From the Lab Bench to the Hospital Bed

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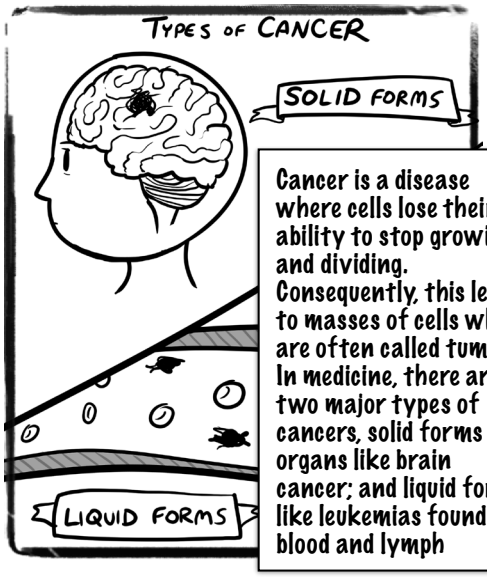

Cancer is a disease where cells lose their ability to stop growing and dividing. Consequently, this leads to masses of cells which are often called tumors. In medicine, there are two major types of cancers, solid forms in organs like brain cancer; and liquid forms like leukemias found in blood and lymph

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Cancer is a very common disease. In fact, 1 in 2 Canadians will develop cancer in their lifetime, and will need anti-cancer treatments. These treatments have undergone extensive testing so that they can be effective, but many also have unwanted side effects.

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Many scientists study how treatments work on cancer cells in controlled laboratory settings: We tend to call them "basic research scientists." However, there are also scientists who take these lab discoveries and assess them on the cancer patients themselves. We tend to call these "clinical scientists".

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Dr. Elizabeth Eisenhauer is a clinical scientist and an expert on how to best evaluate methods used to test treatments. This might include just having great guidelines on which drug candidates are good for testing, as well as strategies and rules on how to test and when to stop testing a drug.

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For instance, Eisenhauer recognized that not everything needs to be new to be better. With this insight, she has developed new standards of cancer treatment in Canada and around the world. This has benefited millions of patients!

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As a leader, she has brought together all sorts of different scientists together (basic and clinical), and also connected these researchers to policymakers. This team building helps make better science and better laws that can make these treatments more efficient and safer for cancer patients.

Art by Armin Mortazavi and text by Zahra Sepehri. October 2021

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The ins and outs of taking an anti-cancer treatment from discovery in the lab to the medicine you give to the patient.

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Art by Armin Mortazavi

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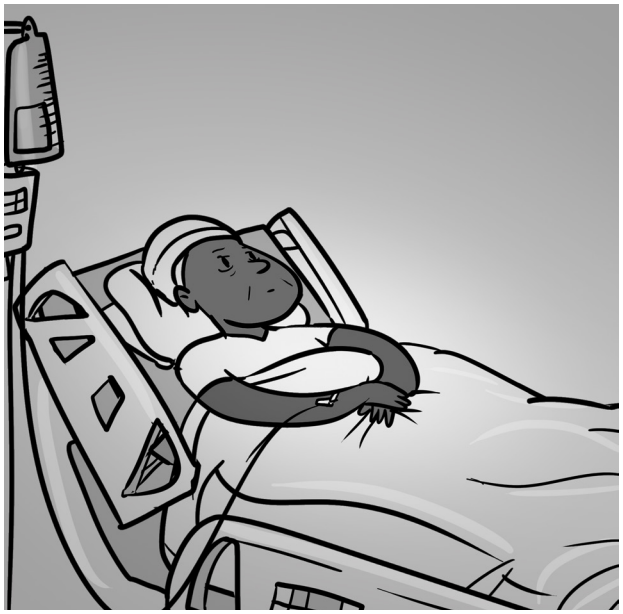
Millions of people from across the world, young and old, suffer from cancer. In fact, during the time it takes for you to read this article (say about 10 minutes), 4 more Canadians will have been diagnosed with this disease. And part of the reason for its ubiquity is because cancer is actually a disorder representing several hundred different diseases.



At its essence, cancer happens because a cell has lost its ability to know when and where it needs to stop dividing. This can lead to abnormal cells that can live much longer, even to the point where they may become immortal, and also where they can grow and divide faster. As a result, this uncontrolled cell division can form masses or growths which are often called tumors.

Here, there are two major types of tumors: **solid** and **liquid**. Liquid tumors occur in your bodily fluids, such as blood, bone marrow, or lymph nodes. Both the bone marrow and your lymph nodes are active sites for immune cells to grow and develop. Consequently, liquid tumours that arise from these tissues constitute many of the cancers that we call **leukemias**. Solid tumors tend to be more compacted together, and usually grow within tissue. Examples include tumours in the brain, skin, breast, and many other organs.

Cancer and drugs

One common strategy for drugs that treat cancer is to take advantage of the disease's core characteristic. Because cancer cells grow and divide rapidly, this also means that they tend to be very active in securing nutrients and other things needed to maintain this level of growth. Consequently, many cancer drugs are ultimately toxic in nature, and administration is a balancing act in figuring out delivery and dosage so that the difference between what a cancer cell and a normal cell takes up is the difference between being killed or staying alive. This is also why when treating tumours, it's not uncommon for the patient to experience serious

side effects: it's a bit like they are being poisoned but in a very controlled fashion.

To minimize side effects, research into how the drug is delivered is just as crucial as the mechanism of the drug itself. Essentially, we want the drug to target the abnormal cells in a way that maximizes its positive effects, whilst minimizing harmful negative effects on the less active normal cells. Because of this, it is important to prescribe the treatment at the **correct dose**, at the **right time**, using the proper **route of prescription**, and for a **suitable duration**. All of these considerations can allow us to better and more precisely deliver the drug against the tumour so that the drug's **efficacy** (how well it works) is optimized, while minimizing the **toxic side effects** (essentially monitoring its **safety**). This is an area that many cancer scientists are working on, sometimes by doing tests on the cancer cells in petri plates but also sometimes by testing the drug on the cancer patients themselves.

Scientists and clinical trials for newly discovered targeted drugs

In medical science, research is sometimes categorized as the work of two major groups of scientists. Some scientists do their work within a strictly laboratory setting, working with cancer cells in very controlled scenarios. For instance, this might be where experimental variables of individual cells can be closely studied by monitoring effects in petri plates. These scientists put their primary focus on the molecular workings of actively growing cancer cells, and are often referred to as **basic research scientists**. In many ways, their work may focus on the treatment, but more often than not, they also represent the active investigation of basic cell functions. Other scientists, however, focus their attention on directly improving the quality of life for patients. They want patients to have longer and better lives, and perform experiments with patients to work out best practices in attaining that goal. These scientists are often referred to as **clinical scientists**.

The two are both equally important because they play roles in the pathway for any new treatment, as it moves from discovery to being used by patients. Basic scientists, working in their lab environment, produce results that lay the foundation for clinical scientists to do their experiments where safety and efficacy can be explored in the patient setting. Indeed, before being approved for final use, any novel therapy needs to pass through a variety of different phases of clinical trials.

Still, one of the challenges is coming up with guidelines to determine which therapies should progress from basic science discovery to clinical

science testing. At any given moment, there are very large numbers of basic scientists working in their labs, producing data and proposing new and different ways to treat a tumor. Out of all of the proposed ways, who decides which discovery is worth being a candidate to be tested in clinical trials?

Furthermore, these guidelines should not only provide direction on which novel therapies should be allowed to start clinical trials, but they should also dictate how trials need to be worked through, as well as when and why a clinical trial needs to terminate. In other words, it's important to set boundaries for this clinical research, so that the patient's quality of life is always considered above all else.

Team building and optimization of treatments

This is where Dr. Elizabeth Eisenhauer came in. Dr. Eisenhauer is a Professor Emerita in the Department of Oncology at Queen's University and this year's Canada Wightman Gairdner Award winner. For over 30 years, she has made groundbreaking contributions on how anti-cancer drugs are clinically evaluated.

Reminiscing about her early career, she notes, "There was a certain amount of good luck in finding an excellent mentor," referring to her colleague Dr. Joseph Pater who in 1982 offered her a position in helping found the *Investigational New Drug Program* (IND) of the then *National Cancer Institute of Canada Clinical Trials Group*. From there, she oversaw the direction of the IND program and has had many other leadership roles in the field. In all those years, she has tackled cancer from different aspects: treatment, supportive care, and prevention.

As a leader, she saw the importance of bringing basic scientists and clinical researchers together, so that this collaborative approach could lead to better science. Actively connecting the two also allows for better administration of the research: for example, it can help funding organizations navigate new partnerships that allow investments to be more strategic, filling in gaps in the landscape of cancer research.

Dr. Eisenhauer also recognized the crucial task of connecting researchers to policymakers. This was especially important in her work around cancer prevention and tobacco, as the science itself is only as powerful as having government systems in place that can help society adopt healthier habits. Here, her work has led to the *Tobacco Endgame for Canada*, a collection of policy measures aimed at cutting the prevalence of tobacco use to less than 5% of the Canadian population by the end of 2035.

Early on, Dr. Eisenhauer also recognized that not everything needs to be new to be better. Essentially, there may be opportunities to optimize the efficacy of existing drugs, by simply reevaluating treatment approaches. Furthermore, she saw the value in emphasizing patient input in this process.

In this manner, she showed that **Taxol**, already one of the most widely used cancer drugs in the world, could be administered in shorter and safer ways to maintain efficacy but with significantly fewer side effects. These methods are now internationally recognized as standard practice for Taxol to the benefit of millions. In fact, her expertise in clinical evaluation has coordinated more than 170 different clinical trials on a diverse array of anti-cancer medications all across the world. This in turn has been pivotal in establishing many new and effective treatments for ovarian, skin and brain cancers.

Overall, it's clear why Dr. Elizabeth Einsenhauser has been awarded the prestigious 2021 Canada Wightman Gairdner Award. Her scientific leadership and ability to bring different communities together has been responsible for fundamental, impactful and extraordinary contributions in how anti-cancer agents and clinical trial methodologies are evaluated. As she says, to fight a disease as complex as cancer, "It is not just one part of science that has to progress, but all parts of it need to move progressively forward."