

CANCER STEM CELL CONSORTIUM

SCIENTIFIC STRATEGIC PLAN

2009-2014

9 October 2008

(UPDATED)

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Executive Summary

The discovery of a rare subpopulation of tumor cells, termed cancer stem cells (CSCs), in many common malignancies has profound implications for treating cancer patients. Most current anticancer therapies were developed to kill the major tumor cell population that makes up the bulk tumor mass; however, these cells are not responsible for the growth and dissemination of tumors. CSCs are at the root of cancer and account for tumor growth and metastases. CSCs are resistant to the toxic effects of radiation therapy and current chemotherapies. Hence, it is not surprising that tumors often recur, leading to relapse of cancer patients treated with these agents. By developing new therapies that target CSC for eradication, long-lasting cures should be achieved.

According to a recent economic report, a 1% reduction in mortality from cancer would save nearly \$500 billion to current and future Canadians and Americans. A “war on cancer,” which would cost an additional \$500 million for CSC research and treatment over the next 5 years, would clearly yield an excellent return on investment.

Both Canadian and Californian researchers pioneered the discovery of CSCs giving them a powerful historical lead in this rapidly expanding field. Moreover, a significant percentage of the world’s CSC researchers are located in Canada and California. Thus, there is a natural alignment of research prowess and critical mass of researchers in both jurisdictions with which to surmount the challenges posed by CSCs.

The CSC Consortium’s research programs will focus on identifying CSC biomarkers and anti-CSC therapeutic agents. State-of-the-art infrastructure will provide live CSCs from various malignancies for study. This plan also envisions developing a number of novel high-throughput technologies. The scientific community believes that progress will occur more rapidly by supporting several large-scale efforts involving multiple Research Teams (see Figure 3), that will share cutting-edge core Technology Platforms and Facilities and common research goals to generate new knowledge. The CSC Consortium, a not-for-profit corporation with a strong governance and management structure, will provide funding and oversight of the research programs and supporting infrastructure.

This strategic plan recommends that the CSC Consortium invest significantly in translational activities that will accelerate the evaluation of CSC-specific biomarkers and the discovery of anti-CSC therapies. Both Canada and California host Comprehensive Cancer Centres that will provide the infrastructure necessary to validate CSC biomarkers and to clinically evaluate new anticancer therapies targeting CSCs including “First-in-Man” studies.

This plan describes strategically important CSC research and technology programs, and proposes CSC Consortium activities and an organizational structure to manage a budget of sustained and stable funding of \$500 million (CDN) for an initial five-year period, which will be provided by a variety of agencies in Canada and California. Sustained funding is the key to the success of the CSC Consortium because of the unique nature of the expertise and technologies required for this research, and the imperative for rapidly moving discoveries to the clinic. CSC Consortium funding will be bolstered by world-leading business expertise and will lead an exciting wave of new biotechnology companies based on CSC discoveries.

1. Scientific Background

1.1. What are Cancer Stem Cells?

Cancer arises from the accumulation of multiple alterations to the genome of an individual cell leading to clonal tumors. These genetic and epigenetic changes affect genes involved in multiple cellular processes including cell division, DNA repair and cell migration. A spate of recent discoveries suggests that the cell of origin of cancer is an adult tissue-specific stem or progenitor cell (**Figure 1**). Adult stem and progenitor cells are infrequent cells present in tissues and organs that replenish dead cells arising from injury and normal tissue turnover. Unlike embryonic stem cells, which are capable of producing all the cells in every organ of our body, adult stem cells are more restricted in their developmental potential and give rise to progenitor cells that rapidly proliferate and differentiate to generate specialized cells of particular tissues and organs.

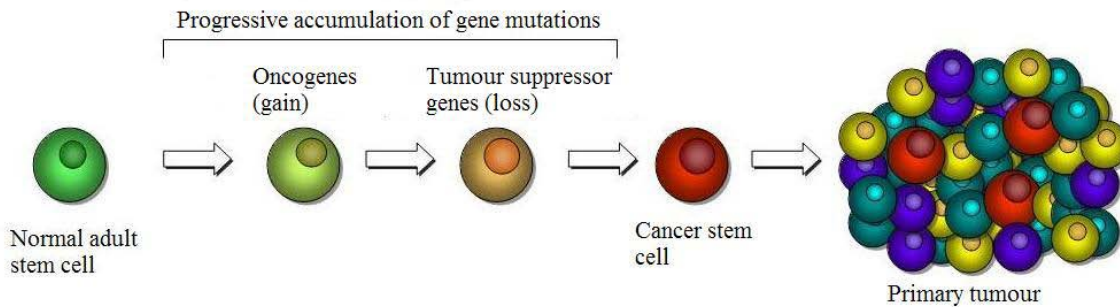


Figure 1: Origin of CSC

Normal adult stem cell self-renewal and differentiation are finely regulated to ensure tissue homeostasis. Cancer arises as a result of the dysregulation of these stem cell processes; self-renewal is increased, whereas differentiation is arrested at particular stages in the cellular hierarchy resulting in the accumulation of abnormal cells.

Cancer stem cells (CSCs) are the transformed descendants of adult stem/progenitor cells. These tumor cells, like their antecedents, possess the capacity to self-renew and to differentiate thereby generating the heterogeneous lineages of cells comprising tumors. However, the changes that endow CSCs with malignant properties typically alter the capacity of their progeny to execute the differentiation program pursued by their normal counterparts. In addition, despite their clonal origin, CSCs are genetically unstable and give rise to continuously evolving subclones. Hence by the time cancer is diagnosed, the tumor is likely to comprise genetically- and epigenetically-heterogeneous CSC populations, which may be dominated by only the most aggressive subsets of tumor cells.

CSCs are operationally defined by their capacity to generate a new tumor, similar to that from which they were isolated, after transplant into immune-compromised animals. Current estimates suggest that cancer stem cells are a minor fraction of all the cells in tumors; the vast majority of cells comprising tumors – the bulk tumor cell population – are not tumorigenic and comprise the aberrantly differentiated descendants of CSCs.

CSCs have been found in all malignancies examined thus far including common cancers such as those of the breast, prostate and colon. It is thought that CSCs not only fuel tumor growth, but also seed metastases, which accounts for the death of most cancer patients.

1.2. The Importance of Cancer Stem Cell Research

The implication of the stem cell model for treating cancer is profound. Mounting experimental evidence suggests that our current therapies do not target CSCs, but instead eradicate the bulk tumor cell population, which are not intrinsically tumorigenic cells. CSCs have a heightened ability to repair damaged DNA and hence, are resistant to radiation, and possess means to rapidly efflux many different chemotherapeutic agents, thus evading their toxic consequences (**Figure 2**). Consequently, to successfully treat cancer, scientists have to reorient their energies to eradicate CSCs.

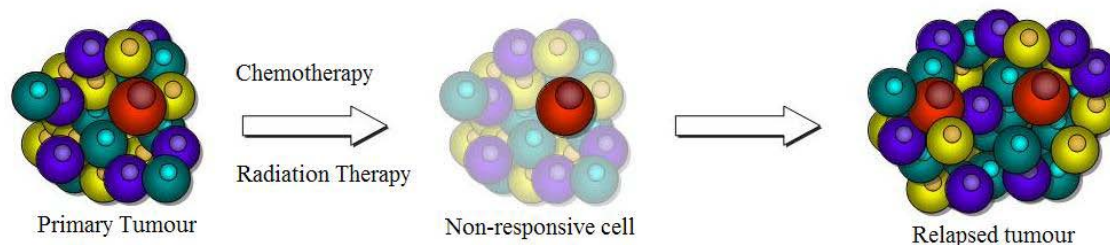


Figure 2: CSCs May Not be Targeted by Current Anti-Cancer Agents

Ideal anti-cancer drugs should kill CSCs, but not their normal adult stem cell counterparts or any other tissue-specific stem or progenitor cells and hence would have few side effects. The path to this desired outcome hinges on being able to purify and subsequently characterize CSCs in intimate detail using state-of-the-art tools to identify the molecular differences between adult stem cells and CSCs, and to then exploit these biological and biochemical differences to develop new anti-CSC therapies, which disrupt molecular pathways active in these cells. The availability of pure CSC populations would also allow scientists to find biomarkers (proteins or gene signatures) that uniquely identify these cells. The availability of CSC biomarkers would permit rapid estimates of the frequency of CSCs in a patient's tumor, which could be of diagnostic/prognostic value, and to track the effectiveness of anti-cancer treatments in eliminating these cells.

1.3. Challenges

The discovery that CSCs represent a rare subset of tumor cells poses several challenges. First, these cells constitute a minor proportion of all the cells comprising tumors. Second, many tumors (i.e., prostate and breast tumors) are small at the time of resection and provide few bulk tumor cells for CSC purification. Third, means of purifying CSCs to homogeneity – a requirement for many types of analyses such as gene expression profiling and genome sequencing – have yet to be achieved. And finally, most tumor cells cannot be propagated in tissue culture under conditions that either maintain or exceed the CSC frequency of the tumors from which they were isolated. These obstacles have stymied CSC researchers and have substantially impeded investigation of CSC and discovery of CSC biomarkers and anti-CSC therapeutic agents.

To surmount these challenges will require assembling the appropriate Research Teams and infrastructure to collect and store live tumor cells from a number of cancers and to purify, and if

necessary, expand the number of these cells in immune-compromised mice and/or tissue culture to enable investigation of CSCs using a variety of cutting-edge technologies and research tools. This plan anticipates that by working together in a collaborative and open fashion, whereby scientists share their research findings at an early stage, Research Teams will be able to mount several major research thrusts to realize the primary objectives of identifying candidate CSC biomarkers and new lead therapeutic anti-CSC agents, and of rapidly translating their use in the clinic.

2. Societal Need to Invest in Cancer Stem Cell Research

A substantial targeted investment in CSC research is necessary to surmount the barriers impeding progress in identifying and developing CSC biomarkers and more effective therapies targeting these cells. To overcome this roadblock, large repositories of live tumor cells from specific malignancies are needed as a source of CSCs for research as a prelude to moving discoveries into the clinic.

CSC research has enormous potential to significantly reduce health care costs and human suffering. As the population increases, incomes grow, health improves and the baby-boomer generation approaches the primary ages of disease-related death, the social value of improvements in health will continue to rise. Prospectively, even modest progress against diseases such as cancer will have enormous social values. According to a recent economic report, a mere 1% reduction in mortality from cancer would save nearly \$500 billion (\$89,300 per life saved) to current and future Canadians and Americans (Kevin Murphy, University of Chicago and Robert Topel, US National Bureau of Economic Research: *Journal of Political Economy*, 2006, vol. 114, no.5). An infusion of \$500 million over the next 5 years (2009-2014) to wage a more effective “war on cancer” by conducting CSC research could thus clearly yield an excellent return on investment.

CSC research also has the potential to expand the growth of the biotechnology and pharmaceutical sector. Investment in CSC research is expected to greatly enhance the expansion of a nascent private sector community in Canada and California. Both the generation of highly trained personnel, and the development of new technologies and products will be important drivers of commercial activity and key deliverables of a successful CSC research program.

3. Cancer Stem Cell Consortium

A CSC Consortium was established in 2007 as a not-for-profit corporation to secure and manage the allocation of an estimated \$500 million (CDN) during an initial 5-year period (2009-2014) to accelerate research focussed on CSCs and to facilitate the rapid translation of research findings into clinical application. The scientists involved in founding this Consortium included pioneers in CSC research, who have attained global recognition for their contributions to this field. The funding agencies that form the CSC Consortium currently include Genome Canada, the Canada Foundation for Innovation (CFI), Canadian Institutes of Health Research, the Stem Cell Network - a Canadian National Centre of Excellence - and the Ontario Institute for Cancer Research (OICR). Other funding agencies, both governmental and non-governmental, are expected to join the Consortium as it develops.

A strategic partnership between the CSC Consortium and the California Institute for Regenerative Medicine (CIRM), a state-sponsored stem cell research funding organization, was negotiated to catalyze strategic research partnerships among the world-class stem cell researchers in both jurisdictions. This partnership will accelerate advances in CSC research from discovery to pre-clinical and clinical trials. Funding for CSC research is anticipated from both Canadian and Californian funding agencies under the umbrella of the Canada-California Strategic Innovation Partnership (CCSIP).

4. Scientific Capacity in Canada and California to Advance Cancer Stem Cell Research

Canadian and Californian researchers pioneered the discovery of CSCs and are leaders in this rapidly expanding field. Collaborations already exist between many of these investigators; there are unique possibilities for aggregating their expertise and resources to build a critical mass of researchers to accelerate the rate of research discoveries to the benefit of cancer patients.

5. Rationale for Multi-Disciplinary and Multi-Jurisdictional Research Teams

It is widely recognized that cancer is a major and complex worldwide problem. Undertaking research in the context of a multi-jurisdictional, multi-institutional research consortium offers many advantages over world-class Canadian and Californian researchers (who are widely viewed as global leaders in this field) working in isolation and/or in direct competition. These advantages include:

- **Building on existing expertise:** Canadian and Californian researchers pioneered the discovery of CSCs and are leaders in this rapidly expanding field. Collaborations already exist between some of these investigators and there are unique possibilities for further capitalizing on their expertise by building on the existing collaborative foundation.
- **More efficient use of resources:** A critical mass of expert researchers working in collaboration within the context of a strategic research initiative focused on specific goals allows researchers to assemble large, multidisciplinary teams with the ability to tackle complex research challenges, efficiently leverage state-of-the-art core facilities and infrastructure, thereby accelerating the pace of discovery and development.
- **More effective use of resources:** A consortium approach has the potential to focus and align research funding opportunities with strategically important research projects identified in the context of an overarching research program that experts agree will move the field of CSC research forward from discovery to pre-clinical and clinical development at a rate not otherwise possible by researchers working in isolation.
- **Enhanced capacity to build opportunities for current and future generations of cancer stem cell investigators:** Over time, the CSC Consortium will facilitate new meaningful and lasting working relationships between world leaders in the fields of normal stem cell and CSC research that would otherwise not develop given the highly competitive, individualized and localized nature of the traditional research process supported in North America. Likewise, research trainees will have unique opportunities to work in the context of large Research Teams thereby learning valuable research,

coordination, management and teamwork skills from multiple researchers in multiple institutions and across disciplines.

- **Accelerate rate and intensity of cancer stem cell research findings and their translation to clinical application, commercial products and public policy:** The consortium approach will act as a magnet opportunity, attracting world-class researchers and research trainees to CSC research. Building new Research Teams and clustering of excellence and expertise in CSC research will create conditions to trigger and accelerate additional, trans-disciplinary follow-on research and development. Research Teams will benefit significantly from the commercialization know-how of the California biotechnology sector by developing relationships with Californian CSC researchers, funding agencies, technology transfer and management experts, and venture capitalists.
- **Create growth opportunities for Canadian and Californian biotechnology:** The CSC Consortium will promote the commercialization of intellectual property to ensure economic benefits to Canada and California as well as the rapid translation of research discoveries from bench to bedside. California is home to the largest and Canada is home to the third largest concentration of biotechnology firms in the world. Fortunately, the outlook for near-term commercialization in Canada is strong because of new federal and provincial initiatives in intellectual property development and commercialization. At the Federal level, the Canadian government has announced a new Science and Technology policy, and funding for Centres of Excellence in Commercialization and Research, which both have a strong focus on commercialization. At the provincial level, a life-science commercialization development fund has recently been announced in Quebec. Similar funding vehicles are close to being launched in Ontario and Alberta. With strong science and coordination between the two principal geographic centres of CSC biology, associated clinical expertise, world-leading business experience and newly created early stage funding mechanisms, the prospects are excellent for developing an exciting wave of new biotechnology companies based on novel CSC technologies and therapeutic interventions. The latter is underscored by a swell of recent CSC patents for therapeutic claims in nine cancer types and diagnostic claims for 17 cancer types.

6. Mandate

The CSC Consortium will initially fund outstanding, large-scale CSC research programs involving centres in both Canada and California. However, it is anticipated that a sign of success of this Consortium will be the subsequent inclusion of other international partners. The CSC Consortium will encourage a diversity of initiatives spanning a wide spectrum of basic and clinical research activities, as well as pre-commercialization activities and analyses of relevant legal, ethical and policy issues. The latter may be governed and funded independently in different jurisdictions, but they will be linked by common goals and shared materials, information, protocols and principles. The CSC Consortium will thus promote synergies among participants and groups with related interests. The CSC Consortium will create new opportunities for the scientific community at large to access the results of such large-scale CSC investigations and promote the rapid translation of basic findings into clinical results through the design of efficient pre-clinical testing programs.

7. Mission

The mission of CSC Consortium-supported Research Teams is to assemble world-class investigators and physicians to discover diagnostic and prognostic CSC biomarkers and anti-CSC therapies, which will reduce the prevalence, morbidity, mortality, and social and economic burden of cancer.

8. Vision

By 2013, the CSC Consortium will have enabled Canadian and Californian Research Teams to discover new diagnostic and prognostic markers of CSCs and to identify novel therapeutic agents that target these cells as a first step to improving cancer treatment.

9. Values

The values that guide the decisions, strategies and actions of participants in the CSC Consortium are:

- Excellence: Model excellence and embrace peer review
- Accountability: Effective communication among funding agencies, scientists and the public
- Relevance: Focus on activities aligned with the CSC Consortium mission and mandate
- Creativity: Emphasize the importance of continuously searching for new paradigms and technological advances
- Relationships: Partner and collaborate with others in all we do
- Empowerment: Empower CSC Consortium participants and collaborators by exchanging knowledge and sharing expertise
- Enablement: Catalyze and support new opportunities in CSC research that would not be readily supported otherwise

10. Cancer Stem Cell Research Program Priorities

The research programs of the CSC Consortium will focus on identifying CSC biomarkers and anti-CSC therapies. State-of-the-art infrastructure will be developed to provide live CSCs for study and to translate research findings into clinical application. The support of large-scale efforts will enable Research Teams to link patient clinical data to basic advances in CSC biology by sharing cutting-edge technology platforms and pursuing common research goals. Both Canada and California operate Comprehensive Cancer Centres and Programs, which together will provide unique opportunities to accelerate the clinical evaluation of novel anti-CSC targeted therapies and the validation of CSC biomarkers.

The CSC Consortium will embrace the development of a diversity of approaches and adopt as a fundamental principle open collaboration across a wide range of disciplines including those that address ethical, legal and social issues. This emphasis is based on an appreciation of the rapidly evolving knowledge of CSCs and the development of a range of new methods applicable to their characterization (genomics, epigenomics, imaging, proteomics, microfluidics and nanotechnology). Parallel efforts by different Research Teams will stimulate comparisons and may lead to new insights that could be missed if CSC Consortium efforts were designed to minimize overlap among these research groups.

Important elements that the CSC Consortium will enable include:

- Access to bio-banks of “live-cells” consisting of annotated, high quality normal tissue and tumor samples obtained with appropriate informed consent
- Compilation of CSC definitions, frequency measurements and characterization data
- Development and access to new technologies
- Development and availability of compatible data structures
- Early and open sharing of research methods and data amongst CSC Consortium participants to accelerate the discovery of approaches to understand, prevent, diagnose and treat cancer
- Use of non-exclusive, non-transferable, royalty-free licenses that allow participants to transfer intellectual property to academic groups in the CSC Consortium
- Enhanced interdisciplinary training programs with particular emphases on physician scientists and health policy and ethics scholars
- Effective communication among funding agencies, scientists and the public

11. Mechanisms to Launch Initiatives and Promote Collaboration and Coordination

CSC Consortium funding organizations will jointly coordinate requests for applications (RFAs). RFAs will encourage the development of Research Teams with goals that can best be achieved by an integrated large-scale approach not feasible through individual investigator-initiated grants. Applications from Research Teams comprising both established and new investigators will be encouraged; specific application criteria will be developed by the funding agencies regarding requirements for preliminary data, funding levels, progress reports and deliverables. Applications may be co-submitted to the multiple funding agencies participating in the CSC Consortium. Following a competitive peer review process, the source of agency funding will be determined in accordance with the mandates of these agencies. Funding agencies will promote efficiencies through common review panels and similar reporting structures. Funding agencies will seek assurances that funded groups participate in CSC Consortium activities (i.e., annual meetings and workshops). The first CSC Consortium RFA will be launched in the Fall-Winter of 2008-09 and will include Canadian and Californian funding agencies that have expressed an interest in supporting research programs to enhance collaborations between Canadian and California scientists.

12. Research and Development Programs

12.1. Introduction

The CSC Consortium will achieve its goals by sponsoring a number of initiatives that will collectively define its research program. These initiatives will span basic to clinical research and will include developing tools, technologies and infrastructure in aid of the research programs. Training of high-quality personnel and commercialization of research findings will also constitute key components of the research enterprise.

12.2. Understanding Cancer Stem Cell Biology

There is general agreement that much of our understanding of CSC biology is relatively primitive. CSCs were discovered about 10 years ago in blood-borne cancers but only within the

last 5 years in more common solid tumors. Moreover, in most malignancies where CSCs have been identified relatively few individual tumors have been the subject of investigation. Determining how CSCs function in their environments is critical to understanding how to identify and target these cells. The availability of CSCs, especially CSC-enriched cell cultures, coupled with the results of genomic and proteomic analyses of these cells will provide a rich information database to launch new research programs. These research programs may be centered on establishing the origin of CSC, studying their progression to full-fledged malignant cells capable of metastasizing and elucidating the molecular events accompanying these processes. Identifying signalling pathways required for key stem cell processes such as survival, self-renewal and differentiation are of paramount importance. This will also require parallel efforts to identify, isolate and characterize the normal stem and progenitor cells in various tissues and the mechanisms whereby their survival, self-renewal and differentiation are regulated. Efforts to elucidate the biology of CSCs will be essential to the success of translational research activities.

12.3. Identifying Cancer Stem Cell Biomarkers and Anti-Cancer Stem Cell Therapeutics

The availability of highly enriched CSC populations from multiple diverse tumors of particular malignancies and their comparison to normal stem and progenitor cells from the same tissues will enable comparative genomic and proteomic analyses of these cells, a required first step to discover CSC biomarkers and molecular therapeutic targets. Genomic and epigenomic studies might include identifying all the genes that are expressed or differentially regulated in CSCs and learning how their transcriptomes differ between CSCs and the non-tumorigenic cancer cells from the same tumor, and between the CSCs and the normal adult stem and progenitor cells of the tissue of origin of the tumor.

Candidate biomarkers and molecular therapeutic targets can be validated using patient tumor samples and cell cultures isolated from these tumors. For example, the expression of candidate CSC biomarkers will be assessed in organ-specific tumors of a large numbers of cancer patients to ensure that they truly identify CSCs. Verified CSC biomarkers will then be linked with clinical parameters such as patient prognosis and treatment outcome to firmly establish the clinical relevance of CSCs. Similarly genome-wide libraries of interfering RNAs (RNAi) will be employed to validate molecular therapeutic targets. Validated molecular targets with druggable qualities will then be used in *in vitro* assays amenable to high-throughput screening (HTS) with compound libraries from various sources to identify lead anti-CSC agents. Lead anti-CSC therapies can also be identified by establishing CSC-enriched cell populations capable of being propagated in tissue culture, developing phenotypic screens and subjecting such cell cultures to HTS with chemical libraries.

Genomics and epigenomic datasets generated from CSCs from various malignancies will identify genes whose mutation might be implicated in the genesis or early progression of CSCs. The CSC genomics research program will be linked to large-scale cancer cell resequencing programs such as the NIH-funded project called The Cancer Genome Atlas (TCGA) project and the International Cancer Genome Consortium (ICGC) that was recently launched by funding agencies in over 10 countries including the USA (National Cancer Institute and National Human Genome Research Institute) and Canada (OICR and Genome Canada).

The management, analysis and sharing of data among researchers funded by the CSC Consortium funding agencies (and eventual dissemination to the larger research community) will require significant support to existing and/or new informatics and bio-computing teams, which will be distributed among the Canada and California Research Teams. The establishment of a data coordination centre (centralized or disseminated) that is well integrated with CSC Consortium operations at participating centres will be critical to assure secure and effective management of datasets that will be produced, exchanged and analysed by members of the CSC Consortium. Effective and interactive tools will be required to support hypothesis-driven research by CSC Consortium researchers that accommodate a range of bioinformatics skills.

13. Infrastructure Enabling Research Programs

Successful pursuit of the CSC Consortium's research and development programs will require establishing new technology platforms and tools to isolate, purify and characterize CSCs. In addition, the CSC Consortium will support new emerging technologies to enable investigation of CSCs. A partial list of shared core facilities and technology platforms required to support CSC research is listed below.

13.1. Live-Cell Bio-Repositories

The small size of most tumors at the time of their surgical removal from cancer patients coupled with the generally low frequency of CSC in these tumors is the major impediment to achieving the goals of the CSC Consortium. Hence, new infrastructure will be required to collect and store large numbers of human tumor samples from an ethnically diverse population under conditions that preserve the viability of the cells in these samples. This effort will require developing novel and standardized ways of processing fresh human tumor tissue to enable the subsequent purification of live CSCs. These cells will be essential both for their initial biological characterization and also later as pre-treatment samples to assess new candidate prognostic indicators or predictors of treatment responses. Given the importance of testing normal stem and progenitor cells in determining the selectivity of candidate therapeutic agents or targets in CSCs, it will be essential to also bank normal tissues. The latter may be achieved by adopting the Rapid Autopsy Program, which has recently been developed at Stanford and elsewhere in California. This program can serve as a valuable guide to Canadian efforts to design and implement a similar system with appropriate handling of the logistics as well as associated social, legal and ethical issues.

To be maximally useful, it will be critically important that Live-Cell Bio-Repositories are equipped with robust systems to link clinical and pathological data to each stored tumor sample. The reason for this is that malignancies may be continuously diversifying at the CSC level. Thus, the CSCs in any given patient are likely to be heterogeneous and display different phenotypes, treatment responses and other biological properties at different times or at different sites, or perhaps within the primary tumor itself. These data storage and retrieval systems will also need to allow both prospective recording of data and the ability to add and search for accrued data retroactively. Standardization of prospective data entry and the use of common software programs will be particularly important for identifying samples with a defined set of features among bio-repositories and hence facilitate access to those of interest for particular studies. The ability to perform retrospective data searches will also allow correlation of analyzed samples with clinical outcomes and interrogation with more detailed pathologic data. The development of

these systems will require careful consideration of the ethical and legal issues around patient privacy and informed consent, which must be compatible with both Canadian and Californian standards.

13.2. Xenotransplantation Core Facility

Another key infrastructure component will be a Xenotransplantation Core Facility to provide immune-compromised experimental animals at minimal cost to Research Teams. Long-lived strains of highly immune-deficient mice allow human tumors to be propagated as xenografts with high efficiency. Other less expensive xenogeneic hosts (e.g., zebrafish) genetically engineered to improve the support of human tissues will also be developed. Adjacent facilities for monitoring tumor growth by various imaging methods will also be required. Xenotransplant systems are essential elements to: develop CSC assays; obtain expanded CSC populations; develop novel CSC purification strategies; examine the biological properties of CSCs; and as model patients to assess *in vivo* responses to new therapeutics developed to target CSCs.

13.3. Cancer Cell Culture Platform

The Consortium will need to establish core cell culture facilities and support new initiatives that exploit, advance and develop procedures for detecting, maintaining and expanding CSCs *in vitro*. Both suspension and stromal-based culture methods that allow some types of CSCs to grow *in vitro* have been pioneered by Canadian scientists. These will provide important opportunities to develop more rapid assays for quantifying CSC frequency, and for assessing their responses to factors that may induce their death or differentiation, or alternatively allow their controlled expansion. Several groups in Canada have developed gene transfer and Tat-protein methods for expanding normal hematopoietic and leukemic CSCs *in vitro*. These and other novel culture strategies (e.g., microfluidics systems able to handle tens of thousands of micro-cultures in a postage stamp area) will be crucial to many aspects of CSC investigations. The latter include generating sufficient CSCs and suitable culture conditions to identify new anti-cancer drugs in cell-based screening campaigns with chemical compound libraries, as well as experiments designed to better understand CSC biology.

13.4. Cancer Stem Cell Purification Facilities

The purification of CSCs for their specific investigation is paramount to any means of directly analyzing these cells. Whereas methods for purifying CSCs from blood-borne malignancies (leukemia and lymphomas) are well established, the means of purifying CSCs from solid tumors are far less developed and fraught with difficulties. Improved methods of dissociating solid tumors and cryopreserving CSCs are needed. The CSC Consortium will support facilities dedicated to solid tumor cell fractionation to obtain homogeneous populations of CSCs. Achieving this objective will require a concerted effort to identify new CSC surface markers fuelled in part by transcriptome analyses. This facility will also be central to producing antibodies to cell surface proteins to enable CSC purification and to developing new therapeutic antibodies to proteins essential for CSC survival.

13.5. High-Throughput Screening and High-Content Imaging Facilities

Screening assays will be developed and cell-based HTS implemented using chemical libraries from various commercial and academic sources. Central to the HTS activities will be the availability of CSC-enriched cell populations. Screening campaigns will be performed at HTS

centers supplemented with infrastructure tailored for CSC screens. Chemical hits that kill, block the proliferation or induce the differentiation of CSC (thereby abrogating their tumorigenicity) will be identified. Promising “hits” (i.e., compounds that look promising as cancer drugs), will enter a drug-development stream to include medicinal chemistry/ADME (absorption, distribution, metabolism, excretion)/toxicology (TOX) to identify lead compounds for pre-clinical and clinical development. HTS will also be used in conjunction with iRNA to identify and/or validate candidate therapeutic targets fingered by gene expression profiling of CSCs. Alternative routes to developing new therapies to CSC targets will also include developing specific antibodies, oncolytic viruses and peptides (i.e., peptide aptamers) to CSCs.

13.6. Imaging Facilities

Rapid advances in imaging technologies (Positron Emission Tomography [PET] and Magnetic Resonance Imaging [MRI]), which use labelled probes to identify specific cells and their environment will be used to study CSCs. The availability of CSC biomarkers in conjunction with imaging technology platforms will enable CSCs to be identified among the various cells in the tumors of experimental animals and human subjects, thus providing significant new knowledge about CSC biology and the efficacy of novel therapeutic agents targeting these cells.

13.7. Data Compilation and Management Systems

As noted above, data acquisition and management will be a requisite feature of many of the scientific activities of the CSC Consortium. In addition, real-time access to a shared database will be an important and defining goal of the entire operation requiring development of appropriate software, program maintenance and support for data entry, quality assurance and protection of patient confidentiality.

13.8. New Technology Platform Development

The development of new technology platforms and tools will facilitate both basic and clinical CSC research. The CSC Consortium will promote developing new tools and technologies to: characterize single cells (genomics, proteomics, etc.); efficiently propagate and expand CSCs both *in vitro* and *in vivo*; purify large numbers of CSCs; develop antibodies to cell surface proteins and intracellular biomarkers; assess the status of signalling pathways in CSCs; and measure CSC frequency, genetic instability and differentiation, to name a few.

13.9. Ethical, Legal and Social Issues (ELSI) Support and Research

Both Canada and California have strong ELSI communities that have been involved in research that is highly relevant to the proposed activities of the CSC Consortium. In Canada, for example, Genome Canada and the Stem Cell Network – both CSC Consortium funding partners – have extensive ELSI programs that involve numerous interdisciplinary research teams. The CSC Consortium can draw upon this expertise to facilitate accountability and satisfy regulatory standards (e.g., consent and research ethics review); and to take on original research in relevant ELSI areas. As noted throughout the proposal, the planned research activities may generate a variety of legal, ethical and regulatory issues, including those associated with clinical trials and the formation of bio-repositories. In addition, the CSC Consortium commercialization mandate creates new opportunities to explore the challenges associated with industry-funded research, such as models of governance and conflicts of interest.

To ensure the integration of ELSI issues, research teams will be expected to either include an ELSI research component that will be supported in the context of individual projects/programmes of research or link with an existing ELSI team.

In addition, the CSC Consortium will establish an ELSI Advisory Committee that can provide independent advice and guidance to the Research Management Committee and Board of Directors with respect to ELSI issues and can facilitate Consortium-wide coordination of ELSI issues arising in the context of CSC Consortium supported research. The ELSI Advisory Committee will also facilitate links between CSC Consortium research teams and the wider ELSI community. Finally, it is envisioned that the CSC Consortium's ELSI Advisory Committee will have a modest discretionary budget enabling it to commission small, translationally relevant position papers and workshops as CSC Consortium-supported research results move towards clinical application.

14. Clinical Applications of Cancer Stem Cell Research

An important aspect of the CSC Consortium is to ensure that the results from basic research are rapidly translated to the clinic. The CSC Consortium will promote phase I and II clinical trials as lead anti-CSC therapies and CSC biomarkers are discovered, and deemed suitable for testing in patients. The Research Teams will work closely with research ethicists to develop appropriate processes to ensure an efficient and ethical trials process. The latter would include ethicists working closely with physicians.

Basic research on CSCs may have an impact in a variety of areas including:

- Improved *diagnosis* of malignancies and means of distinguishing pre-cancerous and cancerous conditions
- Improved *prognosis* regarding outcomes to currently available treatments
- Improved *understanding* of patient and familial susceptibility to cancer leading to improved early detection and prevention strategies
- Directing patients to different forms of currently available *therapy* so that cancer treatment can be better individualized for patients leading to improved outcomes
- Assessing response to *treatment* based on persistence of CSCs so that subsequent patient follow-up and additional treatment can be improved
- As new therapies are discovered and deemed suitable for testing in patients, the CSC Consortium will work with collaborative clinical groups to develop new generations of treatments for cancer, which attempt to *change outcomes* by directly targeting CSCs, which may sustain the disease and be responsible for recurrence.

Through all these mechanisms, work on CSCs may lead to both near-term and long-term improvements in cancer care and outcomes.

The CSC Consortium will invest significantly in translational activities that investigate the clinical relevance of CSCs and accelerate the evaluation of CSC-specific therapies. For example, CSC Consortium support will enable teams to determine whether the abundance of CSCs in tumors account for tumor aggressiveness, metastases and relapse following therapy. The availability of validated CSC biomarkers will make this task significantly simpler than is now

possible; currently, CSCs are identified by transplanting varying numbers of tumor cells into immune-compromised mice, an expensive and time-consuming activity.

At this time neither current nor new anti-cancer therapeutics in clinical trials are being evaluated for their capacity to eradicate CSCs. Prior to assessing new agents in cancer patients, the CSC Consortium will work with cancer centres and bio-pharmaceutical companies developing new drugs and conducting clinical trials to evaluate their efficacy in targeting CSC.

Furthermore new anti-CSC agents (i.e. antibodies, oncolytic viruses and small molecules) identified in the discovery and characterization phases of the proposed research program will undergo rigorous pre-clinical evaluation to obtain comprehensive ADME and TOX profiles, prior to filing Investigational New Drug (IND) applications with the FDA.

Candidate therapeutics to be entered into clinical trials may include existing drugs now used for indications other than cancer. Indeed several CSC investigators have discovered new agents and existing drugs that affect hyper-activated molecular pathways in CSCs. These novel agents are investigational in nature and have not been tested in man, and hence will require detailed medicinal chemistry, manufacturing, and control information, as well as ADME and TOX studies. Coordination among CSC laboratories, partner biotechnology firms and clinical trials centres will accelerate these processes by months, if not years.

Both Canada and California host Comprehensive Cancer Centres with world-leading expertise and infrastructure for evaluating candidate CSC biomarkers and testing new cancer therapies, including “First-in-Man” studies (i.e., the first introduction of a new drug in human subjects). Networking among cancer centres in university hospitals provides extensive resources, such as biomarker investigations, state-of-the-art imaging, molecular pathology, pharmacogenomics and other technologies that allow rapid monitoring of tumor response. The availability of these cancer centres will provide unique opportunities to study novel CSC therapies and to understand the response of CSCs to these treatments in patients.

15. Training of Highly Qualified Personnel (HQP)

Training of HQP will be an integral component of the research programs. CSC researchers in both jurisdictions have an outstanding record in training HQP, who include undergraduate and graduate students, post-doctoral fellows and research assistants and associates. Many of their graduates have gone on to productive careers in academia or the bio-pharmaceutical industry.

The expansion of CSC research will require new funding for trainees at all levels. The CSC Consortium will also provide a platform for workshops, conferences and trainee exchanges between the leading laboratories of the field, enhance knowledge transfer and make the leading basic, translational and clinician scientists accessible to all trainees. Workshops may include instruction in new technologies, procedures and CSC isolation. Trainees will also be exposed to hands-on training through student exchanges between laboratories. Conferences will provide opportunities to exchange ideas and keep abreast of research that is rapidly progressing in the field. Collectively these training opportunities and means for knowledge transfer will result in enriched environments within which to train HQP for both the academic and industrial sectors. In this regard, training of HQP through research has long been known to be crucial for the

development of the biotechnology industry, which will be an active partner in the growth of the CSC Consortium. The CSC Consortium also will invest in an outreach initiative to enhance public awareness of advances made in the field. Attempts to extend understanding of CSC to medical student curricula, and to residency and fellowship training programs will be pursued, and efforts to provide educational materials and interactive opportunities for students and teachers at all levels as well as the public will also be undertaken, with assistance from the Consortium Secretariat.

16. Commercialization Strategy

A strategic priority of the CSC Consortium is to enhance the value of intellectual property (IP), which will arise from the research programs described above. These collaborative research programs led by world-class scientists and clinicians are expected to significantly enhance the scale of valuable IP with the potential for broad alliances with the pharmaceutical and medical device businesses as well as launching new start-up companies. The CSC Consortium does not intend to take an ownership participation in IP arising from the research programs; IP ownership will reside with the inventor and/or his/her institution. Several partners in the Consortium will, however, play an active role in the development of IP by funding proof-of-principle (POP), Proof-of-Concept (POC) and validation studies (i.e., potentially supported by the Stem Cell Network and the OICR through its Investment Commercialization Program).

Equally important, the CSC Consortium can position itself as a vehicle to coordinate commercialization interactions and to secure investments. The Steering Committee believes that it will be essential to work proactively with industry and the venture community to promote strategic industry investments in both Canada and California. Some specific examples of initiatives that the scientific community will focus on are:

- Determine the feasibility of setting up a structure to enhance opportunities for IP bundling
- Develop a strategy to increase the visibility and credibility to the investor community to secure funding for commercialization
- Support IP development related to biomarkers and therapeutic targets by collaborating to develop supplementary and complementary preclinical and clinical data for CSCs from tissues of different origin
- Expand and accelerate the testing of novel prototype diagnostic and imaging devices
- Identify opportunities for early stage research collaborations that more efficiently lead to joint IP.

Whereas IP ownership will continue to reside with the inventor and/or the host institution, most Technology Transfer Offices lack CSC-specific scientific knowledge and relationships with biopharmaceutical companies and investors in the CSC space. Therefore, to support the researchers and university based Technology Transfer Officers in the process of commercializing CSC Consortium-supported research outcomes, the CSC Consortium will appoint a number of Commercialization Officers (COs). COs will have both the scientific and business knowledge to act as expert advisors and will be dedicated to working with CSC Consortium funded researchers and institutions on a project (Research Team) specific basis. Initially it is recommended that there be only 1 or 2 COs in the CSC Consortium who will focus on existing IP that is ready for commercialization. Over time the number of COs will increase as new and valuable IP is

developed. It is envisioned that the support of COs will come directly from funding agencies as a small percentage of the grant moneys allocated to specific Research Teams. COs will provide leadership and coordination to develop a strategy to work with business receptor networks, principally the bio-pharmaceutical sector, for primary investments and clinical trials.

Specifically COs will:

- Promote collaboration between CSC Consortium members in Canada and in California (Intra-CSC Consortium collaboration)
- Support IP bundling and identify new opportunities for partnering, licensing and spin-out entities
- Gain in-depth knowledge of, and develop deep relationships with, the needs and interests of biopharmaceutical companies and the investment community
- Communicate knowledge to CSC Consortium researchers and funding agencies
- Bring business expertise to CSC Consortium members helping them to license or partner IP
- Increase the visibility and credibility of the CSC Consortium and its researchers to the international scientific and investment community
- Develop contract research and/or service models for CSC Consortium members to work with external collaborators (for example, a biopharmaceutical testing pipeline focused on CSCs).

There will be a focus on developing a strategy to work with the business receptor network principally the bio-pharmaceutical sector for primary investments and to develop clinical trials. There is strong interest from the biopharmaceutical sector in CSCs. For example the following companies are involved in CSC research or are contemplating sponsored research projects with Canadian and Californian CSC researchers: OncoMed Pharmaceuticals; ChemGenex; Geron; Genentech; Raven Biotechnology/MacroGenics; Immunocellular Therapeutics; Novocell; ARIUS (Roche); GlaxoSmithKline (GSK); Micromet, Inc.; Stemline Therapeutics; and Aggregate Therapeutics, Inc.

Venture capital investors, such as StemCell Ventures and Forward Ventures, are also likely to participate as discoveries mature. California is the home of the largest VC community in the world (over 500 firms) and Canada has a very active though smaller industry with many life science investors.

As indicated in Section 14, the CSC Consortium will participate with the bio-pharmaceutical industry in setting up a clinical trials coordination function for CSC investigational treatment studies. This will be a considerable investment from this sector in both Canada and California.

Roughly 10% of the CSC Consortium budget should be targeted for early phases of the commercialization process including support for specialists to coordinate commercialization activities. It is anticipated that this investment will yield multiples in financial benefits for both Canada and California. This is because start-up biotechnology firms will have to locate close to the Research Teams, as evidenced by the location of biotech firms in California, to take full

advantage of rapidly evolving biological understanding and to have access to state-of-the-art research infrastructure.

To maximize the full value of academia-based intellectual property sufficient time for the development of intervention strategies targeting CSCs must be allowed. Here again the importance of sustained funding over an extended period is critical to the mission of the CSC Consortium. In addition, sustained research funding will be a pivotal factor in attracting industrial and venture funding in both Canada and California.

17. Governance and Management Structure

The proposed organizational structure (see Figure 3, below) will facilitate the basic and clinical translational activities of world-leading Research Teams and Technology Platforms/Facilities. The CSC Consortium has been established as a not-for-profit corporation with the following management structure:

17.1. Board of Directors

The Board comprises representatives of the major funding agencies (both governmental and non-governmental) and may also include research and business leaders from the international community and patient advocates. Criteria will be developed to define the composition, selection and succession of board members. The Board is responsible for overseeing the overall scientific direction, setting specific goals and milestones and fiscal management. One of the main objectives of the scientific strategy will be the dissemination of new knowledge to ensure that new cancer therapies and improvements to existing therapies are quickly commercialized. The Board will also be responsible for overseeing the development of Consortium policies covering: confidentiality and conflict of interest, partnership policies and agreements, intellectual property, data release and resource sharing.

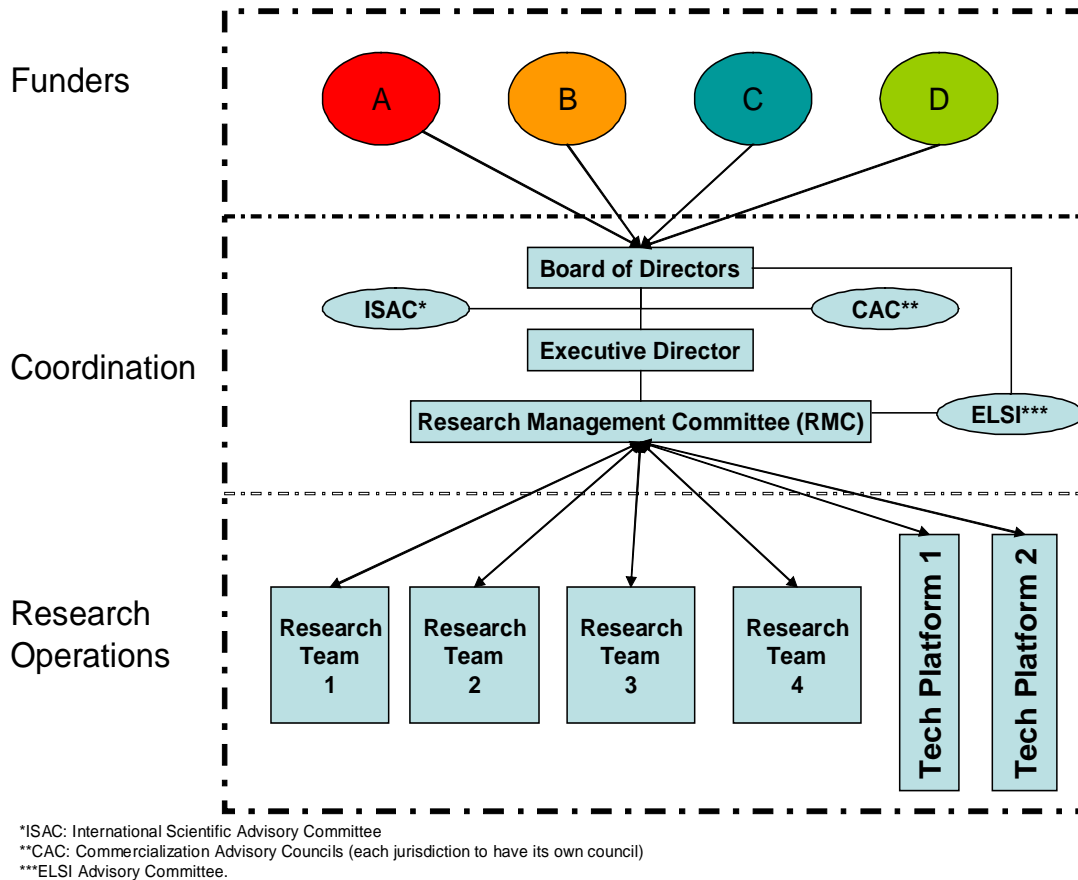
17.2. International Scientific Advisory Committee (ISAC)

An ISAC will be independently constituted to provide informed, critical and formative advice and guidance to the Board on scientific directions.

17.3. Commercialization Advisory Councils (CAC)

Because of the importance of commercialization for the CSC Consortium, Commercialization Advisory Councils (CAC) comprising leading members of their respective industrial and venture capital communities should be established in Canada and California. The primary role of each CAC, one in each jurisdiction, would be to provide recommendations on developing commercial opportunities in cooperation and proximity to the Research Teams and Technology Platforms/Facilities. A commercialization manager will be appointed in both Canada and California for coordination among the CACs and between CACs and the CSC Consortium.

Figure 3: CSC Consortium Organizational Structure



17.4 Executive Director (ED)

The ED will be responsible for overall coordination between the various Research Clusters and Technology Platforms (see Section 17.7) of the Consortium, and in establishing operational policies as prescribed by the Board. The ED will be supported by a relatively small **Secretariat**, which will be responsible for administrative matters including coordination, statistical tracking and reporting for accountability purposes and serving as a communication hub for the CSC Consortium at both the national and international level. In addition, the Secretariat will oversee activities with respect to building linkages with new stakeholders.

17.5. Research Management Committee (RMC)

An RMC will be established with representation from Research Teams and Technology Platforms/Facilities to ensure that milestones are achieved and that research projects are appropriately coordinated across Research Teams and Technology Platforms/Facilities.

17.6. Ethical Legal and Social Issues Advisory Committee (ELSI)

An ELSI Advisory Committee will be established to provide independent advice and guidance to the Research Management Committee and Board of Directors with respect to ethical, legal and social issues.

17.7. Research Teams and Technology Platforms

The CSC Consortium will have well-defined research and technology development programs organized as Research Teams and Technology Platforms/Facilities. A Research Team will either be a regional or thematic grouping of investigators. The Research Teams will consist of researchers, including biologists, bio-informaticians, clinician scientists, surgeons, pathologists and technical experts. Technology Platforms/Facilities will be closely linked to the research programs and will focus on technology development and automation leading to increased capacity for research activities. Each Research Team or Technology Platform/Facility will identify a Leader for coordination purposes with the CSC Consortium. The Research Teams and Technology Platforms/Facilities will be funded based on competitive peer review, which will be undertaken by CSC Consortium funding agencies and will include inter-agency participation.

18. Proposed Budget (2009-2014)

Sustained funding will be the key to the success of the CSC Consortium. A key operational principle for the CSC Consortium will be that funding organizations will disburse funds according to their respective mandates and jurisdictions. This implies that funds will not flow through a central organization. Instead funds will flow from a funding agency to the desired Research Team or Technology Platforms/Facilities. Furthermore, it is anticipated that, where feasible, joint-funding mechanisms will be set up between complementary funding agencies in each jurisdiction. The CSC Consortium will facilitate coordination among its funding partners to ensure that essential expertise is developed and that technological resources are fully utilized. It is anticipated that funding of the proposed research programs and technology platforms and facilities will require a minimum budget of \$500 million (CDN) over a 5-year period (Table 1).

Canadian funding is anticipated to be “modular,” meaning that it will be directed for specific periods and towards discreet components of the CSC Consortium. Overall, 50% of the funding would come from Federal sources and 50% would come from the provinces and philanthropic non-governmental organizations. Several funding agencies have already begun to collaborate to create a framework for this new structure – Genome Canada, the Canadian Institutes of Health Research, the CFI, and the OICR, to name a few. Additional public and private entities, such as provincial funding agencies, cancer charities and pharmaceutical and biotechnology companies based in Canada and California, are expected to join the CSC Consortium providing experience and funding in their areas of expertise. For example, Genome Canada would support initiatives such as the sequencing of the CSC genome. The Canadian Institutes of Health Research will support the CSC biology and translational clinical research and training programs. The CFI will play a major role with its provincial partners in supporting infrastructure needs in Canada from its existing programs. Commercialization support may come from the newly announced Centres of Excellence in Commercialization and Research.

Table 1 CSC Consortium Budget Outline (2009-2014)

Targeted sustained funds over five years - spending to be divided between Canada and California	Budget Allocation	Million \$ CDN
1. Research Teams operating and training funds for HQP	30%	150
2. Research infrastructure (space, equipment, maintenance and support costs), including tissue/live cell banking,	27%	135

Targeted sustained funds over five years - spending to be divided between Canada and California	Budget Allocation	Million \$ CDN
science and technology platforms (genomics, proteomics, high-throughput screening, bioinformatics, etc.)		
3. Clinical Translation Programs	30%	150
4. Innovator, Accelerator and Commercialization Opportunities	12%	60
5. Secretariat – Administrative and Communications Hub	1%	5
Total	100%	\$500

Strong participation is anticipated from several Canadian provinces. There is confirmed participation from the OICR of \$30 million over five years. The Alberta Heritage Foundation for Medical Research and the Fonds de Recherche en Santé du Québec (FRSQ) are also in the process of exploring whether or not support for an undertaking such as described herein fits with their strategic priorities. In addition, support can be sought from other philanthropic organizations in Canada such as the Terry Fox Foundation and the Michael Smith Foundation for Health Research.

Funds for participation of California in the CSC Consortium could come from several sources including CIRM, philanthropic foundations, health charities, individual donations, patient driven research organisations, university funds and from California’s extensive biotechnology sector. In the November 2005 state election, California voters approved \$3 billion over 10 years to support stem cell research through CIRM. As indicated in the commercialization section, this strategic plan anticipates significant interest from the private sector in the downstream development of intellectual property and human intervention strategies.

19. Deliverables

The CSC field holds great promise for ushering in a new era of cancer diagnostics and treatments. Some areas are more advanced (such as leukemia) but many others are in an embryonic state. The CSC Consortium is poised to capitalize on both the advances as well as the challenges to make major advances in understanding CSC biology, identifying new targets for therapy and in some of the more advanced areas, initiating early clinical trials designed to improve cancer care outcomes. At the completion of the first phase of this project in 2013, the CSC Consortium will aim to have accomplished the following goals:

- Procedures for collecting large volumes of tumor samples established
- Methods for isolation of progressively well characterized populations of potential CSCs developed and validated
- Banks of live tumor cells for CSC research with direct and efficient linkage to the associated clinical information created
- Web-based methods for sharing data, methodologies and standard operating procedures among CSC Consortium researchers
- New cost effective and efficient xenotransplant models for expanding and assessing CSCs developed
- *In vitro* methods for expanding CSCs for genomic/proteomic profiling, drug screening efforts and other studies established and validated

- Lead candidate compounds with selective-CSC activity identified
- Initial commercial and regulatory partnerships needed to shepherd candidate compounds into the clinic established
- Suitable genomics/proteomics technologies for analyzing small numbers (hundreds to thousands) of cells developed and applied to CSCs
- Integrated tumor groups established to include scientists, pathologists, clinicians and others aimed at developing improved approaches to accessing and studying CSCs as well as the first generation of CSC-based clinical trials instituted
- First early phase clinical trials attempting to validate CSC-specific information in cancer diagnosis, prognosis and therapy underway
- Groups of ethicists, legal experts and others created to improve education of the public and policy makers about issues related to tissue collection and clinical information and tissue exchange established
- A first cohort of next generation of scientists and clinicians trained in CSC biology and the use of this knowledge for clinical application established.

20. Timeframe

The Canadian scientific community is preparing to launch the collaborative research program under the auspices of the CSC Consortium in partnership with member organizations (to date Genome Canada, CFI, CIHR, SCN and OICR) in the Winter of 2008/09.

Appendix A: Cancer Stem Cell Consortium Steering Committee Membership

CSC Consortium Steering Committee Members				
Last Name	First Name	Title/Institution	Prov/State	Country
Caulfield	Tim	Canada Research Chair in Health Law & Policy Research Director, Health Law Institute Professor, Faculty of Law, Faculty of Medicine & Dentistry University of Alberta, Edmonton	AB	Canada
Crooks	Gay	Professor, University of Southern California (USC) Gene Therapy, Pediatrics The Saban Research Institute Children's Hospital, Los Angeles	California	USA
Dick	John	Senior Scientist Division of Stem Cell and Developmental Biology Toronto General Research Institute Affiliate Scientist Division of Cellular & Molecular Biology Ontario Cancer Institute (OCI) University Health Network, Toronto	ON	Canada
Eaves	Connie	Director, Department Head, Terry Fox Laboratories, Vancouver	BC	Canada
Hassell (CHAIR)	John	Professor and Director Centre for Functional Genomics Department of Biochemistry and Biomedical Sciences McMaster University, Hamilton	ON	Canada
Hudson	Tom	President and Scientific Director, Ontario Institute for Cancer Research, Toronto	ON	Canada
Kung	Hsing-Jien	Director, UC Davis Cancer Center Basic Sciences Deputy Director, UC Davis Cancer Center and Professor, Biological Chemistry University of California, Davis	California	USA
Sauvageau	Guy	Canada Research Chair in the Molecular Genetics of Normal and Cancer Cells Université de Montréal, Montréal	QC	Canada
Smith	Clay	Director, Leukemia/BMT Program of British Columbia Senior Scientist, Terry Fox Laboratories Vancouver	BC	Canada
Weiss	Sam	Director Hotchkiss Brain Institute Professor Department of Cell Biology & Anatomy/Pharmacology & Therapeutics Member, Genes and Development Research Group Faculty of Medicine	AB	Canada

CSC Consortium Steering Committee Members				
Last Name	First Name	Title/Institution	Prov/State	Country
		University of Calgary, Calgary		
Weissman	Irv	Director, Stanford Institute for Stem Cell Biology and Regenerative Medicine Director, Stanford Comprehensive Cancer Center Director, Stanford Ludwig Center for Stem Cell Research Professor of Pathology and Developmental Biology Stanford University School of Medicine, Menlo Park	California	USA
Witte	Owen	President's Chair in Developmental Immunology, Microbiology, Immunology & Molecular Genetics Distinguished Professor, Microbiology, Immunology & Molecular Genetics Professor, Molecular & Medical Pharmacology Member, California NanoSystems Institute University of California, Los Angeles	California	USA