The University of Chicago Genetic Services Laboratories

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SRCAP analysis for Floating Harbor syndrome

Clinical Features:

Patients with Floating Harbor syndrome [OMIM #136140] typically have short stature, delayed osseous maturation and expressive-language deficits (1). Distinctive facial features of affected individuals include a triangular shaped face, short philtrum, wide mouth, and a long nose with a broad base, full tip and low hanging columella (1). The majority of affected individuals have some degree of intellectual impairment or learning disability, ranging from moderate intellectual disability to borderline normal intelligence (2). Other associated features include skeletal anomalies, genitourinary anomalies, celiac disease, congenital heart defects, and a high-pitched or nasal voice (2). Floating Harbor syndrome shares many key clinical features with Rubinstein-Taybi syndrome [OMIM #180849], including short stature, a long nose with low hanging columella, and anomalous thumbs (1).

Inheritance:

Floating Harbor syndrome is an autosomal dominant condition. The majority of affected individuals have a *de novo* mutation, however some familial cases have also been reported (3). Recurrence risk for parents in cases with a confirmed *de novo* mutation is <1%. Recurrence risk for affected individuals is 50%.

Molecular Genetics:

Hood *et al.* (2012) identified mutations in the *SRCAP* gene (SNF2-related CBP activator protein) [OMIM #611421] in 13/13 (100%) patients with Floating Harbor syndrome. Goff *et al.* (2012) identified *SRCAP* mutations in 6/9 affected individuals (67%). *SRCAP* has 34 coding exons and is located at 16p11.2. It encodes a switch/sucrose nonfermentable-type chromatin-remodeling ATPase, which is a potent coactivator for CREB-binding protein (CREBBP, the major cause of Rubenstein-Taybi syndrome) and CBP-mediated transcription (1). All mutations reported to date are truncating mutations that occur in exon 34 (1, 2).

Additional Resources:

Floating Harbor Syndrome Support Group
Website: www.floatingharborsyndromesupport.com
Phone: 336-831-6955
Email: littleflock7@gmail.com

Test methods:

We offer full gene sequencing of all 34 coding exons and intron/exon boundaries of *SRCAP* by direct sequencing of amplification products in both the forward and reverse directions. Deletion/duplication analysis is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

SRCAP sequencing analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$2,550
CPT codes:	81407
Turn-around time:	4 weeks

SRCAP deletion/duplication analysis

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$1000
CPT codes:	81406
Turn-around time:	4 weeks

Note: The sensitivity of our assay may be reduced when DNA is extracted by an outside laboratory.

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

References:

1. Hood RL, Lines MA, Nikkel SM et al. Mutations in SRCAP, encoding SNF2-related CREBBP activator protein, cause Floating-Harbor syndrome. Am J Hum Genet 2012: 90: 308-313.
2. White SM, Morgan A, Da Costa A et al. The phenotype of Floating-Harbor syndrome in 10 patients. Am J Med Genet A 2010: 152A: 821-829.
3. Le Goff C, Mahaut C, Bottani A et al. Not all floating-harbor syndrome cases are due to mutations in exon 34 of SRCAP. Hum Mutat 2013: 34: 88-92.