



MEDIA RELEASE

Autism and schizophrenia: Scientists measure gene mutation rate

New study from University of Montreal shows family history not always a good indicator

Montreal, August 26, 2010 – An international study led by University of Montreal scientists suggests family history may not be a good predictor of the presence of mutations predisposing to autism or schizophrenia. The findings show how new or *de novo* gene mutations – alterations of the cell's DNA – play a role in these devastating conditions. Published in the *American Journal of Human Genetics*, this study has implications for disease prevalence and severity.

“This study emphasizes the importance of *de novo* mutations as genetic factors predisposing to autism and schizophrenia. We found an increased frequency of severe *de novo* mutations in critical brain genes in both of these diseases,” says senior author and University of Montreal professor, Guy Rouleau.

“Harmful *de novo* mutations, as observed in this study, may in part explain the high global incidences of autism and schizophrenia,” adds Dr. Rouleau, who is also director of the Sainte-Justine University Hospital Research Center and a scientist at the University of Montreal Hospital Research Centre.

Investigating human mutation rate:

The team analyzed 400 genes that are turned on in nerve cells from patients with autism or schizophrenia spectrum disorders. Their results showed that there is an excess of *de novo* gene mutations associated with the two diseases.

Their study revealed that DNA taken directly from the patient's blood was superior to that taken from patient-derived cell lines. “The source of biological material is crucial for these types of experiments,” says lead author Philip Awadalla, a University of Montreal pediatrics professor, scientist at the Sainte-Justine University Hospital Research Center and scientific director of the CARTaGENE project.

“In the process of confirming our findings, we were also able to provide one of the first direct estimates of the human mutation rate,” continues Dr. Awadalla. “The number of mutations per generation is extremely small but on the order of what was previously indirectly inferred for human-chimpanzee comparisons. We also discovered that mutations can be introduced when cell lines are produced, which creates false-positive results. This artefact can significantly bias results and therefore great care needs to be taken when analyzing these samples.”

About *de novo* mutations:

Mutations are alterations of the cell's DNA that can occur because of errors in the DNA replication, which happen prior to cell division. Once DNA is changed, this mutation is passed down to a next generation. A mutation that is newly formed and therefore not inherited from either parent is called a *de novo* mutation.

Contributing authors of this investigation were from the Montreal Heart Institute, McGill University, North Carolina State University, Stanford University, Nathan S. Kline Institute for Psychiatric Research, Université Paris Descartes and INSERM.

Note to editors:

The Université de Montréal name can be adapted to University of Montreal (never Montreal University).

Partners in research:

This study was funded by Genome Canada, Génome Québec, the University of Montreal and the Canada Foundation for Innovation.

About the study:

The paper, "Direct Measure of the *de novo* Mutation Rate in Autism and Schizophrenia cohorts," published in the *American Journal of Human Genetics*, was authored by Philip Awadalla, Julie Gauthier, Rachel A. Myers, Ferran Casals, Fadi F. Hamdan, Alexander R. Griffing, Mélanie Côté, Edouard Henrion, Dan Spiegelman, Julien Tarabeux, Amélie Piton, Yan Yang, Adam Boyko, Carlos Bustamante, Lan Xiong, Judith L. Rapoport, Anjené M. Addington, J. Lynn E. DeLisi, Marie-Odile Krebs, Ridha Joober, Bruno Millet, Éric Fombonne, Laurent Mottron, Martine Zilvermit, Jon Keebler, Hussein Daoud, Claude Marineau, Marie-Hélène Roy-Gagnon, Marie-Pierre Dubé, Adam Eyre-Walker, Pierre Drapeau, Eric A. Stone, Ronald G. Lafrenière and Guy A. Rouleau.

On the Web:

- *American Journal of Human Genetics*: www.cell.com/AJHG
- University of Montreal: www.umontreal.ca/english
- University of Montreal Hospital Research Centre: www.chumtl.qc.ca/crchum.en.html
- Sainte-Justine University Hospital Research Center: www.recherche-sainte-justine.qc.ca/en
- Synapse to Disease Project: www.synapse2disease.ca
- CARTaGENE: www.cartagene.qc.ca

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