

# The Hallmarks of Cancer

The Research Information Outreach Team (RIOT) of the local Canadian Cancer Society, Elgin Middlesex Community Office, is pleased to present a 12-part series on the Hallmarks of Cancer, which will begin this month. This concept of a set of characteristics in cells that are essential for their development into

cancer was proposed by Drs. Douglas Hanahan and Robert Weinberg in 2000, and later updated in 2011. Both papers were published in the prestigious medical journal Cell.

Each month a local researcher will focus on one of the Hallmarks of Cancer as it relates to his or her research. Occasionally,

we will invite a researcher from outside of London to participate in the series. We will conclude the series with another overview of the hallmarks and the role that research is having on the discovery of ways to prevent, detect, diagnose, and treat this dreaded disease. We would like to take this opportunity to thank

all of the researchers for taking the time to participate in the series. It is our hope that by providing a better understanding of the Hallmarks of Cancer and the amazing research that is going on to combat cancer, we will spread a message of hope, inspired by the progress and promise in cancer research today.

The series begins with an overview of the ten 'Hallmarks of Cancer' by Dr. David Rodenhiser, an Associate Professor at Western University in the Schulich School of Medicine and Dentistry. He is also a scientist with the London Regional Cancer Program and Children's Health Research Institute, where his research on epigenetics is

focused on how genes are turned on and off in cancer cells. Dr. Rodenhiser presented an informative and accessible overview of the Hallmarks of Cancer at our Ignite Cancer event last March. The audience response was very positive, and we've asked him once again to give an overview of this important topic.

It goes without saying that a cancer diagnosis is a life-changing event. The daily routines and priorities for the patient and the patient's family are dramatically changed as they deal with the realities of medical intervention and treatment for this life-threatening disease. Adding to the overwhelming events for these patients, they also face such perplexing questions as 'Why me?', 'What causes cancer?' and 'Can this be treated?'

Cancer is complex at many levels, and today we have a much better understanding of the over 200 different types of cancer that do occur. Thousands of genes working together in different networks are involved in cancer. Some cancer types, such as breast cancer, may actually exist as four or five specific cancer types that have different causes, progressions and responses to treatment. An individual's cancer can also change over time, meaning that cancers that reoccur years later may be quite different from the patient's initial cancer. Even for cancer researchers and the medical teams who treat cancer patients, the scale of this complexity is daunting.

Fortunately, we now understand that there are 10 general features that can change in normal cells to become cancer cells. These ten Hallmarks of Cancer offer us better insight into how cancer is



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David Rodenhiser

caused and provide us with better targets for developing new patient-specific treatments to control and cure cancer. The first three hallmarks of cancer have to do with the fact that when compared to normal cells, cancer cells grow uncontrollably. That faster growth creates the solid clump of cancer cells that we know as a tumour or the overabundance of cancer cells in the blood that we know as leukemia. Instead of being carefully controlled in how they grow, divide and multiply, cancer cells are like a car with its gas pedal stuck to the floor. They grow and multiply uncontrollably. This first hallmark of 'sustained growth and cell division' is made even worse because cancer cells are also like a runaway train, lacking the brakes to stop dividing. This is because cancer cells have lost the genes that allow them to 'slow down and grow at a normal rate'. In other words the cancer cells have lost their brakes. Cancer cells have also increased their 'energy metabolism'. This third hallmark re-programs cancer cells to make them hungrier and makes them require more

fuel for their faster rates of cell growth and multiplication.

The next two hallmarks of cancer involve the lifespan of cancer cells. While normal cells die when they are injured, cancer cells can resist signals to die. This natural process of programmed cell death or 'apoptosis' is lost in cancer cells. Cancer cells hang around longer, almost zombie-like, becoming more unpredictable and more resistant to treatment. Cancer cells can even become 'immortal', in that they don't die at the age that normal cells do. Together, these two hallmarks of resistance to cell death and the ability to become immortal allow cancer cells to extend their natural lifespans while growing and dividing uncontrollably.

Of particular concern to cancer patients is the next hallmark of 'metastasis'. Cancer cells can leave the site of the original tumour and travel throughout the body to find new sites in the body in which to grow. There, these metastatic cancer cells may lie dormant or undetected, only to start growing again uncontrollably, sometimes years after initial treatments may be successful, these elusive metastatic cells may be missed. If the cancer comes back, new blood vessels are triggered to grow at these new cancer sites; a process called 'angiogenesis'.

This new blood supply provides the necessary oxygen and nutrients to allow these metastatic cells to grow and develop into new tumours. Together, these two hallmarks allow cancer cells to migrate to and invade new organs, leading to the growth of cancer cells throughout the body. In fact, metastatic cells are responsible for most cancer deaths, as they are the most difficult cancer cells to locate, identify, and treat.

Cancer cells can also hijack the immune response. They are able to 'avoid immune detection' by our ever-alert immune system, which can usually identify cancer cells as if cancer was an invading bacteria or virus. Somehow cancer cells can disable this immune surveillance, much like cutting the wires on a burglar alarm. As well, cancer cells can 'cause inflammation'. Unfortunately, such inflammation may be beneficial to the cancer cells, by providing them with growth factors and other molecules that improve their ability to survive, grow, and metastasize. As a result, new batches of cancer cells are born that are more evolved and more deadly. The abilities of cancer cells to both evade the immune system and to hijack it to improve cancer cell growth are now under intense study by cancer researchers.

Finally, all these hallmarks described above are able to occur because cancer cells within the tumour are

'unstable, constantly mutating and evolving'. The sets of genes (known as the 'genome') possessed by cancer cells are very unstable, resulting in many new mutations that create new species of cancer cells within a tumour. In some combinations, these mutations create cancer cells so unstable that they die. Unfortunately, new combinations of gene mutations can also lead to new cancer cells that can survive cancer treatment. We can think of the tumour as a nest in which new, more deadly and unique cancer types are born. These are the cells that cause cancer to reoccur, with patients needing to go back onto treatment to fight these new cancers, perhaps following years of cancer-free health.

The Hallmarks of Cancer have provided cancer researchers with a way to organize their approaches to target cancer. It is sobering to think about the complexity of cancer. The good news is that each of these hallmarks is a potential Achilles heel for the cancer cell, offering the possibilities for new, targeted cancer treatments to kill those cells and shrink those tumours. Already, drugs are being developed to target the hallmarks necessary for tumour growth and progression. A major challenge is that cancer is a moving target, with certain drugs failing to kill all cells in a tumour because resistant cancer cells

can survive, evolve and eventually grow into new tumours. New treatment strategies involve combining therapies that target several hallmarks at the same time, preventing the development of cancer cells that are resistant to treatment. These approaches, combined with our better understanding of the environmental and genetic contributions to cancer are allowing us to take the new approaches developed in our labs and translate them into better, more effective treatments for our patients.

*Stay tuned for monthly articles written by local cancer researchers who are studying different aspects of or ways to target each of these hallmarks.*

### 10 Hallmarks of Cancer

1. Sustaining Proliferative Signaling (April)
2. Evading Growth Suppressors (May)
3. Deregulating Cellular Energetics (March)
4. Resisting Cell Death (June)
5. Enabling Replicative Immortality (July)
6. Activating Invasion & Metastasis (August)
7. Inducing Angiogenesis (September)
8. Avoiding Immune Destruction (October)
9. Tumour-Promoting Inflammation (November)
10. Genome Instability & Mutation (February)

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