

# Methylated markers in Fragile X

January 6 2011

---

A "fingerprint" on a key gene in certain groups of people with Fragile X syndrome may be a litmus test for which patients can benefit from a new drug, reports a recent study of 30 patients with the syndrome. Fragile X is the most common cause of inherited intellectual retardation, affecting one in every 5,000 children worldwide.

Without a cure, Fragile X is caused by a mutation in a single gene, Fragile X Mental Retardation-1 or FMR1, where part of the gene is made longer than normal by additional repeats of DNA sequence. The degree of gene elongation varies from person to person; some individuals have little expansion and do not display symptoms of Fragile X whereas others have much more expansion, known as "full mutation."

For individuals with full mutation the FMR1 gene is shut down, resulting in severe Fragile X symptoms, and abnormal development of neuronal connections in the brain important for learning and memory. Normally, the FMR protein keeps a protein called mGluR5 in check. mGluR5 belongs to a family of proteins called mGlu5 receptors that is essential for many aspects of normal brain function; yet in patients with Fragile X, the FMR protein is absent, causing over-activation of mGluR5 in the brain, leading to symptoms of the disease.

Here, Sébastien Jacquemont and colleagues treated a group of 30 patients with [Fragile X syndrome](#) with a new drug that reduces the activity of mGluR5 in the brain. Not all patients showed improvement, but an analysis of those that did revealed that the promoter of the FMR1 gene (the control switch that that interacts with DNA to turn on gene

activity) in those patients was fully tagged with methyl groups.

The methyl group tags signaled that the FMR1 gene was completely shut off in these patients, providing a possible signature of people with Fragile X who could benefit from mGluR5-blocking drugs. The team also ran a large set of tests designed to detect changes in behaviors, like hyperactivity and inappropriate speech in the patients.

While the new drug had no effect on behavior as measured by the first slew of tests, it did show an effect on a secondary group of tests, when compared to a group of patients given a placebo treatment. Taking a closer look, the authors found that each member of the group of patients with fully methylated FMR1 promoters showed improvement in behavior.

The group with partially methylated promoters showed no such changes. This correlation between response to treatment and methylation status of the FMR1 promoter sets the stage for future studies designed to test whether methylation can serve as a predictor of positive drug response in patients with Fragile X syndrome.

**More information:** "1 Epigenetic Modification of the FMR1 Gene in Fragile X Syndrome Is Associated with Differential Response to the mGluR5 Antagonist AFQ056," by S. Jacquemont et al., *Science Translational Medicine*, 6-Jan-2011.

Provided by AAAS

Citation: Methylated markers in Fragile X (2011, January 6) retrieved 25 April 2024 from <https://medicalxpress.com/news/2011-01-methylated-markers-fragile.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.