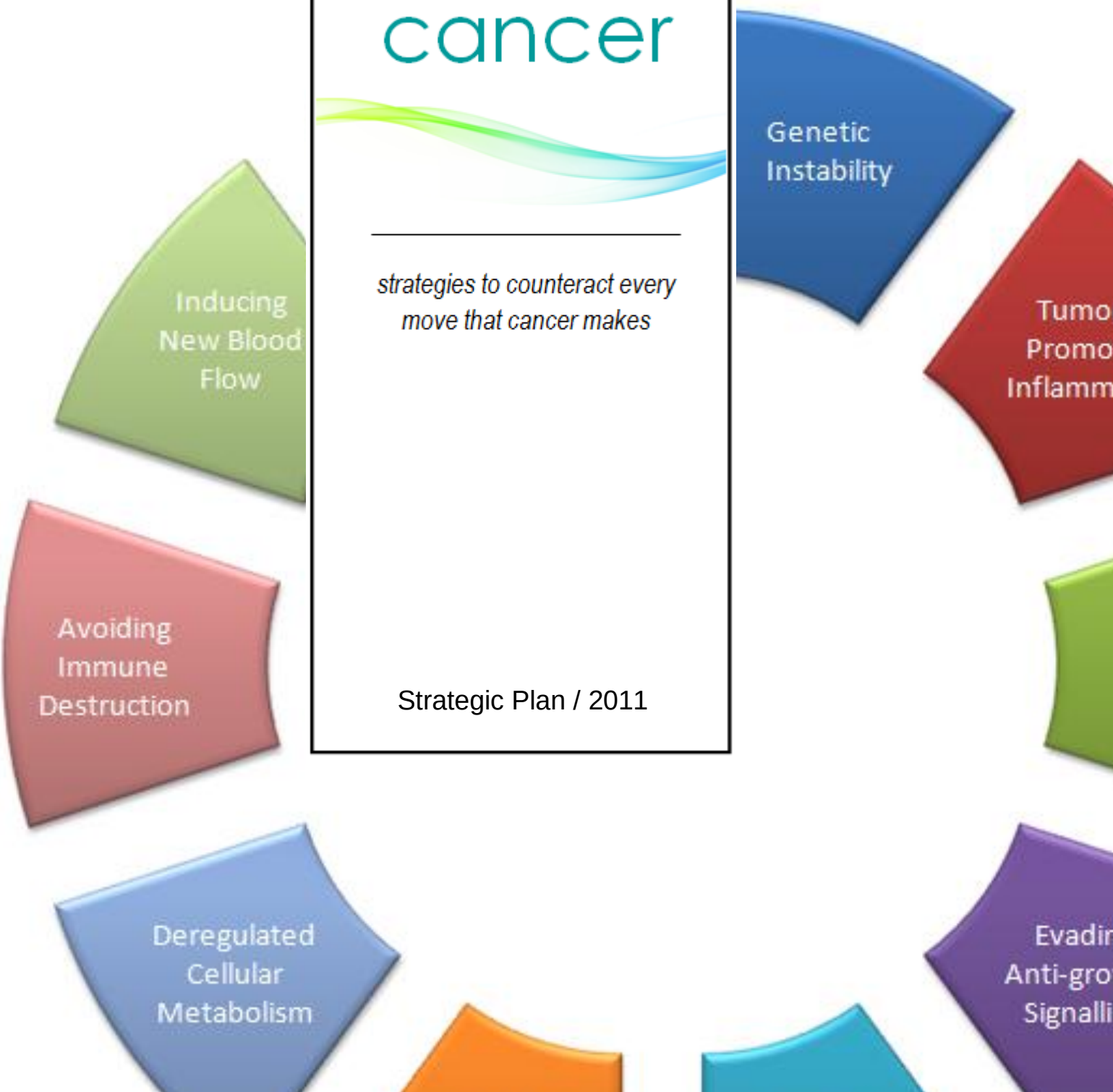
getting to know cancer

strategies to counteract every move that cancer makes

Strategic Plan / 2011



New science brings a fresh perspective

The World health Organization International Agency for Research on Cancer (IARC) has indicated that cancer has stubbornly persisted as one of the leading causes of death worldwide. And the global burden of cancer has more than doubled in the past 30 years, with the majority of that burden now being shouldered by low-medium resource countries that are ill-equipped to respond to the problem (World Cancer Report, 2008).

Fortunately, there have been some remarkable advances in the science of cancer in the past two decades and that has given us some hope. We now know that only a very small percentage of cancers are caused by hereditary defects. Most cancers are caused by environmental exposures that people encounter on a day-to-day basis. Many factors contribute to this complex disease including various types of radiation, man-made chemicals (e.g., chemicals in certain foods, pesticides etc), and a number of biological agents (e.g., viruses, bacteria etc.). These disruptive exposures result in insults to cells within the body and/or they interfere with chemical signalling within and between cells. In fact, we now understand in precise biochemical and genetic terms, how many of these agents are involved in disease causation.

However, our collective efforts to prevent and treat cancer to date have not been nearly as successful as most of us had hoped. Part of the difficulty in making progress on these fronts has been due to the fact that cancer is much more complex than anyone ever envisioned. In essence, all cancers are comprised of a grouping of misbehaving (immortalized) cells that are growing, dividing and replicating repeatedly (thereby forming tumours). And while there are many types of cancer, all cancer types are known to share ten common ***hallmark*** characteristics:

1. The cells in cancer have become genetically unstable;
2. They are frequently found in an inflammatory environment;
3. They are growing uncontrollably;
4. They are able to avoid/ignore anti-growth signalling;
5. The cells have a self-destruct mechanism that is not functioning properly;
6. The cells have bypassed a replication limit that is not functioning properly;
7. The metabolic machinery with the cells is not functioning normally;
8. The cancerous cells are able to evade immune system surveillance;
9. Cells that are oxygen-deprived within a tumour will signal for new blood flow; and
10. The cancerous cells invade nearby tissues, and ultimately enter the blood stream or lymph system, which allows them to spread and colonize in other parts of the body.

Hanahan, D, and Weinberg, R - The Hallmarks of Cancer: The Next Generation
Cell - 4 March 2011 (Vol. 144, Issue 5, pp. 646-674)

This elegant and holistic framework appears relatively straightforward, but it represents the culmination of many decades of research, and it belies the underlying complexity of the disease. There is actually a great variety of aberrant genetic pathways that can be used to achieve each of these hallmarks, and these different pathways can vary significantly in the cells within any given cancer, and when comparing various instances of cancer. Nonetheless, the framework helps us to visualize these discrete, but interrelated, characteristics that collectively allow the cells to grow and divide with impunity. Also, two substantive conclusions can immediately be drawn from this enhanced understanding of the disease.

Environmental Exposures and Regulation

The first conclusion relates to the current regulatory approach that has been used to identify cancer-causing agents within the environment. Historically, regulatory agencies around the globe have sought to identify and limit our exposures to carcinogens (i.e., individual agents that can cause cancer). However, as the decades have passed, we have come to realize that relatively few chemicals are complete carcinogens (i.e., have the potential to enable all of these hallmarks on their own). Rather it is now known that many of the hallmarks of cancer can be independently enabled by individual

chemicals, and that fact changes everything. While the identification of complete carcinogens will always be an important activity, we also need to be seriously concerned about the ways in which exposures to combinations of disruptive, but otherwise non-carcinogenic, environmental agents are able to act in concert with one another to instigate the disease.

Unfortunately, regulatory systems around the globe are lagging behind the science in this regard, and most of them simply do not have policies that address the carcinogenic effects of the many individual chemical exposures that we face. Most existing regulatory agencies still rely on the identification of "mutagens" through laboratory screening (i.e., search for carcinogenic agents that cause genetic damage/instability, the first hallmark noted above), and they typically rely on feeding studies aimed at finding individual agents that can cause cancer in small mammals (i.e., mice and rats). Most of these agencies also have methods to determine the extent to which the population is exposed to any of the agents that appear to be complete carcinogens. However, now that we understand that each of the hallmarks of cancer can be instigated by individual chemicals, it has become obvious that exposures to complete carcinogens are only the tip of the iceberg.

In other words, the hallmarks framework illustrates that we need to also be concerned about exposures to non-carcinogenic agents that can disrupt the cellular machinery that is associated with any number of these hallmarks, because a multitude of exposures of this nature can easily instigate cancer. This requires a much more nuanced appreciation of the complexity of the disease (from a regulatory perspective), but it is an issue that must be addressed quickly if we really hope to protect the public from environmental exposures that can cause cancer.

To that end, our top priority needs to be to identify disruptive agents that can disable or suppress our own cancer defence mechanisms. Our own cancer defences are so effective that a large percentage of people who are routinely exposed to known carcinogens (e.g., long term smokers who do not get cancer) are still able to fend off the disease. And an analysis of the various hallmarks of cancer shows us that there are many lines of defence (i.e., DNA repair, inflammation suppression, anti-growth mechanisms, programmed cell death, cellular replication limits and several immune system components) that have been disrupted, blocked, suppressed, breached or somehow overwhelmed in every type of cancer. Yet, we have very few regulatory measures that actually focus on preventing population-level exposures to chemicals or other agents that have the ability to specifically disrupt these mechanisms. So this is a critical regulatory gap that needs to be immediately addressed.

Therapeutic Options

The second important conclusion that can be drawn from the hallmarks of cancer framework relates to the new chemotherapy options for cancer that are being researched and developed for clinical use.

Some of the early approaches to cancer treatment focused mainly on the eradication of the cancerous cells by removal or obliteration. For example, surgery, radiation and cell-killing chemotherapy (aimed at tumours) are all strategies that have been used for many years. However, with an enhanced understanding of the mechanics of the disease, somewhat less-toxic therapeutic options that target the individual mechanisms within the hallmarks of in cancer framework are being aggressively pursued. Some of these therapies are aimed at specific receptors on the surface of cancer cells, while others target specific pathways inside of these cells. And, in some instances, these therapies have been quite successful.

Unfortunately, however, cancerous cells are prone to ongoing mutation, and therefore most cancers are comprised of a variety of subpopulations of mutated cells. Consequently, relapses are still quite common after treatment with targeted therapy, even if the disease has been put into remission. This is because targeted therapies tend to only be effective on certain subpopulations of cells, while other (unaffected) subpopulations use alternate pathways to achieve the same hallmark characteristics.

This has resulted in a considerable push towards "personalized medicine", where rapid diagnostics are to be used to identify the most prominent subpopulations of mutated cells in any given instance of cancer, and tailored therapies are then to be used to attack those cells. Yet, this approach is not without its challenges. There are many possible subpopulations, or strains of mutated cells that are known to exist, which means that many tailored therapies will ultimately be needed, and it isn't at all clear that we will ever be able to address the many subpopulations of cells that will need to be reached. Furthermore, not all cancers are easily characterized because ongoing mutations are somewhat random, so knowing which therapy to use will likely never be a straightforward decision. Furthermore, the therapies that are being developed are destined to be used by smaller and smaller numbers of patients, who will have very narrowly defined set of needs, so that is going to continue to drive the cost of therapy upward (as research and development costs will need to be recovered from smaller groups of patients).

An attractive alternative (or possible complementary) approach, would be to design a broad-spectrum therapy or regimen that could act on many pathways simultaneously (i.e., act favourably on many different strains of mutated cancerous cells). Much in the same way that we have come to rely on broad-spectrum antibiotics to suppress rapidly mutating bacteria in many infections, we need a broad-spectrum of mechanistic action in cancer therapy if we really want to address the many different subpopulations, or

strains of mutant cells that occur in the many different types of cancer that are seen in the clinic.

Combination chemotherapy is a strategy that is already used by some physicians in certain instances to reach multiple cellular targets. However the narrow margins of safety associated with most synthetic chemicals in use today severely restricts the number of therapies that can be realistically combined without excessive toxicity. As a result, this approach has limited potential, and given the range of mutations that are known to be present in most instances of cancer, a much broader spectrum of therapeutic action is desperately needed.

One solution to this challenge would be to look to the many chemicals that have been found in foods (and other plants) that have been shown to target the very same cellular machinery. Many of these chemicals have been shown to have impressive anti-cancer potential and many have wide margins of safety. This makes them ideal candidates to be considered for use in combination with one another to achieve a truly broad-spectrum therapeutic result (potentially reaching scores of mechanisms simultaneously). Unfortunately, these naturally occurring chemicals cannot be patented, and they are therefore of little interest to bio-tech and pharmaceutical firms.

As a result, there is an urgent need for government and/or private funding agencies that can instigate applied research along these lines – even in the absence of profit potential. This may be contrary to the current approach, which relies heavily on public funding for ongoing cancer research, and then on private industry to make use of that research to drive drug development. However, a low-cost, patent free, low/no-toxicity, broad-spectrum mixture or regimen that could be used therapeutically (or in a prophylactic manner) against many different cancer types with good efficacy would represent a breakthrough of profound significance. Such a therapy would be welcomed by physicians and patients, and it would help many of the westernized countries contain costs at a time when healthcare costs are rising exponentially. It would also be extremely valuable for low-middle resource countries, where the burden of cancer is greatest, and the ability to pay is severely constrained. So this is an important challenge that definitely warrants international collaboration and cooperation.

Accordingly, the remainder of this document lays the foundation for a non-profit, advocacy organization called "Getting to Know Cancer" that will be focused on making sure that both of these important goals (i.e., progressive environmental regulatory reform and the development of broad-spectrum cancer chemotherapy) are realized.

getting to know cancer

A Strategic Plan (2011)

Vision

We envision a world where an in-depth knowledge of cancer biology has changed our approach to managing chemical exposures which, in turn, has caused a dramatic reduction in the incidence of cancer at the population level. We also foresee a time in the future when this same knowledge will serve to help us to effectively control, and inexpensively cure cancer without causing substantial adverse side effects.

Mission

To share holistic, scientific knowledge about cancer with key stakeholders who have an interest in the disease in a manner that ultimately results in societal changes that reduce the public's exposure to disruptive environmental agents that can act in concert with one another to instigate cancer. And to inspire funding, and applied research that will lead to a "broad-spectrum" plant-based therapeutic that can help us reduce the incidence of cancer, and treat the disease more effectively.

Values

CARING - We are passionate, considerate and empathetic towards all who have been touched by cancer. We are respectful to one another and to everyone with whom we interact. We foster an encouraging and supportive virtual work environment to ensure that everyone involved in the organization thrives in their role and has a chance to make a meaningful contribution to the organizational mission and to society.

SERVICE - We place an emphasis on volunteer service and great value on the efforts of those who act unselfishly to serve others who are in need.

LEARNING - We draw lessons from the past and strive for continuous improvement at all levels of the organization. We draw our knowledge from the scientific literature and we embrace creativity, innovation and learning as we seek to find better solutions that will help us achieve our mission.

STRENGTH - We have strength and courage and are undaunted by the scale of the global cancer problem. We believe that teamwork, strength of character, an optimistic problem-solving disposition and determination will allow us to effect meaningful change.

COURAGE - We encourage our volunteers to act cautiously and prudently at all times but also to take bold, carefully measured steps to effect positive change.

COLLABORATION – We believe that collaboration leverages untapped potential and we value the possibilities that are unearthed by synergy. We believe that our mission will be achieved with the help of many other individuals and organizations who are equally passionate about solving the cancer problem.

INTEGRITY - We are honest and ethical. We adhere to the highest standards of professionalism and do everything we can to ensure that our credibility is never questioned. We are fully transparent as an organization and accountable to the public in all that we do.

Strategic Direction One:

PROGRESSIVE REGULATORY CHANGE – We will work with scientists, NGOs and progressive regulatory agencies around the globe to inspire funding and instigate research that exposes the need for stewardship practices that address the fact that many environmental chemicals/agents that are not pure carcinogens may still have an important role to play in the instigation of cancer.

- Identify environmentally-minded NGOs that have an interest in the role that chemical exposures play in cancer causation, show them how the biological mechanisms of cancer change our understanding of regulatory needs and recruit them to help us build public support for progressive regulatory change in countries where change is possible

- Work directly with regulatory agencies in countries that are open to change, and bring them together with scientists to encourage knowledge sharing, scientific collaboration and funding for research that illustrates the importance of exposures to chemical mixtures (as it relates to cancer causation) and the need for the adoption of a more progressive framework that assesses the degree to which aggregate chemical exposures are contributing to the enablement of each of the hallmarks of cancer

- Place an emphasis on the importance of the natural biological defence mechanisms that should stop cancer and the importance of guarding against exposures that disrupt these capabilities. For example, environmental exposures that disable or suppress DNA repair, proper stress-axis function (inflammation suppression), the cellular mechanisms that recognizes anti-growth signalling (e.g., cell-cycle checkpoint signalling), the cellular self-destruct mechanism (apoptosis), the cellular copy-limit (senescence) and various key components of the immune system need to be identified, regulated and minimized or eliminated to the extent possible.

Strategic Direction Two:

BROAD SPECTRUM ONCOTHERAPY - Work with scientists, physicians, NGOs, and national health agencies around the globe to inspire funding, collaboration and research that demonstrates the viability and importance of attacking cancer using complex therapeutic mixtures or a regimen of plant-based chemicals in anticipation of the many mutations that can enable the hallmarks of cancer in any given cancer, and to achieve a broad-spectrum result.

- Identify cancer focused funding agencies that have an interest in finding a "cure" for cancer, show them how the biological mechanisms of cancer necessitate a need for broad-spectrum onco-therapy, help them understand why private industry is not taking this approach and the logic behind the use of plant-based chemical for this purpose. Encourage them to fund research that demonstrates the viability and importance of attacking cancer using complex therapeutic mixtures of plant-based chemicals

- Identify national health agencies that are struggling with the escalating costs of cancer chemotherapy, and bring them together with scientists to help them to understand why the biological mechanisms of cancer necessitate a need for broad-spectrum cancer therapy, and the logic behind the use of plant-based chemicals for this purpose. Encourage them to collaborate with one another to fund research that demonstrates the viability and importance of attacking cancer using complex therapeutic mixtures of plant-based chemicals

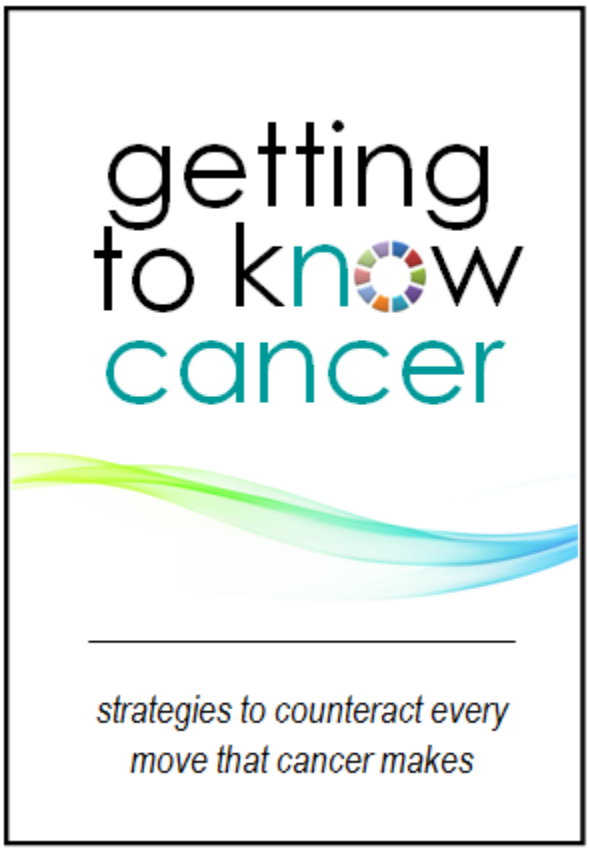
Strategic Direction Three:

PUBLIC OUTREACH / GRASS ROOTS SUPPORT - Broadly promote and foster a holistic understanding of the biological mechanisms of cancer to the general public, and to the many stakeholders who care about the disease. Our objective is to generate a wide base of understanding and support for progressive regulatory change that fully acknowledges the cancer-causing potential of exposures to combinations of chemicals and others agents that collectively contribute to cancer. Further, we will seek support for applied cancer research that is focused on the anti-cancer potential of mixtures of plant-based chemicals that can be employed for chemotherapeutic and prophylactic purposes.

- Use social media tools to build public awareness for the organizational mission and to drive traffic to the organizational website

- Use online learning tools to engage interested stakeholders and ensure that they understand the biological mechanics of cancer well enough to appreciate the importance of the solutions being proposed

- Build a globally distributed grass roots network of support for our mission (directly and through partnerships), and identify influential stakeholders (individuals and organizations) that can help us achieve the organizational mission



"Getting to Know Cancer" is an independent, all-volunteer, non-profit organization. It was initiated as a service learning initiative** by Nova Scotia Community College (NSCC) faculty, alumni and students, along with a number of other courageous volunteers. The organization is academically supported by a large advisory board of cancer researchers from prominent scientific research institutions around the globe.

www.gettingtoknowcancer.org

***NSCC is a province-wide system of training and education established in 1988 in Nova Scotia, Canada. The college's vision is to provide every learner with an opportunity to experience community engagement that will enhance her/his critical thinking, leadership development, ethical decision making, social consciousness and civic responsibility. To that end, Service Learning is a program-level outcome in all of NSCC's core programs. It integrates active, meaningful community service with instruction and reflection to promote a sense of civic responsibility and strengthen communities.*

nscc