Hallmarks of Cancer Series

Scholl Research Group from left to right: Adam Farag, Yonathan Araya, Thien Dang, Heeseung Lim, Justin Peterson, Francisco Martínez and Timothy Scholl (Dr. Scholl is an Assistant Professor of Medical Biophysics at Western University and an Investigator with the Ontario Institute for Cancer Research.)

Altered Energy Metabolism in Cancer

By Timothy Scholl

Glucose (sugar) and oxygen are the chief nutrients required for cells to function and grow. In a series of steps inside the cell, glucose is broken down and combined with oxygen to provide the energy necessary for the cell to survive. Cancer cells are able to adjust this energy metabolism (i.e. how and what the cell uses for energy) in response to a tumour's demand for rapid and sustained cellular growth. This altered energy metabolism is a hallmark of cancer.

In tumours, blood vessels are hastily created to match the fast cellular growth. These new vessels are often poorly formed and can't provide sufficient nutrients to surrounding cells. This leads to oxygen-starved (hypoxic) regions within the tumour. To adapt to hypoxia, cancer cells re-program themselves to produce energy without oxygen. This reprogramming results in increased glucose consumption in cancer cells compared to those of neighbouring healthy cells giving them a competitive advantage for growth.

Changes in energy metabolism in tumour cells can be mapped using new diagnostic methods, known as molecular imaging. Molecular imaging methods have the ability to differentiate regions containing cancer cells from healthy tissue based on certain indicators, such as their increased use of glucose. The ability of molecular imaging to monitor changes in tumour energy metabolism may be an accurate method to both detect the presence of some cancers, and assess the effectiveness of cancer treatment.

Recent advances in our understanding of cancer have led to the development of new "targeted" treatments designed to attack specific characteristics possessed by cancer cells causing them to die. Unfortunately, our knowledge of the biology of tumours is still incomplete. Very often, different patients exhibit widely varying responses to a particular therapy despite having similar types of tumours. Therefore, accurate and early assessment of cancer treatment is essential for identifying effective therapies, eliminating the toxic effects of ineffective ones and the reduction of treatment costs.

Dr. Timothy Scholl and his research group at the Robarts Research Institute (Western University) are developing new molecular imaging methods for magnetic resonance imaging (MRI) to detect and assess cancer. This research has shown that the energy metabolism in tumours changes quickly in response to clinical treatments such as chemotherapy and radiotherapy. Using these new methods, they have identified significant changes in tumour energy metabolism as soon as one or two days after the start of treatment, which can be linked to changes in oxygen-starved regions in the cellular environment due to effective cancer therapy.

Increased glucose metabolism causes the spaces surrounding cancer cells to become more acidic, which eventually leads to changes in the concentration of sodium (salt) in tumours. Increased sodium levels in brain and breast tumours have been previously observed, but sodium levels have not been measured in prostate cancer until now. Dr. Scholl's team has developed specialized technology to measure sodium in the prostate using MRI. They have observed increased sodium levels in human prostate tumours prior to surgery which were related to aggressive cancer identified under the microscope. This is a significant finding since prostate tumours are often slow growing and, as a result, many men die with but not because of prostate cancer.

Presently, men whose doctors find something suspicious during a prostate examination or who have an elevated prostate-specific antigen (PSA) blood test, undergo a biopsy. This invasive procedure takes sample tissue from the prostate to establish the tumour grade (the aggressiveness of a tumour). Although biopsy is the "gold standard" for diagnosis, it often misses smaller scattered clusters of cancer cells, which may be aggressive. Better identification of patients as low-risk ("watchful waiting") or high-risk (treatment) will reduce unnecessary surgery and healthcare costs while increasing quality of life. Non-invasive molecular imaging methods such as sodium imaging might supplement biopsy to help reduce the over-treatment of this disease.

The 2015 Hallmarks of Cancer Series is brought to you by the Elgin-Middlesex Canadian Cancer Society Volunteer Research Information Outreach Team (RIOT). All of the past Londoner articles in this series can be found at riotteam.blogspot.ca