SickKids | Genome Diagnostics

CAFFEY DISEASE (INFANTILE CORTICAL HYPEROSTOSIS)

Caffey Disease is an autosomal dominant disorder characterized by episodes of massive subperiosteal new bone formation, usually involving the diaphysies of long bones, mandible and clavicle. It typically presents before 5 months of age and clinical features resolve spontaneously around 2 years of age. A single pathogenic mutation, c.3040C>T (p.Arg1014Cys) has been found in the *COL1A1* gene. Penetrance of the mutation is only ~80%, with an inflammatory event as the proposed mechanism to elicit clinical presentation.

GENETICS

Caffey Disease is an autosomal dominant disorder caused by mutations in the collagen 1A1 (*COL1A1*) gene located on chromosome 17 (17q21).

In some cases, Caffey disease may be the result of new mutation, when the parents are not affected. In these cases the risk of having another affected child is low.

A person with Caffey disease whose partner is not affected with Caffey disease has a 50% chance of having a child with Caffey disease. In some cases, a parent may carry a *COL1A1* mutation but not be identified as affected with Caffey disease, due to the reduced pentrance (~80%) of the disease. In these cases, if the partner is not affected with Caffey disease there is a 50% chance of having a child with Caffey disease.

In rare cases a parent may carry the mutation only in their germ cells (gonadal mosaicism). The risk for gonadal mosaicism is ~1-2%. In cases of known gonadal mosaicism, if the other partner is not affected with Caffey disease, the couple has up to a 50% chance of having a child with Caffey disease.

TEST METHODS

- Direct mutation detection assay using DNA sequencing to test for the recurrent c.3040C>T (p.Arg1014Cys) mutation in the *COL1A1* gene

TEST SENSITIVITY

The c.3040C>T(p.Arg1014Cys) mutation in the *COL1A1* gene is the only mutation currently known to cause Caffey disease.

WHO SHOULD BE TESTED?

- Individuals clinically suspected of being affected with Caffey disease

- Parents of individuals with Caffey disease due to reduced pentrance

POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

***COL1A1* Gene Mutation**	**Explanation**
None detected	This result does not support a diagnosis of Caffey Disease
Mutation detected (c.3040C>T; p.Arg1014Cys)	This result supports a diagnosis of Caffey Disease

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/ Item # 114000

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

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1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of Caffey Disease.

2. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.

3. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.