Seeds4Hope

A program of the Windsor Essex County Cancer Centre Foundation

2013 Seeds4Hope Grant Recipient

Dr. Luis Rueda

"Transcriptomic Analysis of Prostate Cancer using RNA-Seq Data"

SUMMARY OF RESEARCH PROJECT

Prostate cancer is a very complex disease that is becoming progressively more prevalent, particularly in Windsor-Essex County. Studying prostate cancer at the molecular level helps researchers uncover the genetic regulatory mechanisms involved in the tumour biology. An important task that prostate cancer researchers face is to discover "biological indicators" or biomarkers that can help health professionals distinguish between benign and malignant tumours, and their different subtypes. This is of great significance, since the lack of reliable biomarkers to distinguish, at early stages, tumours that are not likely to grow from those that are most likely to grow is a major challenge in prostate cancer treatment. As a result, many men who are at low risk of their prostate cancer progressing are undergoing surgery unnecessarily, which can lead to side effects ranging from temporary pain and weakness to permanent impotence and urinary incontinence.

There are exciting new biotechnological techniques that can help researchers learn more about the biomarkers that affect the way tumours develop. The growth of new approaches that combine bioinformatics with traditional hands-on lab techniques has revolutionized the way that researchers study the "expressions of the genes" or transcriptome. One such tool called "RNA-seq technology" assists researchers in revealing unexplored territories by "reading" the transcriptome at a remarkable single-nucleotide resolution. It's like reading a book about several thousand gene products of a prostate tumour, all at once. The power of this technique can help researchers better understand the known regulatory mechanisms of gene expression (transcription) and discover new gene products that can't be detected by conventional tools alone.

This project focuses on the regulatory mechanisms of gene expression in prostate cancer using computational biology techniques on RNA-seq public datasets from the most recent studies. The project will have particular emphasis on known and novel ways in which genes are expressed in prostate cancer, and the associated machinery that can help researchers identify benign from malignant tumours. Furthermore, the approaches used in this project will also be used to distinguish among different types of prostate cancer such as low or high-risk, localized or metastatic and benign tumours. Using computational approaches to predict the growth of prostate tumours and their associated risk will open an unexplored territory for finding novel regulatory methods of gene expression and potential new biomarkers for prostate cancer progression.

HOW THIS RESEARCH HELPS ADVANCE QUALITY CANCER CARE IN OUR COMMUNITY

More people develop and die from prostate cancer in Windsor-Essex County than in the rest of Ontario. Due to increased efforts in research, the five-year prostate cancer survival in the region has also increased steadily in the past two decades. This proposal will support the Windsor Essex County Cancer Centre Foundation initiatives, which focus on the genomics and transcriptomic aspects of cancer. This study will have a significant impact on controlling the growth of prostate cancer in our region, in other areas in Ontario and across Canada. Using the proposed computational approaches for prediction of malignancy and growth rate of prostate tumours will lead to improvements in prostate cancer diagnosis, especially in early detection. Finding new biomarkers will help in the development of novel therapeutic strategies and lower recurrence. This project will also bring together bioinformaticians, biologists and clinicians in the region and other places, laying the foundation for future research collaborations.

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PROGRESS REPORT

We have developed a computational model used to detect different ways in which genes are expressed in benign versus malignant prostate tumours. The computational model uses machine learning techniques for classification, which simulates a diagnosis system using only a few genes as cancer indicators. The model has been tested on a dataset generated using the latest RNA sequencing technologies, obtaining a perfect prediction accuracy. As a result, we have identified a very small subset of genes as drivers of prostate cancer, which have been validated using human protein data repositories. Proteins associated with three of these genes have been categorized as having moderate to strong relationships to prostate cancer and weak relationship to noncancerous tissue.

Our aim for the second year is to validate the drivers we found by means of biological experiments on prostate cancer cell lines. In addition, we are currently deploying a set of integrative computational tools that will be used to simulate the next steps in the molecular biology of the cells, involving potential proteins whose functions are involved in cellular processes associated with prostate cancer. We are also planning to extend our studies to other studies for which clinical information is available, including demographics, pathological information and patients' data. We aim to identify a more robust set of drivers of prostate cancer that can be used as potential targets for diagnosis, drug development, therapeutic procedures and clinical follow up.