Seeds4Hope

A program of the Windsor Essex County Cancer Centre Foundation

2011 Seeds4Hope Grant Recipient

Dr. Andrew Swan

"Probing the tumour suppressive functions of a known oncogene: Skp2 interacts with cyclin dependent kinases to maintain diploidy."

SUMMARY OF RESEARCH PROJECT

To understand and eventually find cures for different cancers, it is important that we identify the genes that protect cells from cancer or that contribute to cancer. Most cancer-related genes fall into either of these two opposing categories. However, we found that an important cancer causing gene called Skp2 also has cancer protective abilities. Our interest is in understanding how Skp2 provides this critical tumour suppressive function. Our results to date implicate this gene in a pathway with one of the key regulators of cell division, cyclin A-Cdk1, and in opposition to a well known tumour suppressor, Cdh1. This latter finding means that just as the tumour promoting gene, Skp2 acts as a sometime tumour suppressor, the tumour suppressor Cdh1 can sometimes act as a tumour promotor. The goal of this research is to test this novel hypothesis and in doing so, to determine the precise relationship between Skp2 and other key cellular proteins during tumour progression. Our findings will lead to a better understanding of cancer that will lead to improved treatments in the long term.

HOW THIS RESEARCH HELPS ADVANCE QUALITY CANCER CARE IN OUR COMMUNITY

This research will have immediate and long-term importance in our fight against cancer. We are studying a very important cancer gene that several research groups are currently working to selectively inhibit as a treatment for cancer. Our findings indicate that inhibiting this gene may actually cause cancer. It is critical to understand how this happens in order to be able to evaluate the safety of the current proposed treatments. For this reason, there is an immediate and urgent reason for this research. In the long term we are asking questions about the most fundamental workings of a cancer cell. This will provide understanding that will, in the long run, lead to effective treatments.

2011 Seeds4Hope Grant Recipient - *Dr. Andrew Swan*

PROGRESS REPORT

This Seeds4Hope grant focused on the study of a tumour promotor gene or oncogene called Skp2. Skp2 had been previously found to play a cancer promoting role in a number of cancers and several research groups have begun investigating the possibility of targeting this protein to fight cancer. Our work was based on observations that we made in the fruit fly model the loss of Skp2 leads to cancer. Our objective was to study this tumour suppressing role of Skp2 - to identify proteins that interact with Skp2, and to determine how these proteins function to protect cells from cancer. We have now shown that Skp2 interacts specifically with the S-phase kinase, Cdk2. Interestingly, the Skp2-Cdk2 complex appears to function during entry into cell division (i.e., mitosis), indicating a previously unappreciated role for Cdk2 in this stage of the cell cycle. We are currently seeking funding from the Cancer Research Society (application due Feb. 15, 2014) to continue this important research. Our primary objective will be to establish how Cdk2-Skp2 interacts with another key cell cycle regulator, APC/C to promote mitotic entry, and to determine how failed mitotic entry in these mutants leads to cancer progression.

The research conducted under this research grant has now been presented at two meetings (1,2). Two more meeting presentations will be presented later this year. We are currently in the process of putting together a manuscript based on our findings sketched out above (3).

Conference presentations:

1. Vasavan, B., Das, N., and Swan, A. (2012). *Role of SCF-Skp2 in Maintaining Genome Stability*. In Annual Drosophila Research Conference (Chicago).

2. Vasavan, B., and Swan, A. (2011). *Role of Cks85A and Skp2 in Maintaining Diploidy in Drosophila*. In Canadian Drosophila Research Conference (Ste. Catharines).

Manuscripts:

3. Das, N., Vasavan, B., and Swan, A. (2013). *SCFSkp2 and Cyclin A Antagonize APCFzr to Maintain Diploidy. Manuscript in preparation.*

Grant Applications: We are currently seeking funding from Cancer Research Society (Feb. 15, 2014) to continue this important research.