The Donor Difference

A publication of the Windsor & Essex County Cancer Centre Foundation

January 2012

Seeds4Hope Year One Progress Reports 2010 Grant Recipients - Part 1

"Inhibition of neutral sphingomyelinase 2 can lead to breast cancer cell survival through plasma membrane steroid receptor stabilization on cholesterol rafts"

- Dr. Bulent Mutus

Recent studies indicate that the use of cholesterol lowering drugs, or *statins*, inhibit the growth and progression of prostate cancer as well as reducing breast cancer incidence by up to 18%. Despite these exciting correlations, the manner in which increased cholesterol leads to breast cancer initiation and / or progression is not well understood. Our goal in this project is to determine if elevated cholesterol in cancer cells protects these cells from death and increases their ability to grow. We also want to identify processes that are responsible for elevating the levels of cholesterol in cells so that we can target these to make cancer cells easier to kill.

In the past year, we have discovered that the enzyme termed *neutral sphingomyelinase* is responsible for keeping cholesterol levels low in normal cells. Furthermore, we found that cancer cells produce more of this enzyme, especially when they are stressed with drugs or hormones, but that the enzyme is unable to do its job, i.e. lower cholesterol, because it has been damaged or inactivated in the cancer cells. Another very important finding we made was that the neutral sphingomyelinase enzyme, which is normally found on the inner surface of the membrane that surrounds all cells, moves to the outer surface of the cell in cancer cells. This is very significant since we can now use antibodies for this enzyme to identify whether cancerous cells are present in breast tissues. In other words, ***this discovery makes it possible to detect cancer***.

"Regulation of the expression of Plks in Myelodysplastic Syndromes (MDS) and hematological malignancies"

- Dr. John Hudson

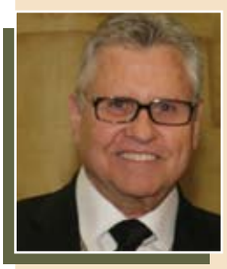
Myelodysplastic Syndromes (MDS, formerly known as pre-leukemia) and other hematological (blood related) cancers often involve changes in the expression levels of important genes. The expression levels of many proteins from these key genes can be either increased or decreased, thus destroying the perfect balance required for the proper function of cells. Changes in a protein's function(s) may occur due to physical damage to DNA that results in a mutation or altered expression of a gene or due to changes in its regulation that don't involve mutation. One type of modification that can alter how a gene functions is by *DNA methylation*. This is known as an "epigenetic" modification. Unfortunately, treatment for these disorders is complicated in many individual patients by the fact that many develop resistance to the standard forms of treatment.

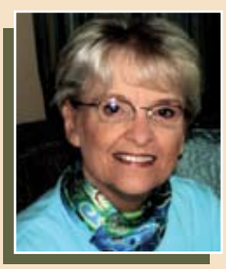
Through funding from Seeds4Hope, our research group initiated a survey to determine whether our genes of interest (the plks) have normal expression in cell lines derived from patients with a previous history of myelodysplastic syndromes or other blood cancers. These cell lines are also being exposed to drug treatments, which parallel the treatments patients receive in the clinical setting. We have determined that the plks display different patterns of DNA methylation in different cell lines and that this pattern is altered in response to therapeutic drugs. We have also begun the more long term aspect of our investigation, which is to examine the expression levels of the plk genes in clinical samples such as bone marrow aspirates and whole blood when available. The major goal here is to first establish the baseline expression for each of the plks in a given patient at the time of diagnosis and then to follow up the initial results, with during and post treatment analysis. We are focused on determining whether the levels of the plks provide clues as to why some patients respond to treatment, some development resistance to prolonged treatment, or why others don't respond at all.

WHAT'S NEW IN 2012

Please join us as we say goodbye to long-time Foundation Administrator, ***Nancy Gibbons***. Nancy has announced her retirement, with her last day being January 5th. Nancy has worked for the Foundation since its incorporation 15 years ago and is an integral member who will be missed very much. Please stop by the office to thank Nancy for all of her years of hard work and dedication to the Foundation.

Please join the Foundation as we welcome ***Renata Sznajkart*** to our team as our new Event Coordinator. Please stop by the office to say hello and look for her at upcoming events!





Congratulations!

Congratulations to our Foundation's Past President, Margaret Williams, and Seeds4Hope Administrator, Dr. Michael Dufresne. Margaret and Michael were honoured at a recent dinner of the Essex County Medical Society. Margaret received a *Community Service award* and Michael an *Honorary Membership award* from the **Ontario Medical Association**. Congratulations to you both!

Campaign Planning Underway!

The Foundation will soon be launching a community appeal to raise funds for a new **Regional Comprehensive Men's Health Program**, which will include the *da Vinci® Robotic Surgical System*, initially to be used for prostate cancer. We invite input from groups and individuals who would like to be involved in this $4 million campaign which will lead to shorter wait times and provide the most up-to-date tools available for the treatment of men with prostate cancer.

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Cancer Facts & News – Part 5: Dimensions of Cancer

By: Dr. Michael Dufresne, Seeds4Hope Administrator

This month I want to review what research tells us about why cancer is more prevalent in aging populations. First, it can take years - researchers estimate as many as 30 - to accumulate a sufficient number of cancer-causing mutations in a cell's genetic information to transform it from a normal cell to a cancer cell (i.e., ***transformation***). So a transformation event that begins during our teens or early 20's may not be completed until we are in our 40's or 50's. Secondly, once a cancer cell is formed, the development of "cancer" from that cell (i.e., ***carcinogenesis / cancer progression***) can involve several stages. For example, in the case of a solid tumour such as breast cancer, tumour progression can involve: **i)** the formation of a mass of billions of cells from the division of the original cancer cell and its progeny cells (i.e., ***primary tumour formation***); **ii)** the breaking away of cancer cells from the primary tumour (i.e., ***detachment***); **iii)** invasion of cancer cells into surrounding healthy tissue (i.e., ***invasion***), and **iv)**, the spread of cancer cells from the primary site to other parts of the body (i.e., ***metastasis***). Each of these different stages takes time and rarely proceeds uninterrupted. Cancer cells must overcome built in genetic mechanisms to repair or destroy them, as well as the body's immune response to destroy them. They must also overcome limitations imposed by their own altered growth patterns. For example, during formation of a primary tumour in the breast, the tumour will increase in size only if the majority of the cells within the tumour have access to blood vessels that carry nutrients to, and toxic by products from, the cells. However when the tumour reaches a certain size, cells in the central region may compact, become cut off from such blood vessels, and die. As cell death increases, the overall rate of tumour growth slows, and in some cases, stops. Such "steady-state" tumours can appear dormant for long periods of time, producing few if any detectable symptoms. However, some of these tumours begin growing again. **Research tells us why.** Through a normal process termed ***angiogenesis***, cells in all parts of the tumour - not just the cells in the outer section - acquire access to blood vessels and are able to grow and divide. In the coming months, I'll discuss what is involved in ***angiogenesis*** and the role this process plays in the other stages in carcinogenesis - ***invasion*** and ***metastasis***.

Exciting Events!

Our Foundation is privileged to partner with wonderful people in our community for fund raising events. We gratefully acknowledge our event partners:

We had several cheque presentations during the month of December from events that have taken place earlier in the year:

Durocher Charity Classic
$8,000 for Seeds4Hope

Do Good Divas
$46,000 for (5) I.V. Pumps and Patient Assistance Fund

Jillian Stratichuk & Alexis Marra's Friendship Pins
$1,700 for Patient Assistance Fund

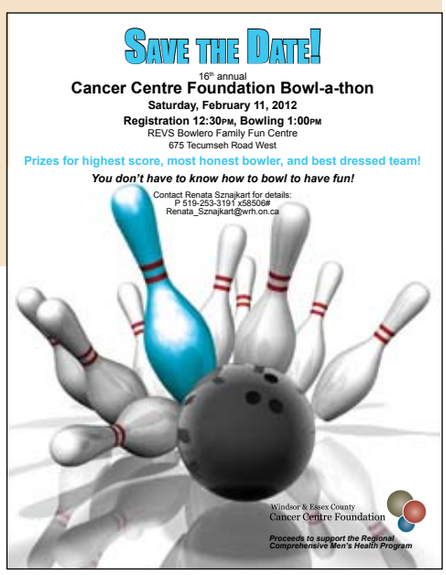
A Breast or Knot Dragon Boat Team
$1,000 for Patient Assistance Fund

Coming Events

Jan. 14th & 15th – the **25th annual Wedding Extravaganza** will be held at the Caboto Club. Visit our booth and learn how you can create customized favour cards that will let your wedding guests know you have made a donation to our Foundation in lieu of traditional wedding favours.

Registration is now taking place for the **16th Annual Bowl-a-thon**. The Bowl-a-thon will once again take place at REVS Bowlero Family Fun Centre on February 11th. Late registration begins at 12:30pm, bowling starts at 1:00pm. New this year – register yourself or your team online! You can also collect pledges and donate online. Check it out at www.WindsorCancerFoundation.org.kintera.org/bowlathon

Would you like to attend an event? Do you want to organize an event? Call, email, or visit Renata in the Foundation office!



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