# Chromosome 12 mutation linked to familial diarrhea

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(HealthDay) -- An activating mutation in *GUCY2C*, encoding guanylate cyclase C (GC-C), is thought to cause a novel familial diarrhea syndrome seen in a Norwegian family, according to a study published online March 21 in the *New England Journal of Medicine*.

Torunn Fiskerstrand, M.D., Ph.D., of the Haukeland University Hospital in Bergen, Norway, and colleagues describe the cause of a novel dominant disease in 32 members of a Norwegian family. Linkage analysis was used to identify a candidate region on chromosome 12, and *GUCY2C* was sequenced. Exome sequencing of the entire region was performed for three affected family members. Functional studies of mutant GC-C were carried out using HEK293T cells.

The researchers found that all affected family members had a heterozygous missense mutation in *GUCY2C*. In the candidate region, there were no other rare variants seen in exons of genes. There was a markedly increased production of cyclic guanosine monophosphate (cGMP) on exposure of the mutant receptor to its ligands.

"Increased GC-C signaling disturbs normal bowel function and appears to have a proinflammatory effect, either through increased chloride secretion or additional effects of elevated cellular cGMP," the authors write. "Further investigation of the relevance of genetic variants affecting the GC-C-cystic fibrosis transmembrane regulator pathway to conditions such as Crohn's disease is warranted."

Several authors disclosed financial ties to the pharmaceutical and biotechnology industries.

**More information:** Abstract
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