Regional Cancer Program
Programme régional de cancérologie

Functional Analysis of a novel protein that is downregulated in lobular breast carcinoma.

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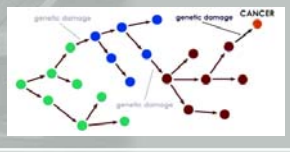
Presentation Outline

- What is Cancer; Breast Cancer?
- Programmed cell death
- RNA Binding Proteins
- Previous Research
- Current Research
- Future Directions
- Acknowledgements and Questions

What is Cancer?

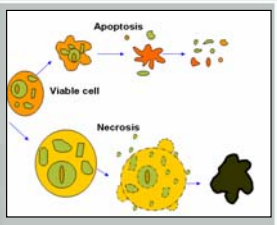
- Cancer: Refers to diseases characterized by the development of abnormal cells that divide uncontrollably and are unable to die.
- These abnormal cells infiltrate (metastasize) and interfere with normal body functions.



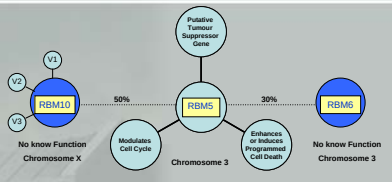
http://www.barrettsinfo.com/content/5_how_does_cancer_develop_in_barretts.htm

Programmed Cell Death

- Apoptosis
- Genetic process involving gene and gene product interactions
- Not to be confused with necrosis (cell death caused by trauma)
- Deregulation can lead to cancer



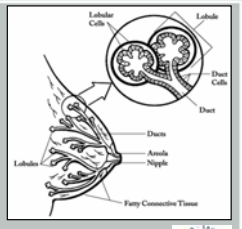
RNA Binding Motif (RBM) Proteins



- Is the expression of RBM5 modulated in aggressive breast cancer?
- What is the relationship between RBM5 and the other RBM family members?

Lobular Vs. Ductal Breast Carcinomas

- **5000** Canadian women will die from breast cancer this year
- **70%-80%** Ductal
- **5%-10%** Lobular



http://www.au-kbc.org/research_areas/bio/projects/bcinfoldig_breast.gif

Expression of RBM-Related Factors in Primary Breast Tissue

- Rintala-Maki N.D., et al. 2006. J Cell Biochem 100(6): 1440-1458
- Paired non-tumor and tumor breast specimens
- Kind donations HRSRH, Sudbury Regional Breast Clinic in 2002-2004
- Patients from North East Local Health Integration Network (LHIN 13)
- Expression of RBM5, RBM6 and RBM10 was analyzed

Intriguing Findings

RBM10v1 and RBM5

- Expression levels were significantly positively correlated
- Expression of RBM10v1 is significantly lower in lobular compared to ductal carcinomas

RBM10v2 and RBM6

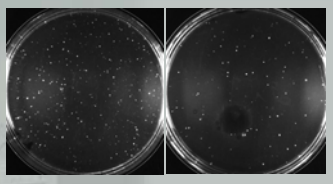
- Expression was significantly positively correlated
- Significance increased in relation to a number of clinicopathological parameters normally associated with poor prognoses

Does RBM10v1 function in a similar fashion to RBM5?

Will RBM10v1 sensitize cells to programmed cell death?

Preliminary observations

Control RBM10v1



Observation:
Cancer cells artificially induced to express more RBM10v1, either are unable to grow as fast or are dying.

Question:
Is RBM10v1 inducing apoptosis and/or causing cell cycle arrest?

Current Research

Objective 1: Artificially induce more RBM10v1 expression in cancer cells

- Integrate plasmid containing gene of interest into a cancer cell line.

Objective 2: Determine the effect of RBM10v1 on the cell cycle or programmed cell death

- Quantify the amount of cells in different stages of cell cycle (via flow cytometry).

Results: Transfected cells do not appear to undergo cell cycle arrest
There are dramatically fewer viable cells in the transfected group

Objective 3: Delineate programmed cell death signaling pathway

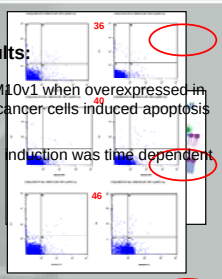
- Quantify expression levels of various programmed cell death related genes (via PCR array)

Results: Change in expression levels of 4 related genes.

Current Research

Results:

- RBM10v1 when overexpressed in the cancer cells induced apoptosis
- This induction was time dependent

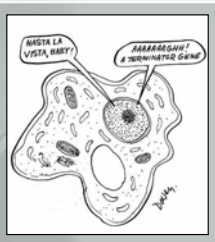


http://www.sabiosciences.com/pcr_details.php?catalog_no=10085K

Future Directions

- Further experiments at narrower time points to determine the onset of apoptosis
- Utilize different apoptosis assays to confirm RBM10v1 as an apoptotic inducer
- Identification of molecules effected by RBM10v1.
- Analysis of RBM10v2 as an apoptosis inducer

The Big Picture



Identifying and understanding the function of the genes that induce programmed cells death will help in the development of novel cancer treatments and ultimately a cure for cancer.

Acknowledgments

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- All interested minds here today

Questions?