A genetic defect in sex cells may predispose to childhood leukemia

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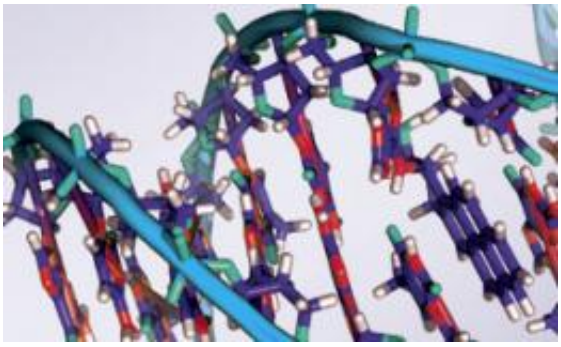

Researchers at the Sainte-Justine University Hospital Center and the University of Montreal have found a possible heredity mechanism that predisposes children to acute lymphoblastic leukemia (ALL), the most common type of blood cancer in children. According to their findings published in Genome Research, the presence of a genetic defect in the egg or sperm from which children having ALL arise may be a prerequisite for the disease to develop. A significant number of children with ALL are thought to inherit a rare PRDM9 gene variant responsible for the abnormal sex cells–a gene variant that puts their own children at risk of having ALL-predisposed offspring.

"Our findings indicate ALL susceptibility to be partially hereditary. However, it is not classic heredity in the sense that the abnormal genetic

variant does not need to be passed from parent to child for offspring to have the disease," explains Julie Hussin, a doctoral student in Genomics under the direction of Dr. Philip Awadalla, a genetics researcher.

"Instead, the genetic defect in the egg or sperm from which the children developed is thought to predispose them to leukemia," continues Julie Hussin. "However, only the children who inherit the genetic variant run the risk of transmitting ALL predispositions to their offspring." According to the study, more than three fourth of families with affected children have an atypical form of the PRDM9 gene, but only half the patients inherited this genetic variant. The defect is expressed by chromosome recombinations at unusual points during gamete formation (eggs in girls, sperm in boys).

While an abnormal gamete may lead to ALL development, this condition alone is not enough. "Triggering the process of cancer cell proliferation inevitably requires a second hit, such as other mutations or environmental factors," explains Julie Hussin.

Until now, few pediatric cancer studies have analyzed data from parents, as scientists generally focus on studying children, their tumors or their environment, especially during pregnancy. "Parents have to be included in these studies. Our findings demonstrate the importance of including parents' genetic information for the understanding of childhood leukemia, as well as other early childhood diseases," added Dr. Philip Awadalla, the lead principal investigator on the study.

The findings were replicated in a cohort of American children with ALL through a collaboration of the Sainte-Justine University Hospital Center in Montreal, Canada, and St. Jude Children's Research Hospital in Memphis, USA.

More information: Rare allelic forms of PRDM9 associated with

childhood leukemogenesis in *Genome Research*, December 5, 2012. genome.cshlp.org/content/early … .144188.112.abstract

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