Computational analysis of epigenetic patterns facilitates diagnosis of unknown hereditary disorders

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A new sophisticated computational model, developed by scientists at Lawson Health Research Institute, is bringing an innovative method of diagnosing rare hereditary conditions.

Genome-wide testing of DNA methylation, a mechanism of the epigenome, has been shown to facilitate the diagnosis of previously unsolved cases of neurodevelopmental or congenital abnormalities. The epigenome is any process that can change the expression of a gene without changing the gene sequence.

The latest in a series of research publications around the theme of epigenomic testing applied the new pattern recognition model to DNA samples of 965 patients with neurodevelopmental and congenital anomalies that did not have a definitive diagnosis despite extensive clinical genetic testing. Their DNA, acquired through blood samples, was examined using the new model, and dozens of new cases were resolved.

Current testing of patients who present with neurodevelopmental and congenital anomalies leaves a number of cases undiagnosed or unexplained. "Many families spend years going through repeated testing and assessments, in search of a diagnosis. This process is hard on patients and families, and is a great cost to our health care system," explains Dr. Bekim Sadikovic, Associate Scientist at Lawson, and Head of the Molecular Genetics Division in the Department of Pathology and Laboratory Medicine, London Health Sciences Centre (LHSC).

While currently there are limited treatment options associated with many of these conditions, providing a specific diagnosis can help physicians better predict the course of the disease, allowing for better planning and support for the patient. This research highlights the value of epigenomic testing in the routine assessment of neurodevelopmental and congenital disorders.

From this research, LHSC will be the first site in the world to offer this type of genetic testing. "We are excited to make this testing accessible to local patients, and across the world. Our lab has partnered and licensed

this technology to Greenwood Genetics Laboratories in the United States and Amsterdam University Medical Centre Laboratories in the European Union", says Dr. Sadikovic. 100 per cent of revenue will be funneled back to support local testing for patients and ongoing research.

The study, "Diagnostic utility of genome-wide DNA methylation testing in genetically unsolved individuals with suspected hereditary conditions" is published in the *American Journal of Human Genetics*.

This is one example of how Lawson is contributing to making Ontario Healthier, Wealthier and Smarter.

More information: Erfan Aref-Eshghi et al, Diagnostic Utility of Genome-wide DNA Methylation Testing in Genetically Unsolved Individuals with Suspected Hereditary Conditions, *The American Journal of Human Genetics* (2019). DOI: 10.1016/j.ajhg.2019.03.008

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