PIP Digest

Canadian Cancer Research Alliance
Alliance canadienne pour la recherche sur le cancer

Patient Involvement in Cancer Research Program
Programme de Participation des Patients à la recherche sur le cancer

CANCER RESEARCH: Types of Research

In this PIP Digest, we describe major types of cancer research and current priorities in cancer research.

Key Concepts

- Major types of cancer research
- Research priorities, national and international

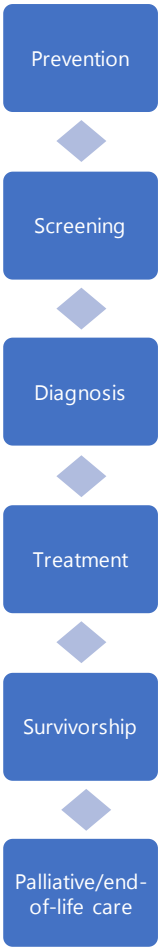
Related PIP Digest

- Cancer Research: Cancer Research Funding

"Cancer research has always been among the most interdisciplinary of fields, mirroring the complexity of the many diseases it addresses."[1]

Many classifications are used to describe different types of research. In this PIP Digest, we use the definitions of the four major research pillars used by the Canadian Institutes of Health Research. Every aspect of cancer research, from prevention through to end-of-life care, is captured under these research pillars. Each pillar of research involves many different disciplines and provides important opportunities to engage patients.

[1]From: National Academy of Sciences, National Academy of Engineering, and Institute of Medicine. (2005). *Facilitating Interdisciplinary Research*. Washington, DC: The National Academies Press. https://doi.org/10.17226/11153.



BIOMEDICAL	CLINICAL	HEALTH SYSTEMS AND HEALTH SERVICES	SOCIAL, CULTURAL, ENVIRONMENTAL, AND POPULATION HEALTH
This type of research studies normal and abnormal human function from the level of cells and molecules all the way up to the whole body. Basic biomedical researchers do their work in a laboratory using test tubes, cell samples, microscopes, chemical analysis, and other applicable tools or methods.	Clinical research is health research on people, typically to evaluate the effectiveness of drugs, medical devices and practices. It may involve researchers asking questions, administering drugs, taking blood or tissue samples, or checking the progress of patients as they take a treatment according to a study's protocol. Clinical research studies often have specific criteria to define who can be recruited or enrolled in a particular study.	This is a type of research that seeks to improve the efficiency and effectiveness of health professionals, such as doctors, nurses, or physiotherapists, or the health care system itself through changes to practice and policy. Health services researchers often use surveys, focus groups, randomized controlled trials, and comparisons of data from health records and other sources in their studies.	This research works to enhance the health of Canadian populations (or subpopulations, such as those from a particular region or ethnic group) by understanding how social, cultural, environmental, work-related, and economic factors affect people's health. It also involves the evaluation of certain health interventions such as the effect of tobacco control programs on populations.
Disciplines: Biology, Computer Science, Genetics, Mathematics, Microbiology, Oncology, Pharmacology, Physiology, Zoology	Disciplines: Biostatistics, Clinical Epidemiology, Kinesiology, Medical Biophysics, Nursing, Oncology, Psychology, Social Work	Disciplines: Anthropology, Bioethics, Geography, Health Economics, Political Sciences, Public and Health Administration, Sociology	Disciplines: Epidemiology, Nutrition, Law, Performing Arts, Philosophy, Psychology, Public and Population Health, Sociology, Visual Arts

Adapted from: CIHR's *Health Research in Canada and You* (2014) available at http://www.cihr-irsc.gc.ca/e/documents/Health_Research_in_Canada_and_You_e.pdf

The example below shows how research on cancer metastases can involve all four pillars:

BIOMEDICAL	CLINICAL	HEALTH SYSTEMS AND HEALTH SERVICES	SOCIAL, CULTURAL, ENVIRONMENTAL, AND POPULATION HEALTH
A study looking at the biological mechanisms that cause cancer cells to invade nearby tissue and migrate to other areas of the body	A clinical trial on a new combination therapeutic designed to reduce metastatic disease	Research on the benefits of a telemedicine approach designed to support patients with metastatic disease	A population-based study to determine the prevalence of metastatic disease among different ethnic groups

Research Prioritization

Many cancer research funding organizations identify priority areas for research funding. These priorities relate to the organization's mandate — that is, if the organization funds only biomedical research, its research priorities will fall in that area; if the organization supports research on a specific type of cancer (for example, ovarian), the research priorities will relate to that type of cancer.

Decisions about priorities often involve assessing the state of existing knowledge and determining where a funding organization thinks it can best make a difference. Funders may come together to support research areas of mutual interest. This is a good way to close gaps in under-supported areas. Patients often identify different priorities than either clinicians or researchers, which makes their involvement in priority setting particularly important.

The CCRA member organizations all have strategic priorities for research funding. The CIHR Institute for Cancer Research, for example, has three priority areas for 2015–2020: high fatality cancers; health economics and health services research in cancer control; and redressing cancer risk factor disparities and prevention service inequities.

In its 2016-2021 strategic plan, the Ontario Institute of Cancer Research, identifies three research priorities: finding new ways to treat difficult cancers; optimizing cancer patient management and treatment decisions; and driving improvements in cancer prevention and care delivery.

Collectively, the CCRA members have also developed a broader pan-Canadian strategy, *Target 2020*,[2] that identifies a series of action items grouped around six themes. They are also developing a new vision and new strategic plan.

Addressing research gaps is critically important in advancing cancer science at the global level. When you attend cancer research conferences in Canada, you will no doubt hear from Canadian researchers about their work in these areas.

[2] *Target 2020* can be accessed at the CCRA website: www.ccra-acrc.ca.

Target 2020 Themes

International Perspective

At the international level, research prioritization has taken many forms. In the United States, the National Cancer Institute (NCI) established a Provocative Questions (PQ) Initiative in 2011. The goal of the PQ initiative is "to support research projects designed to use sound and innovative research strategies to solve specific problems and paradoxes in cancer research." The PQs are not intended to represent the full range of NCI's priorities in cancer research but rather to challenge cancer researchers to explore specific problems in key areas of cancer research that are deemed important but have not received sufficient attention. There are nine questions in the 2020 round of provocative questions.[3]

PQ1: **What are the causes for the rising numbers of cancers in people younger than 50 years of age?** Research here will be designed to improve our understanding of why certain cancers are occurring in younger populations, beyond hereditary factors, and to identify markers for early detection and better screening approaches.

PQ2: **How does intermittent fasting affect cancer incidence, treatment response, or outcome?** Research in animal models has shown that a long-term reduction in food intake as well as intermittent fasting reduces cancer incidence. Research here will be focused on understanding how restricting our food intake to specific hours of the day or days of

[3]For more, see https://provocativequestions.cancer.gov/current-rfas-and-pqs.

the week or month affects cancer risk factors, cancer incidence, treatment response, toxicity, and/or other related cancer outcomes.

PQ3: **How can selective pressures – things within or outside of cells - affect how cells compete and cooperate during the start and development of cancer?** Cells interact with each other in response to selective pressures to drive competition and cooperation. This results in the survival of the more "fit" cells at the expense and loss of less fit cells. Understanding this mechanism in relation to cancer initiation is the goal of research addressing this question.

PQ4: **What mechanisms explain sex differences in cancer incidence, tumour location, or response to treatment?** There is a growing literature that suggests that males and females differ in the kinds of cancer they get, the characteristics of those cancers, the progression and response to treatment, and their overall survival. Research here will help us better under the biological mechanisms across sexes that could be used to inform approaches to cancer prevention, diagnosis and treatment.

PQ5: **What strategies can block or reverse changes to tumour cells that are created by cancer treatments and lead to treatment resistance?** Research here will focus on better understanding the fundamental pathways and molecular drivers of the changes in the cancer cell and the drugs and drug combinations that will prevent these changes.

PQ6: **How can cancer cachexia be reversed?** Cancer cachexia - the loss of body weight and muscle mass, and weakness - associated with many types of cancer is often a signal of poor long-term survival. The goal for this research is to understand cancer cachexia at a mechanistic level so that our ability to identify those at risk of cachexia and prevent or halt cachexia will be enhanced.

PQ7: **What methods can be developed to integrate patient-generated health data into electronic health records?** Patient-generated health data are health-related data created, recorded by, or gathered directly from patients. These include patient-reported data and passively collected physical measures from mobile and wearable devices. Best practices for using patient-generated health data is limited. Research on new analytic and data science methods to improve the capture and use of patient-generated health data within existing electronic health records will help to predict and monitor cancer-related outcomes, and ultimately, inform a precision medicine approach.

PQ8: **What strategies can be implemented to ensure better care for cancer patients with complex needs?** The research here will develop and test interventions that would improve the coordination of healthcare for people with complex health needs throughout their cancer journey (diagnosis to survivorship). These interventions would be aligned with patient preferences, goals and needs as well as the goals of the broader health system. Determinants of health – the broad range of biological, behavioural, socioeconomic, cultural, and environmental factors that determine an individual's health – are a key component of this research.

PQ9: **What methods can be developed to effectively study rare cancers?** The research here will identify new study designs, statistical approaches or computational tools to describe, analyze and monitor small groups of people with rare cancers and interpret how these groups are affected by certain exposures or treatments.

The United Kingdom's largest cancer charity, Cancer Research UK, is partnering in 2020 with the U.S. NCI to fund four multidisciplinary research teams from around the globe that will tackle one of more of nine identified research priorities.[4] The Cancer Grand Challenges is an international initiative to address profound and unanswered questions in cancer research. The challenges are developed through a series of international workshops and an open call online that collected ideas from the cancer research community and people affected by cancer. The 2020 challenges are:

CANCER GRAND CHALLENGES

CANCER RESEARCH UK | NIH NATIONAL CANCER INSTITUTE

1. **Understand how cells and tissues maintain "normal" phenotypes while harboring oncogenic mutations and how they transition to become a tumor.** Why some cells but not others can resist becoming cancerous remains a mystery. Researchers suspect that factors such as aging, the immune system, and a cell's location could all contribute. Understanding what makes cells "normal" can help in our understanding of what exactly transforms ordinary cells into cancer cells.
2. **Systematically deliver macromolecules to intracellular targets for therapeutic benefit in cancer.** Getting drugs inside the cancer cells they need to destroy is a major problem that scientists face when designing new treatments. This task is particularly challenging for larger and more complex drugs—known as macromolecules—that are too big to slip into cells without help. Scientists, working from across disciplines, can develop new ways to deliver the most promising macromolecule drugs to every cell in the body, including hard-to-reach places like the brain.
3. **Understand and exploit senescence to improve cancer treatment.** When cells are put under stress, such as when their DNA is damaged, they can enter a state called senescence, in which they stop dividing. Senescence can help protect us against cancer, as it forces potential cancer cells to stop dividing before it is too late. Research suggests that cancer cells can become senescent too, halting their growth. This raises important questions: can we trigger senescence in cancer cells and are there ways to target and eradicate these cells from the body?
4. **Determine the potential benefits and risks of e-cigarette use.** The effects of e-cigarette use on tobacco use behavior and tobacco-related health outcomes are still emerging and much remains to be learned. Bringing together global experts can help answer crucial questions about the harms and potential benefits of e-cigarette use, including: How do e-cigarettes influence overall tobacco use, including initiation, dual use, and cessation? What are the short and long-term health consequences of e-cigarette use? How does the regulatory context affect the extent of harms and potential benefits of these products?
5. **Determine how inflammation causes cancer.** Despite being crucial to our health, inflammation can cause serious damage to our body if it spirals out of control, making it a major risk factor for cancer. Astoundingly, an estimated 20–25% of cancers are linked to chronic inflammation globally; however, we do not understand the

[4]Adapted from: https://www.cancer.gov/grants-training/grants-funding/cancer-grand-challenges.

relationship between inflammation and cancer, and is important that research untangle the complex web of interactions involved in inflammation and pinpoint which processes cause cancer.

6. **Develop novel therapies to target unique features in solid tumors in children.** Solid tumors in children are very different from those in adults. By understanding more about these differing elements and finding ways of targeting them, new drugs or repurposed drugs may be identified to better treat children's cancer.
7. **Understand the biology of extrachromosomal DNA (ecDNA) generation and action and develop approaches to target these mechanisms in cancer.** New research has revealed that cancer cells create vast numbers of extrachromosomal DNA (ecDNA) loops, often containing many copies of genes that help the cancer grow and survive. By learning how ecDNA forms and changes in cancer, new therapies that target it can be identified and developed.
8. **Identify and target dormant cancer cells.** Even after apparently successful treatment, cancer can return, sometimes growing and spreading rapidly many years after the initial diagnosis. This makes it very difficult to detect. But what causes these cells to become dormant, how and where they hide, and what revives them are all unknown. By unravelling the mystery of cancer cell dormancy, researchers could find ways to detect these dangerous cells and then eliminate them or stop them from waking up.
9. **Understand and reverse cachexia and declining performance status in cancer patients.** In the late stages of cancer, people often experience extreme weight loss and muscle wasting—a condition called cachexia. These individuals' general well-being can also deteriorate in other ways. Better ways to help people whose health deteriorates in this way and new ways to understand the complicated pathways involved is needed to address this serious problem.

In summary, cancer research takes many forms, and different organizations may prioritize different areas of research given their mandates or the processes they use for identifying priorities. Knowledge sharing, collaborative funding programs, and the involvement of patients are crucial ways to help identify needed research, ultimately, identify successful new approaches to prevention and cure.

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