

OVERVIEW

While rare, cancer remains a significant cause of death by disease in children. In the USA, 15,700 children are diagnosed each year.

Childhood cancer is largely a genetic disease although its pattern of inheritance is not always clearly defined.

These genetic mechanisms of susceptibility are the focus of research for the Cancer Genetics Program at the Hospital for Sick Children (SickKids) in Toronto, Canada.

Research within the Cancer Genetics Program includes identifying and studying genes associated with childhood cancer risk; analyzing molecular and cell biology pathways associated with development and progression of cancers; identifying molecules that might represent viable targets for drug therapies; and developing practical applications of genetic testing of families at risk.

The Program receives more than 190 new cancer referrals each year and to date has consulted on over 1200 families.

Studying the epigenetics of childhood cancer

TECHNICAL SITUATION

Nardin Samuel, an MD/PhD candidate at the Faculty of Medicine, University of Toronto is using QluCore's Omics Explorer in her research on the epigenetics of Li-Fraumeni Syndrome (LFS) cancers at the Hospital for Sick Children, Genetics and Genome Biology, Ontario Institute for Cancer Research. Individuals with LFS have mutations in the TP53 gene that predispose them to a wide spectrum of cancers that can develop as children. TP53 mutations are also found in women who have developed breast cancer under the age of 30. Many people with LFS will be diagnosed with cancer two or more times during their lifetime.

Epigenetics is the study of the chemical reactions that activate and deactivate specific parts of the genome as it develops and also the study of the factors that influence these reactions. It provides insight into regulatory mechanisms that influence gene expression changes, affording the opportunity to study dynamic cellular processes beyond the genome. Epigenetic analysis of LFS provides a unique avenue to study this syndrome since the causative genetic aberration is well identified, according to Samuel.

SOLUTION

Samuel is studying a range of samples including DNA from patient blood, primary tissue from tumours, and patient cell lines. Cell lines are from lymphoid cells or blood-derived cells or fibroblast cell lines taken from skin biopsies.

Various sequencing approaches are applied to understand how cells are primed to transform and become malignant and in particular, how they can be targeted therapeutically.

Studying the epigenetics of childhood cancer, Hospital of Sick Children in Toronto, Canada.
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“The strength of the QluCore software is being able to conduct and validate statistical analyses and also produce a variety of visualizations”

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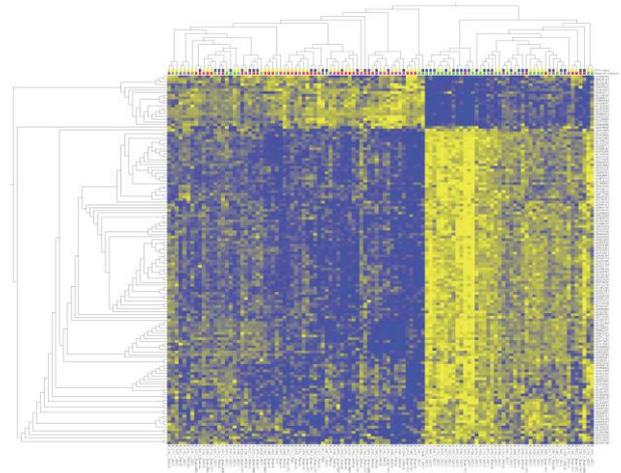
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Heat map showing clusters in methylation data that are generated based on different patient attributes (cancer diagnosis in this case)

“We are doing genetic sequencing, RNA and microRNA analysis, and also experiments in tissue culture in which we are manipulating various genes within the cells lines and analysing their properties,” explains Samuel.

She and her colleagues are dealing with a variety of types and sizes of datasets. Omics Explorer is particularly useful for genome-wide differential methylation analyses, she says.

BENEFITS

“The strength of the QluCore software is being able to conduct and validate statistical analyses and also produce a variety of visualizations, “ explains Samuel. “It has excellent visualization tools that can make very nice depictions of the data and heat maps.”

Samuel adds that the software is particularly useful for people who don't have much experience in computational biology or computation in general.

Epigenetics is a growing field in the arena of cancer susceptibility syndromes and approaches to analyzing genome-scale data are essential, she concludes.

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