ *damage to tumour suppressor genes which normally prevent cells from dividing uncontrollably.*

In addition, cancer cells acquire mutations in genes that regulate apoptosis, the process that normally leads to the death of aberrant or rogue cells. Eventually, accumulated genetic damage leads to populations of cells that multiply in an uncontrolled fashion and are essentially immortal. Recent experiments, carried out by Canadian and other researchers, have suggested that in many cases, if not all, the target cells at the base of all of these processes are the small populations of tissue-specific stem cells. It is probable that the conversion of these cells into cancer stem cells is responsible for promoting the maintenance and progression of human cancer.

Occasionally, damaged DNA is inherited, such as mutations in the BRCA1 and BRCA2 genes that are linked to an increased risk of breast and ovarian cancer. In about 85% of cases however, DNA damage occurs naturally as a result of:

- ❧ *errors in DNA replication (an almost but not quite perfect process);*
- ❧ *production of reactive oxygen species by normal metabolism; or*
- ❧ *mutagenic effects of the earth's natural background radiation.*

Tobacco use is the single largest known cause of cancer, responsible for more than 30% of all cancers. Additional identified causes include infectious agents (bacteria and viruses), radiation (including the sun), hormonal influences and chemical carcinogens (aflatoxins, pesticides, asbestos, hydrocarbons, anilines et cetera). It is also suspected that lifestyle factors such as alcohol abuse, inadequate physical activity, poor diets and socio-economic influences, may be risk factors for cancer.

The word “epidemiology,” which comes from the word “epidemic,” originated in the world of infectious diseases and, simply put, refers to population studies on ‘who gets which disease and why’. Epidemiological studies, which can be descriptive, analytic or experimental, have provided us with a wealth of information on the associations, risk factors and causal effects for many diseases. Early cancer epidemiology can be traced back to the 18th century when it was first noted that:

- ❧ *nuns had an unusually high incidence of breast cancer but a low incidence of cervical cancer due to their celibacy and the associated absence of pregnancy and lactation;*
- ❧ *that chimney sweeps had high levels of cancer of the scrotum caused by exposure to soot; and,*
- ❧ *that people using snuff had high levels of cancer of the nose.*

The first great victory in cancer control was the result of epidemiology studies that clearly linked tobacco use with lung cancer. Because tobacco is such an enormous causative factor, it was possible to evaluate its importance in relatively small population studies. It is widely believed, throughout the epidemiology

community, that in order to identify and evaluate other factors, especially those concerned with lifestyle and environment, a very large cohort of individuals needs to be followed, in the order of 300,000 or more.

Although there is some variation in certain specific cancers, the overall age-corrected cancer rate has not increased over recent decades. However, DNA damage generally accumulates with age and thus cancer is predominantly a disease of older people with most cases diagnosed in the age group over 60 years. This fact has significant implications for our health care system given the aging demographic of the population and the projection that cancer, already the leading cause of *premature* death, will be the single leading cause of death by 2010, with almost half of Canadians at risk for developing cancer in their lifetime.

Can we Prevent Cancer?

In order to prevent a disease, it is generally necessary to understand the cause. For cancer, there is no single cause but rather an array of multiple risk factors operating in combination. We already know the risk factors for an estimated 50% of cancer, with as many as 30% of all cancers being caused by tobacco use alone. Considering that the first alarm about the health effects of tobacco was raised as early as 1761, it is perhaps surprising that over 20% of Canadians still smoke (and many more in some countries). It is of particular concern that young people, still take up the addictive habit for the first time, although they must be fully aware of the health risks. Similarly, people still spend hours in the sun or at tanning salons in search of the perfect tan despite knowing the inherent risks of skin cancer. The current epidemic of obesity would suggest a similar disregard for warnings about diet and physical activity. Perhaps not surprisingly, behavioural change is proving slow to achieve at a population level, although some progress has been made in Canada and the United States of America (USA).

It is likely that cancer control will only be achieved through a combination of approaches: prevention, early detection and treatment. The fact that cancer has existed for so long suggests that it is not a disease that will ever be entirely

prevented by alterations in lifestyle or environment. We cannot prevent the natural aging process and the accumulation of genetic damage over time, especially if we continue to increase our life expectancy, nor can we hope to necessarily effect major social changes in response to known risk factors. For example, hormonal influences are known to play a key role in breast cancer risk. It has been suggested that if women were to return to having five or six children, beginning in their teens and breast fed each of them for two years, we would see a dramatic decrease in breast cancer, but this is not a likely or even desirable scenario in today's society. A drug therapy capable of mimicking twelve years of pregnancy and lactation, with no deleterious side effects is also equally unlikely. Therefore, it is important that, in addition to prevention research, we continue to direct our efforts towards early detection and more effective, less invasive, treatments for those cancers we cannot prevent.

Are we making Progress in the Diagnosis and Treatment of Cancer?

For solid tumours, the most common diagnostic tool is imaging followed by biopsy and histological examination. Recently, there have been major advances in nuclear medicine and imaging technologies that have resulted in sophisticated approaches not dreamed of even 20 years ago. These new technologies are not only capable of detecting smaller tumours at much earlier stages of the disease but are also poised to revolutionize our ability to provide non-invasive imaging in preclinical and clinical situations. Examples include detection and monitoring of:

- ☞ *drug targets;*
- ☞ *drug distribution;*
- ☞ *cancer gene expression;*
- ☞ *cell surface receptor or oncoprotein levels; and*
- ☞ *biomarker predictors of therapeutic responses and prognosis.*

Radiation therapy has also dramatically improved with treatment modalities offering unprecedented sensitivity and specificity, able to zero in on minute tumours with minimal damage to surrounding tissue – a far cry from earlier radiotherapy techniques that often had high patient morbidity. Progress has largely been driven by an emerging new culture of collaboration and multi-disciplinary research involving physicists, chemists, engineers, mathematicians, biologists, geneticists and clinicians.

The process by which new drugs are discovered and tested is also profoundly changing. Scientists have learned more about the molecular processes involved in cancer development in the last two decades than in all the preceding centuries. The sequencing of the human genome has transformed the way we study all life processes. In addition, there has been an explosion in technology that has fast-tracked research progress. Just one example is high-throughput screening which allows millions of biochemical, genetic or pharmacological tests to be performed in a short time. The cytotoxic chemotherapy drugs that are relatively non-specific, killing pretty much every dividing cell and causing enormous collateral damage often accompanied by horrendous side effects, will gradually be replaced by a whole new generation of biological, targeted therapies based on what we now know about the cancer cell at a molecular and genetic level.

Some of the new therapies capitalize on the patient's own immune system to destroy cancer cells or at least lessen the effects of cancer treatments. These approaches include altering the growth patterns of cancer cells, enhancing the body's ability to repair or replace normal cells damaged by therapy and preventing metastatic spread. Included in this category of agents are interferons, interleukins, colony-stimulating factors, monoclonal antibodies, vaccines, gene therapy and non-specific modulating factors.

Other therapies use small molecules to target proteins involved in the dozens of signalling pathways that regulate cell growth. These drugs can act in several ways including killing cancer cells, arresting their growth, making them more vulnerable to other anti-cancer drugs, or inhibiting angiogenesis.

Many of these new therapies show additional promise when used in combination or as an adjunct or follow-up to current standard chemotherapy. For example, Herceptin targets HER2 receptors on the outside of the cell whereas another drug, Lapatinib, targets the part of the receptor inside the cell, making the two drugs complementary. Similarly, a new drug, dasatinib, shows promise in patients who no longer respond to Gleevec or suffer disease recurrence. Most new generation drugs are still in animal testing (preclinical studies) but many are in clinical trials and a few have already been approved for use in patients. It is estimated that there are currently over 400 new cancer drugs, some of which have originated in Canada, at various stages of development.

Eventually the hope is to be able to obtain an individual signature or footprint of a patient's cancer and tailor a therapy that is specific to that individual's unique set of molecular targets, i.e. individualized medicine.

TRANSLATIONAL RESEARCH

What is Translational Research?

Translational research describes that piece of the puzzle that exists between the discoveries made in biomedical research and what happens to the patients in the clinic; in other words, the transition from "bench" to "bedside." Translational research does not necessarily involve the generation of new knowledge, but rather the movement of existing knowledge into clinical interventions and practice. It is a two-way process whereby basic researchers provide clinicians with new tools for use in patients and for assessment of their impact, and clinical researchers make novel observations about the nature and progression of disease that stimulates basic research.

Most improvements in the diagnosis, treatment and care of cancer patients have come from clinical trials focused on prevention, screening and treatment. Translational research is not necessarily based on clinical trials, but could be a study monitoring the expression of a panel of proteins in a group of cancer patients receiving a given therapy in order to see if they have any predictive value. Alternatively, a translational research project could be an addition to an ongoing clinical trial, such as pharmacological/genetic or psychosocial studies designed to provide additional value-added information on prognosis and outcome.

Translational research becomes particularly important in the evaluation of the new generation of targeted therapies to understand their performance in the clinic and identify opportunities for effective drug combinations. It is also important for stratifying patients into those who will respond to a new treatment and those who will not, thus sparing patients (and the health care system) unnecessary treatments that are predicted to have little or no clinical benefit. By understanding how new therapies perform in practice, the basic researcher can return to the laboratory to refine the treatment.

What are Some Examples of Translational Research Projects?

The following list, although by no means exhaustive, describes a few of the many possible examples of translational research projects:

- ❧ *evaluation of new and more effective ways of drug delivery, e.g. liposomal therapy, that improves tumour uptake and reduces damage to normal tissues;*
- ❧ *evaluation of effectiveness of existing and new therapies on cancer stem cells;*
- ❧ *evaluation of drugs or other interventions to reduce the side effects of standard chemotherapy and radiotherapy treatments;*
- ❧ *assessment of agents that overcome multi-drug resistance;*

- ❧ *studies on genes/proteins whose expression predicts severity of disease at diagnosis or that serve as prognostic indicators useful for patient stratification;*
- ❧ *evaluation of the new generation of protein “super chips” to screen cell-signalling proteins associated with malignancy to identify panels and patterns of markers specific for individual tumours;*
- ❧ *evaluation of genes or proteins whose expression changes following drug treatment and correlates with positive or negative responses to therapy;*
- ❧ *evaluation of new methods for determining whether a given therapeutic agent is hitting its target in patients;*
- ❧ *studies on novel molecular and non-molecular diagnostic techniques such as functional imaging with value in determining treatment outcome or detecting microscopic/ sub-clinical disease;*
- ❧ *studies on new and improved radiotherapy techniques that offer increased sensitivity and specificity and a corresponding reduction in harmful side effects;*
- ❧ *studies on the function and potential therapeutic applications of cancer stem cells; and,*
- ❧ *studies on non-drug interventions that enhance patient survivorship.*

Essentially, any project which is designed to take new knowledge gained from discovery research in any area of cancer control and subject it to evaluation in a clinical setting to address a defined problem in patient care, would be considered to be translational research. There is a need for translational research throughout the entire cancer continuum (prevention, early detection, diagnosis, treatment and palliation) in any situation where evidence exists for improved cancer control. The essence of translational research is to link research information and researchers working in non-clinical environments to the clinical setting to facilitate exchanges that translate into benefits for the patient.

What are the Barriers to Translational Research?

The barriers to effective translational research stem in large part from the difficulties in bridging the gap between basic and clinical science and establishing meaningful collaborations between government regulatory authorities, the pharmaceutical industry and research organizations, and between researchers, pathologists, clinicians, and health policy decision makers. More clinical scientists and academic pathologists are needed with adequate time for research in environments that also contain basic researchers with access to the latest knowledge and technologies with applications in the clinical setting. An important outcome of any translational research initiative should be an increase in clinicians and other health care professionals involved in cancer research.

There are, of course, additional barriers to translational research that may be harder to address in the short term such as differences between institutional ethics boards, incompatible databases, fragmented infrastructure, regulatory issues and the high cost of trials. It is estimated that the cost of one trial has increased ten-fold since the Thalidomide tragedy of 1970, largely as a result of new regulations that have extended the time required for preclinical pharmacology and toxicology studies. There is also the challenge of the high cost of the new drugs themselves. In an already strained health care system with significant wait times in a number of areas, the temptation is often to deliver the best available care rather than venturing into new and possibly expensive territory. Despite these challenges, the importance of translational research is increasingly being recognised around the world.

What Examples Exist of Successful Translational Research Initiatives?

The National Cancer Institute (NCI) in the USA has both a Translational Research Working Group, that was established in 2005 to advise the NCI on how best to organize its investment in translational research, and an Office of Translational Research, which promotes collaborations between basic and clinical researchers and facilitates the rapid translation of basic/preclinical observations into practice

through linkage to the NCI clinical trials groups. In addition, the NCI Specialized Programs of Research Excellence (SPOREs) promotes interdisciplinary research that will move basic research findings from the laboratory into clinical settings, involving both cancer patients and populations at risk of cancer. SPORE investigators work collaboratively to plan, design and implement research programs that may impact cancer prevention, detection, diagnosis, and treatment.

In the United Kingdom (UK), Cancer Research UK, in collaboration with the Medical Research Council and the National Health Service, has announced plans to embed translational research studies in late phase cancer clinical trials. Included will be studies that contribute to a mechanistic understanding of treatment outcome within the clinical trial or investigate the value of genotype, novel diagnostic and surrogate markers in determining response and clinical outcome to a trial intervention. In October 2006, the National Cancer Research Institute (NCRI) announced the funding of a major new network, Experimental Cancer Medicine Centres for Translational Research. Following a competitive process, 17 centres were awarded funding (\$4 million each over five years) to fast track the uptake of new cancer treatments into patient care. This initiative, based on the successful work of National Translational Cancer Research Network (NTRAC), established in 2002 to facilitate translational research, will provide vital infrastructure to help basic researchers, clinicians, nurses and support staff accelerate research that benefits patients. The centres will also promote research into the development of new drugs and test individualization of patient care over the next five years.

In Canada, we already have many smaller, highly successful translational research initiatives paving the way for a large-scale national program of translational research. For example:

At the national level, the NCIC Clinical Trials Group (CTG) develops, conducts and analyzes multi-institutional trials of cancer therapy and provides a centralized focus of knowledge, expertise and experience. Over 60 institutions participate in CTG studies and the CTG participates in international trials in North America, Europe and Australia.

- ❧ *CIHR supports a clinical research initiative (CRI) which invests in people, infrastructure, networks, enabling tools and science. Since 2004/2005, CIHR has invested, through the CRI, over \$100 million in clinical research. Also, CIHR and partners support several cancer translational research training centres under the CIHR Strategic Training Programs in Health Research (STIHRs), including those in Montreal, Halifax, and Edmonton/Calgary and Kingston.*
- ❧ *Ontario has just established the Ontario Institute of Cancer Research (OICR) which, building on the work of the Ontario Cancer Research Network (OCRN), plans to significantly increase the number of patients enrolled in cancer clinical trials. OICR will maintain the database of ongoing clinical trials; provide funds to Ontario's hospitals and cancer treatment centres to expand trials programs; work to develop consistent standards, guidelines and processes and increase infrastructure funding through increased support of trials nurses, data managers, research pharmacists, and clinical research associates.*
- ❧ *The Terry Fox Foundation has plans to launch a large (~ \$50 million) translational research initiative with nodes across the country, which will focus primarily on basic science aspects such as biomarkers imaging technologies, et cetera.*
- ❧ *The new BC Cancer Research Centre, one of Canada's largest free-standing cancer research centres, will focus on translational research and encourage collaborations between basic and clinical research teams.*

In addition, Canada has a national tumour bank network (CTRNet) and a health care system that captures cancer patient data across the country. In short, we have all the ingredients necessary to support world-class translational research on our own doorstep. What is required to put it all together is strong leadership and sufficient funds to provide the “glue” needed to bring together the basic and clinical research discoveries.

What does the Canadian Cancer Research Alliance (CCRA) Recommend?

The Research Action Group of the Canadian Strategy for Cancer Control (CSCC), now the Canadian Partnership Against Cancer (CPAC), which in 2004 expanded to become the CCRA, has for more than three years been working to determine

the most pressing research needs in cancer control. Through a process of broad consultation with researchers, health system and health services managers, and stakeholder groups including other CPAC Action Groups and cancer patients, CCRA has come to the conclusion that there are two essential and complementary approaches to cancer control – prevention and treatment.

Cancer Cohort

For prevention to be effective, the risk factors for cancer need to be fully identified and understood. The only way to assess the importance of most genetic, lifestyle and environmental factors causing cancer is through the establishment and analysis of a large cohort involving perhaps as many as 500,000 individuals. One of the best examples of the value of a well-designed cohort study comes from the relatively modest Framingham Heart Study which began, almost 60 years ago, with the recruitment of just 5,208 volunteers living in the small town of Framingham, MA, USA. This study, now into its third generation of recruits, has made major contributions to our understanding of the risk factors for cardiovascular disease.

The complexity of factors linked to cancer and the wide variety of forms of cancer necessitate the use of much larger cohorts to address important cause and effect questions in a meaningful way. However, large cohorts are expensive and the launch of a Canadian cancer/chronic disease cohort would require the support of many Canadian organizations and agencies and a significant long-term financial investment by both federal and provincial governments. The feasibility of designing and launching a Canadian cohort study is currently being investigated.

Translational Research

Translational research, on the other hand, is within our means now, especially considering the availability of new funds within the CSCC, as it would not include the considerable investment needed for discovery research. Rather, a

translational research initiative would take existing knowledge and apply it to important clinical problems, creating a legacy for future generations of researchers. Canada already has both outstanding basic research capabilities and enormous strength in clinical research, concentrated at key locations across the country. What we do not have is an organised plan to take advantage of these capabilities by bridging the gap between basic and clinical environments to use new and existing knowledge to improve cancer control. As noted above, many other countries have recognised this need and have moved to establish translational research initiatives. Canada needs to do the same or we will lose the advantages that our excellent cadre of researchers, strong clinical research base and unique health care system offers.

Following two invitational meetings focused on Canadian translational research needs, CCRA proposes the launch of a competitive process to attract high calibre applications from groups or networks of researchers with experience in translational research. It is recommended that eligible teams be required to demonstrate:

- ☞ that their proposed project addresses an important clinical need or problem in cancer control;*
- ☞ that the team they create will leave a legacy for future translational research initiatives;*
- ☞ that their team incorporates genuine and sustainable collaborations between all the players required to produce an impact on patient care including, but not restricted to, basic researchers, pathologists, clinicians and other health research scientists, and health system managers;*
- ☞ that there is at least a reasonable expectation that, within five years, the results of their research will produce quantifiable improvements in cancer diagnosis, treatment or care; and,*
- ☞ that they recognise existing barriers to translational research and have plans to overcome them.*

In addition, every effort will be made to forge collaborations with existing organizations planning or engaged in translational research initiatives (e.g., OICR, Terry Fox Foundation, NCIC Leadership Fund, CIHR Clinical Research Initiative) and to take advantage, where appropriate, of existing infrastructures such as the Canadian Tumour Bank Network (CTRNet) and the NCIC Clinical Trials Group.

Eligible projects should not be restricted solely to studies applying molecular technologies to develop strategies for personalized medicine, such as drug interventions or clinical trials, but should be open to psychosocial or other interventions, such as dietary changes, shown to have an impact on disease outcome. Clinical evaluation of new imaging techniques and novel radiotherapy treatments would also be an eligible area for translational research projects. Depending on the available funds from CSCC and the ability to increase these funds through partnership, a number of both small (less than \$1 million per year) and larger (between \$1 to 5 million per year) projects might be feasible. Eligible expenses would include anything that was essential for the proposed project, including equipment, materials, information technology, patient databases, tissue banking costs and personnel support (clinician time, nurses data managers, et cetera.).

A strong foundation of translational researchers able to bridge the gap between discovery research and clinical application is essential if we are to move towards individualized treatment using the targeted therapies of the future. The initiative would allow the recruitment and training of clinician scientists and would provide opportunities for the graduates of the existing translational research training programs. Based on funds available, 10 translational research centres might be created across the country, forming a virtual Canadian network for translational cancer research. This structure will catalyze access to new knowledge and interventions and apply them in the Canadian context to improve diagnosis and treatment. The increased numbers of clinician scientists in our key treatment centres, and their interaction with health care systems managers, will facilitate the uptake of new innovations into our health care system, making Canada a leader in individualized cancer care.

