RIOT
Research Information Outreach Team

Ten Hallmarks of Cancer Series

Enabling Replicative Immortality: Hallmark #6

Cancer arises by genetic changes (mutations) in normal cells within our bodies; only a small minority of these are inherited, and the rest happen during our lifetimes. As we are now living longer, our chances of having mutations that lead to cancer are increasing with age. There are many genes in our cells that help them to grow normally and serve vital functions - called "proto-oncogenes." When they mutate, they are called "oncogenes", and the mutation gives the cells potential for unrestricted growth causing cancer. There are also other vital genes that oppose unlimited growth of cells, which protects us from developing cancers. These cells are called "tumour suppressor genes". If they mutate, these genes lose their tumour-suppressing functions, again giving unlimited potential for growth. These two opposing gene sets can be compared with the accelerator and the brakes in a car. If either fails, the car can run amuck.

Stem cells: Our body consists of a variety of tissues, many of which undergo a continuous process of cell renewal, replacing old and dying cells with new ones to maintain normal body functions until we die. An adult human body contains approximately 37 trillion cells, of which 60-70 billion cells die and an equal number are born every day. The rates of cell renewal are different for different areas of the body. For example, the superficial layer of our skin (called epidermis) is replaced every 7-10 days, although we don't see it with the naked eye. We scrub off the dead cells every day while taking a bath. How does this happen? In the base of the epidermis, we have mother cells with the extensive ability for self-renewal. This means they can create two new cells – called daughter cells – that are like the mother. One of the daughter cells will continue on to become a functional cell that will eventually become a skin cell, and then it, too, dies after a week or so. The other daughter cell will become a mother cell and have its own daughter cells, thereby maintaining self-replicative potential. These mother cells are called "stem cells."

Cancer stem cells: In a cancerous tissue, every cell cannot divide and create two new daughter cells. In fact, in the majority of cancers there are very few mother, or stem, cells. Most cancer cells die by a process called apoptosis or "programmed cell death". Traditional anti-cancer agents, such as chemotherapy or radiation, target these regular cancer cells to stop their replication or cause their death. These treatments often succeed in initial responses but may not be permanent. Cancer relapses occur because the surviving stem cells within the cancerous tissue have unlimited self-replicating ability and resistance to these agents. What is the difference between normal stem cells and cancer stem cells? How can we identify cancer stem cells? Can we kill cancer stem cells without hurting normal stem cells? Among many laboratories, we are working hard to answer these questions. Our laboratory is striving to answer them in breast cancer.

Cancer stem cells are a dynamic state allowing exploitation for therapy: Our research into breast cancer has revealed that an inflammation-associated enzyme called cyclo-oxygenase-2 (COX-2) expressed by about half of human breast cancer cases drives tumour progression and its spread to other tissues through multiple mechanisms including activation and growth of cancer stem cells. We also discovered that two small RNA molecules (called micro-RNAs) activated by COX-2 are linked with cancer stem cells in breast cancer. We are currently testing whether these molecules can be used as blood biomarkers to determine if cancer stem cells are present in the patient and if we can monitor cancer progression just by testing a patient's blood instead of an invasive tumour biopsy. We also found that drugs blocking COX-2 were effective in controlling breast cancer stem cell replication, without hurting normal stem cells. These drugs are future candidates for human trials, in combination with traditional therapies.

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