Bringing whole genome transcriptome sequencing (WGTS) to patient care and clinicians: the prospective MOHCCN-O study and Molecular Tumor Board at PM2C.

Scientific Abstract

Background and Rationale: The sequencing of the whole genome and transcriptome (WGTS) of tumors has revealed alterations responsible for cancer. Some of these alterations may be useful for guiding therapeutic approaches. Marathon of Hope has strongly advocated for and supported the prospective use of WGTS to understand tumor biology and offer treatment opportunities to patients. However, factors such as cost, turnaround time, and the need for expertise to interpret results have limited their ability to support therapeutic decisions. MOHCCN-Ontario (MOHCCN-O) aims to bring these analyses to patients, building on the successful experiences of other studies across Canada, such as the POG program in British Columbia.

Objective(s): The primary objective of this study is to prospectively perform WGTS in cancer patients across Ontario to better understand the biology of their disease and explore treatment opportunities based on these analyses. Other objectives include raising awareness within the oncology community regarding the value of precision medicine and providing education to clinicians and scientists about the applicability of these results in clinical practice.

Methods and Results: MOHCCN-O has been recruiting patients since 2023. However, the complexity of accessing the study, interpreting results and returning to patients, the turnaround time, and a lack of awareness about the study have limited its broad applicability. Since October 2024, the study has increasingly recruited patients from diverse tumor sites and healthcare providers, with a special focus (but not limited to) on early-onset and rare tumors. PM2C has simplified the process by implementing an electronic medical health-based order system, expedited approval review, and a dedicated team to track and accelerate analysis. Additionally, shortening the turnaround time for results and providing a complete clinical report—including annotated alterations according to their level of actionability and oncogenicity (based on OncoKB)—have contributed to access to patients. A weekly molecular tumor board has also been launched to review each case for approval, discuss clinical reports, and consider treatment options. This board includes an open discussion between clinicians, scientists, and trainees, and has contributed to increased interest in performing these analyses. It has also provided a unique opportunity for education and raised awareness of the potential benefits of WGTS for patients.

Conclusion(s): MOHCCN-O has become an important opportunity for patients at PM2C to access advanced tumor profiling using WGTS, with improvements in workflow simplification, increased awareness among clinicians, and the introduction of a molecular tumor board to discuss clinical report implications.

Anticipated Impact: This study will have a direct impact on patients by providing real-time tumor profiling through whole genome and transcriptome sequencing, potentially aiding decisions regarding current or future therapies. Additionally, it will contribute to MOH's goal of profiling 15,000

cases by the end of 2026. This study will be expanded across the Ontario Cancer Consortium and will contribute to create a nationwide prospective study.

Plain language abstract

Background and rationale: Cancer is caused by changes in the genes and how they are expressed. Scientists have found that sequencing the entire genome and transcriptome (WGTS) of tumors can reveal these changes and help guide treatment decisions. The Marathon of Hope Cancer Centres Network (MOHCNN) has been a strong advocate for using WGTS to better understand cancer biology and improve treatment options for patients. However, challenges like high costs, long turnaround times, and the need for specialized knowledge to interpret results have made it difficult to use WGTS in routine cancer care. MOHCCN-Ontario (MOHCCN-O) is working to overcome these challenges and bring this advanced analysis to patients across Ontario, inspired by similar successful programs in other parts of Canada, such as the POG program in British Columbia.

Objectives: The goal of this study is to use WGTS in cancer patients throughout Ontario to better understand their disease and identify potential treatment options. It also aims to raise awareness about precision medicine in the oncology community and educate doctors and researchers on how these advanced analyses can be used in everyday clinical practice.

Methods and Results: Since 2023, MOHCCN-O has been recruiting patients, though challenges like the complexity of the process, long wait times, and limited awareness have slowed its progress. Since October 2024, the study has made significant strides by recruiting more patients, especially those with rare and early-onset cancers. The study has been made more accessible through improvements like a simplified electronic ordering system, faster approval processes, and a dedicated team to speed up analyses. Clinical reports are now more comprehensive, with detailed information about cancer-causing changes and their potential treatment options. A weekly molecular tumor board has also been established to review each case and discuss potential treatment strategies, providing a valuable opportunity for education and increasing interest in these analyses.

Conclusion: MOHCCN-O has become an important opportunity for patients at PM2C to access advanced tumor profiling, helping to streamline the process and improve awareness among healthcare professionals.

Anticipated Impact: This study will have a significant impact on patients by providing up-to-date tumor profiling that can help guide treatment decisions. It will also help the Marathon of Hope reach its goal of profiling 15,000 cancer cases by 2026 and will eventually expand to become a nationwide study across Canada, contributing to more personalized cancer care for patients across the country.