PROJECT FACT SHEET

Mapping the Role of Tumor Suppressors in Protecting and Promoting Cancer

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Per capita Nova Scotia has one of the highest incidences of cancer in all of Canada. The statistics are sobering. For example, in 2007, Nova Scotia presented 5,600 new cases of cancer and 2,600 deaths attributed to this family of diseases. There is a clear need to identify the molecular reasons why cancer is prominent in our society.

Cancer is a disease that results from continued growth and multiplication of damaged cells. This occurs when the cell's very own surveillance machinery has been compromised. The major family of proteins involved in maintaining the integrity of the human genome are called tumour suppressors. Researchers are working towards understanding how this family of proteins is able to effectively protect the cell from events that lead to cancer and why when mutated these proteins lose their ability to protect the cell.

Paola Marignani, an Assistant Professor in the Department of Biochemistry & Molecular Biology at Dalhousie University, is focused on understanding how one of these tumour suppressor proteins, LKB1, when damaged leads to the development of cancer. Understanding how tumour suppressors, such as LKB1 suppresses the growth of tumours and how they behave when found mutated is essential for the development of effective treatment strategies as well as for a cure.

"Our main fundamental research interest is to understand how the loss of LKB1 tumour suppressor function leads to cancer," says Dr. Marignani. "We recently discovered a novel function for mutant LKB1, the form of LKB1 found in cancers. Different mutant LKB1 proteins have the ability to turn on the expression of oncogenes, proteins that enhance the ability of a cell to proliferate, and are overactive in cancers.

"Only two other tumour suppressors have been described to have oncogenic properties, p53 and APC," she notes. "p53 is the most frequently mutated tumour suppressor found in cancers while APC is a tumour suppressor responsible for a family of colorectal cancer."

Dr. Marignani and her colleagues are continuing their studies with the hope of identifying new communications pathways where LKB1 and other tumour suppressor proteins are central to maintaining the stability of the genome. "With our new-found information, we can begin to devise targeted therapeutic strategies to deal with cancer at the molecular level," explains Dr. Marignani:

As part of this study, Dr. Marignani has identified new communication partners for LKB1, has developed new technologies, and continues to experimentally determine the role of these new proteins in the development and progression of cancer in the body. Funding Dr. Marignani received from the NSHRF has contributed to a publication in the prestigious scientific journal *Cancer Research*.

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