Mutations That Lead to Congenital Lactose Intolerance

Congenital lactase deficiency (CLD) is a rare severe autosomal recessive disorder, which means you will not have the disorder if you have at least one version of the gene that results in a functional lactase enzyme. Symptoms include watery diarrhea, gas, bloating, and malnutrition, which start a few days after birth by the onset of nursing.

Scientists have studied the human genome—a complete set of DNA in human cells—to determine what causes CLD. CLD is caused by mutations in the *LCT* gene.The *LCT* gene provides instructions for making the lactase enzyme. Mutations that cause congenital lactase deficiency are believed to interfere with the function of lactase, causing affected infants to have a severely impaired ability to digest lactose in breast milk or formula.

In patients with CLD, 5 different mutations in the coding region of the LCT gene have been identified. The most common causes identified for this disorder are missense mutations or premature stop codons in the coding region of the gene. In 27 of 32 patients (84%), they found homozygosity for a nonsense mutation, meaning those patients had two copies of a gene with a mutation that resulted in an early stop codon. In the other patients, they identified different missense mutations in each of the two copies of the gene a patient had. These mutations led to single or multiple amino acid substitutions that can interfere with the proper function of lactase.

This data demonstrates that this inability to digest lactose is the outcome of mutations affecting the structure of the protein leading to inactivation of the enzyme lactase.

References

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