



## CAID Syndrome: Heart and Gut Dysrhythmia



A rare disease affecting both heart rate and intestinal movements has been discovered by researchers from CHU Sainte-Justine, Université de Montréal, CHU de Québec, Université Laval, and Hubrecht Institute. The "Chronic Atrial Intestinal Dysrhythmia syndrome" (CAID) is a serious condition caused by a rare genetic mutation, explained the researchers whose work has been published in *Nature Genetics*.

The researchers have developed a test to effectively diagnose CAID syndrome, which is characterised by the combined presence of different cardiac and intestinal symptoms. "The symptoms are severe, and treatments are very aggressive and invasive," according to Dr. Philippe Chetaille, a paediatric cardiologist and researcher at the university hospital CHU in Québec. These symptoms and treatments include:

- At the cardiac level: Patients suffer primarily from a slow heart rhythm, a condition which will necessitate the implantation of a pacemaker for half of them, often as early as in their childhood.
- At the digestive level: A chronic intestinal pseudo-obstruction will often force patients to feed exclusively intravenously, and many of them will also have to undergo bowel surgery.

### Mutation in the Gene SGOL1

The investigators analysed the DNA of patients of French-Canadian origin and a patient of Scandinavian origin showing both the cardiac and the gastrointestinal conditions. They were able to identify a mutation in the gene SGOL1 that is common to all patients showing both profiles. "To lift any doubts concerning the role of the identified mutation, we also made sure it was ruled out in people showing only one of the profiles," explained Dr. Gregor Andelfinger, a paediatric cardiologist and researcher at CHU Sainte-Justine.

Meanwhile, Dr. Jeroen Bakkers of Hubrecht Institute (The Netherlands), who also collaborated on the project, studied zebrafish with the same gene mutation. "The mutated fish showed the same cardiac symptoms as humans, which confirms the causal role played by SGOL1," Dr. Andelfinger added.

### A Transatlantic Founder Effect

Using the Quebec population BALSAC historical database to analyse the genealogy of eight patients of French-Canadian origin, the research team identified a common ancestor dating back to the 17th century; more precisely, a founder couple married in France in 1620. Molecular genetic tests also proved that the identified French-Canadian and the Swedish mutations share the same origin, suggesting the existence of a founder

effect and the major role played by migration of populations.

Based on the research team's calculations, the genetic legacy would date back to the 12th century, following the migration route of the Vikings from Scandinavia to Normandy, then that of the settlers who migrated to New France in the 17th century.

#### Role of SGOL1 is Focus of Future Research

The SGOL1 mutation acts mechanistically to reduce the protection of specific nerve and muscle cells in the gut and the heart, causing them to age prematurely due to an accelerated replication cycle, the research team said. The study findings indicate an unsuspected role for SGOL1 in the heart's ability to maintain its rhythm throughout life.

The specific role played by the gene and the impact of its mutation will be the focus of future investigations of the research group. A better understanding of the disease would be helpful in identifying new avenues for treatments specifically targeting the underlying genetic and molecular causes, the team said.

Source: ScienceDaily.com

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Published on : Fri, 10 Oct 2014