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Genetic breakthrough for brain cancer in children

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An international research team led by the Research Institute of the McGill University Health Centre (RI MUHC) has made a major genetic breakthrough that could change the way pediatric cancers are treated in the future. The researchers identified two genetic mutations responsible for up to 40 per cent of glioblastomas in children - a fatal cancer of the brain that is unresponsive to chemo and radiotherapy treatment. The mutations were found to be involved in DNA regulation, which could explain the resistance to traditional treatments, and may have significant implications on the treatment of other cancers. The study was published this week in the journal *Nature*.

Using the knowledge and advanced technology of the team from the McGill University and Génome Québec Innovation Centre, the researchers identified two mutations in an important gene known as the histone H3.3. This gene, one of the guardians of our genetic heritage, is key in modulating the expression of our genes. "These mutations prevent the cells from differentiating normally and help protect the genetic information of the tumor, making it less sensitive to radiotherapy and chemotherapy," says Dr. Nada Jabado, hematologist-oncologist at The Montreal Children's Hospital of the McGill University Health Centre (MUHC) and principal investigator of the study.

"This research helps explain the ineffectiveness of conventional treatments against cancer in children and adolescents – we've been failing to hit the right spot," says Dr. Jabado, who is also an Associate Professor of Pediatrics at McGill University. "It is clear now that

glioblastoma in children is due to different molecular mechanisms than those in adults, and should not be treated in the same way. Importantly, we now know where to start focusing our efforts and treatments instead of working in the dark".

Inappropriate regulation of this gene has been observed in other cancers such as colon, pancreatic, lymphoma, leukemia and pancreatic neuroendocrine cancer, and future research could therefore reveal improved treatments for these diseases. "What is significant here is that for the first time in humans we have identified a mutation in one of the most important genes that regulates and protects our genetic information. This is the irrefutable proof that our genome, if modified, can lead to cancer and probably other diseases. What genomics has shown us today is only the beginning," says Dr. Jabado.

"Génome Québec is proud to have contributed to a project whose results will make a significant impact on the treatment of pediatric glioblastoma," underlines Marc Le Page, President and CEO of Génome Québec. "The outstanding contribution of experts in genomics and new sequencing technologies, made by the McGill University and Génome Québec Innovation Centre and as part of Dr. Jabado's project, is further proof that genomics has become essential for development and innovation in medical research. I wish to acknowledge the excellence of the teams involved in this study and the model of interdisciplinary collaboration that was implemented."

"Personalized medicine has amazing potential for many areas of health care, including infection, rare diseases and cancer. Researchers, like this team, play a vital role in translating discoveries into improved patient care," says Dr. Morag Park, Scientific Director of the CIHR Institute of Cancer Research. "Through research advancements like this, there is now greater emphasis on using genetic information to make medical decisions. We congratulate Dr. Jabado and her team on these results".

Brain tumours are the primary cause of death for children with cancer in Europe and North America. The diagnosis of glioblastoma in a child or adolescent remains a death sentence and about 200 children in Canada die every year of this cancer. Most children will die within the two years of their diagnosis regardless of treatment.

Provided by McGill University Health Centre