Floating-Harbor Syndrome

https://www.ncbi.nlm.nih.gov/books/NBK114458/

SummaryClinical characteristics.Floating-Harbor syndrome (FHS) is characterized by typical craniofacial features; low birth weight, normal head circumference, and short stature; bone age delay that normalizes between ages six and 12 years; skeletal anomalies (brachydactyly, clubbing, clinodactyly, short thumbs, prominent joints, clavicular abnormalities); severe receptive and expressive language impairment; hypernasality and high-pitched voice; and intellectual disability that is typically mild to moderate. Difficulties with temperament and behavior that are present in many children tend to improve in adulthood. Other features can include hyperopia and/or strabismus, conductive hearing loss, seizures, gastroesophageal reflux, renal anomalies (e.g., hydronephrosis / renal pelviectasis, cysts, and/or agenesis), and genital anomalies (e.g., hypospadias and/or undescended testes).Diagnosis/testing.The diagnosis is established by identification of a heterozygous SRCAP pathogenic variant in those with clinical findings of FHS.Management.Treatment of manifestations: Early intervention programs, special education, and vocational training to address developmental disabilities; communication rehabilitation with sign language or alternative means of communication; and behavior management by a behavioral specialist/psychologist with consideration of medication as needed. Referral to an endocrinologist for consideration of human growth hormone (HGH) therapy; however, data on use of HGH in FHS are limited. Standard treatment for refractive errors and strabismus, hearing loss, seizures, gastroesophageal reflux, and renal and genitourinary anomalies.Surveillance: Close monitoring of growth, especially in the first year. Annual: ophthalmologic evaluation, hearing screening, blood pressure measurement, and assessment of renal function. Sonographic evaluation for renal cysts in teenage/adult years is indicated.Genetic counseling.FHS is inherited in an autosomal dominant manner. The majority of affected individuals have a de novo pathogenic variant. Each child of an individual with FHS has a 50% chance of inheriting the pathogenic variant. Prenatal testing is possible for families in which the pathogenic variant has been identified.

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DiagnosisSuggestive FindingsFloating-Harbor syndrome (FHS) should be suspected in individuals with the following clinical and radiographic features.Craniofacial appearance (see Figure 1)Figure 1. Facial appearance of a girl age 11 years with FHS (SRCAP pathogenic variant p.Arg2444Ter) A. Note triangular face with deep-set eyes; short philtrum; long nose with narrow bridge and broad base with low-hanging columella; and thin upper lip.Triangular faceDeep-set eyesShort philtrumWide mouth with a thin vermilion border of the upper lipLong nose with a narrow bridge, broad base, broad tip, and low-hanging columellaLow-set ears

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Significant delay in bone age (≥2 SD below the mean) with normalization between ages six and 12 yearsSkeletal anomalies. Brachydactyly, broad fingertips that give the appearance of clubbing, clinodactyly, short thumbs, prominent joints, clavicular abnormalities (See Figure 2.)Short adult stature. 140-155 cm (See Figure 3.)Figure 2. Dorsal (A) and palmar (B) view of the hands of the girl in Figure 1. Note clinodactyly, widened fingertips, and prominent joints. Figure 3. Frontal view of the girl in Figure 1. She has proportionate short stature with height <3rd centile.

Speech and language

Dysarthria and verbal dyspraxia with phoneme imprecisionHypernasalityHigh-pitched voiceSevere receptive and expressive language impairment across all domains of functionIntellectual disability. All individuals have some degree of intellectual impairment and/or learning disability ranging from borderline normal to moderate intellectual disability.Establishing the DiagnosisThe diagnosis of FHS is established in a proband with Suggestive Findings by identification of a heterozygous pathogenic (or likely pathogenic) variant in SRCAP on molecular genetic testing (see Table 1).Note: (1) Per ACMG/AMP variant interpretation guidelines, the terms "pathogenic variants" and "likely pathogenic variants" are synonymous in a clinical setting, meaning that both are considered diagnostic and both

can be used for clinical decision making [Richards et al 2015]. Reference to "pathogenic variants" in this section is understood to include any likely pathogenic variants. (2) Identification of a heterozygous SRCAP variant of uncertain significance does not establish or rule out the diagnosis.Molecular genetic testing approaches can include a combination of gene-targeted testing (single-gene testing, multigene panel) and comprehensive
genomic testing (exome sequencing, genome sequencing) depending on the phenotype.Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas genomic testing does not. Because the phenotype of FHS is broad, individuals with the distinctive findings described in Suggestive Findings are likely to be diagnosed using gene-targeted testing (see Option 1), whereas those with a phenotype indistinguishable from many other inherited disorders with short stature and/or intellectual disability are more likely to be diagnosed using genomic testing (see Option 2).Option 1When the phenotypic and laboratory findings suggest the diagnosis of FHS, molecular genetic testing approaches can include single-gene testing or use of a multigene panel.Single-gene testing. Sequence analysis of SRCAP detects small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. Perform sequence analysis first. If no pathogenic variant is found, perform gene-targeted deletion/duplication analysis to detect intragenic deletions or duplications.A multigene panel that includes SRCAP and other genes of interest (see Differential Diagnosis) is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this GeneReview. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.For an introduction to multigene panels click here. More

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Clinical CharacteristicsClinical DescriptionPrior to the molecular characterization of Floating-Harbor syndrome (FHS) by Hood et al [2012], a number of reports included descriptions of individuals in whom the diagnosis of FHS could be questioned. This GeneReview only includes information on those 73 individuals with molecularly confirmed FHS (i.e., presence of a heterozygous SRCAP pathogenic variant) [Hood et al 2012, Le Goff et al 2013, Nikkel et al 2013, Dong et al 2014, Kehrer et al 2014, Nagasaki et a 2014, Seifert et al 2014, Amita et al 2016, Coughlin et al 2017, Singh et al 2017, Budisteanu et al 2018, Choi et al 2018, Milani et al 2018, Shields et al 2019]. The 41 females and 32 males range in age from eight months to 52 years.FHS is frequently recognized in early childhood because of the characteristic facial features (Figure 1). Infants and younger children are often referred for assessment of poor growth or developmental (predominantly speech and language) delay.Craniofacial features include triangular face, deep-set eyes, short philtrum, wide mouth with a thin vermilion border of the upper lip, long nose with a narrow bridge, broad base, broad tip, and low-hanging columella, and low-set ears.The features become more pronounced with age, especially the length of the nose and the width of the nasal tip.Intellect. Although gross motor and fine motor milestones are within normal limits, affected individuals typically have mild-to-moderate intellectual disability. A disorder of speech and language is the most severe disability. Most aspects of communication are affected; expressive language is most consistently and severely affected. Dysarthria and verbal dyspraxia with phoneme imprecision is most common, with absent speech in some individuals. Voice is described as hypernasal and high-pitched. The majority of affected children receive mainstream education with individualized educational plans. Regression of skills is not typical of FHS.Behavior. Many individuals with FHS have temperament and behavior differences and difficulties: temper tantrums in infancy and

attention-deficit/hyperactivity disorder spectrum with impulsivity, inattention, and restlessness at school age. Aggressive and violent outbursts can occur. Obsessive compulsive disorder and anxiety have been observed. Behavior problems are reported to improve in adulthood.Growth. Short stature is a cardinal sign of FHS. The majority of individuals with FHS have low birth weight (from 3 SD below the mean to 0 SD) and normal head circumference (2 SD below the mean to 0 SD). In the first years of life weight gain and linear growth are poor. A significant delay in bone age is reported (≥2 SD below the mean) with normalization between ages six and 12 years. Average adult height is 140-155 cm.Puberty. Early puberty has been reported; data are insufficient to determine the incidence in either sex.Eye. Five of 73 individuals have been reported with hyperopia and eight of 13 with strabismus. One individual had anterior chamber abnormalities.Hearing. Conductive hearing loss has been seen in eleven of 73 individuals with FHS. Cochlear abnormality has been observed in one of 73.Neurologic. Seizures have been observed in seven of 73 individuals.Gastrointestinal. Reflux can be severe, requiring G-tube feeding in some. Constipation and colonic strictures have been observed. One of 73 individuals had celiac disease; two had transient gluten intolerance.Genitourinary. Renal and genitourinary anomalies can occur and include hypospadias and undescended testes, epididymal cysts, varicocele, and posterior urethral valves in boys. Hydronephrosis/renal pelviectasis and nephrocalcinosis, renal cysts, and renal agenesis have been observed. One adult of the 73 reported individuals developed polycystic kidney disease and end-stage renal disease.Orthopedic. The body habitus is often stocky with a broad chest and short neck. Additional features include hand anomalies such as clinodactyly, brachydactyly, short thumbs, and broad fingertips that give the appearance of clubbing (Figure 2). Clavicular anomalies including pseudarthrosis and clavicular hypoplasia have been observed, as have short metacarpals, 11 pairs of ribs, kyphoscoliosis, prominent joints, dysplastic hips, and dislocated radial heads. Perthes disease has also been reported.Dental. A number of individuals with FHS have dental problems (e.g., caries, microdontia, oligodontia, delayed loss of primary teeth) and orthodontic problems (e.g., maxillary retrusion, underbite).Cardiac. Cardiac malformations are not usually a feature of FHS. Of 73 affected individuals one had mild aortic coarctation, one had mesocardia with persistent left

superior vena cava, two had atrial septal defect, and one individual had tetralogy of Fallot.Genotype-Phenotype CorrelationsPathogenic variants in exons 33 and 34 of SRCAP that are predicted to cause truncation of the protein (removing 3 C-terminal AT-hook DNA-binding motifs while leaving the CBP-binding and ATPase domains intact) result in the FHS phenotype.PrevalenceThe prevalence of FHS is not known. Seventy-three individuals with a heterozygous SRCAP pathogenic variant have been reported to date [Hood et al 2012, Le Goff et al 2013, Nikkel et al 2013, Dong et al 2014, Kehrer et al 2014, Nagasaki et a 2014, Seifert et al 2014, Amita et al 2016, Coughlin et al 2017, Singh et al 2017, Budisteanu et al 2018, Choi et al 2018, Milani et al 2018, Shields et al 2019].The majority of individuals reported with FHS are of European origin, but FHS has also been diagnosed in individuals of Chinese, South American, South Asian, Japanese, and Korean background [Hood et al 2012, Nikkel et al 2013, Nagasaki et al 2014, Amita et al 2016, Singh et al 2017, Choi et al 2018]. Whether the occurrence of FHS is lower in nonwhite populations or the observed difference is the result of other factors is not known.

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Genetically Related (Allelic) DisordersSRCAP truncating variants upstream of exon 33 and 34 have been identified in individuals with developmental and health issues, without clinical features of

Floating-Harbor syndrome [Author, personal communication].

Differential DiagnosisThe distinctive facial features, bone age delay, and characteristic speech disability that make the diagnosis of Floating-Harbor syndrome (FHS) straightforward in early childhood become less distinct with age. Table 2 lists genes and associated conditions that should be considered in children in whom the diagnosis of FHS is suspected.Table 2. Other Genes of Interest in the Differential Diagnosis of Floating-Harbor Syndrome (FHS)View in own windowGene(s) 1Differential DisorderMOIClinical Features of Differential DisorderOverlapping w/FHSDistinguishing from FHS

CCDC8

CUL7

OBSL1

Three M syndrome

AR

Triangular faceShort 5th fingersBone age may be slightly delayed.Males may have hypospadias.Severe pre- & postnatal growth restriction (final height 5-6 SD below mean; i.e., 120-130 cm)

Relatively large head, hypoplastic midface, thick eyebrows, fleshy nasal tip, long philtrum, prominent mouth & lips, pointed chinNormal intelligenceAbsence of language impairmentCharacteristic radiologic findingsShort broad neck, prominent trapezii, deformed sternum, short thorax, square shoulders, winged scapulae, & hyperlordosis, prominent heels, loose jointsHypogonadism in males

CREBBP

EP300

Rubinstein-Taybi syndrome

AD

Facial features (e.g., low-hanging columella)Broad or angulated thumbs5th-finger clinodactylyShort stature

Round face, downslanted palpebral fissures, small mouth openingSevere intellectual disabilityNormal bone ageCardiac malformations

FOXP2

FOXP2 speech and language disorders

See footnote 2.

DysarthriaHypernasalitySevere expressive & receptive language & literacy impairments

Absence of:

Short statureDelayed bone ageFHS characteristic facies Aggression in childhood

Multiple etiologies 3

Silver-Russell syndrome(SRS)See footnote 3.

Pre- & postnatal growth restrictionExpressive language impairment (much more severe in FHS than in SRS)

Body asymmetryCafé au lait maculesBlue scleraAbsence of FHS characteristic facial features & thumb anomalies

AR = autosomal recessive; MOI = mode of inheritance; SD = standard deviation(s); SRS = Silver-Russell syndrome1. Genes are listed in alphabetic order.2. Recurrence risk for sibs of

proband with a FOXP2 speech and language disorder depends on the causative genetic alteration.3. Silver-Russell syndrome (SRS) has multiple etiologies including: epigenetic changes that modify expression of genes in the imprinted region of chromosome 11p15.5, maternal UPD7, and (infrequently) autosomal dominant or autosomal recessive inheritance. When a proband has SRS as the result of paternal hypomethylation at IC1 or maternal UPD7, both parents are predicted to be unaffected, the risk to the sibs is not increased over that of the general population, and the risk to offspring is probably low.

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ManagementEvaluations Following Initial DiagnosisTo establish the extent of disease and needs in an individual diagnosed with Floating-Harbor syndrome (FHS), the evaluations summarized in Table 3 (if not performed as part of the evaluation that led to the diagnosis) are recommended.Table 3.

Recommended Evaluations Following Initial Diagnosis in Individuals with Floating-Harbor SyndromeView in own windowSystem/ConcernEvaluationComment

Constitutional

Measurement of growth & plotting of growth parametersSyndrome-specific charts are currently not available for children w/a SRCAP pathogenic variant.

Eyes

Ophthalmologic exam

ENT

Audiology eval(See Hereditary Hearing Loss and Deafness Overview for details of eval.)Dental eval

Genitourinary

Renal ultrasound examBlood pressure assessmentAssessment for cryptorchidism in males

Musculoskeletal

Orthopedic assessmentEval for hip dysplasia & clavicular anomalies

Other

Multidisciplinary developmental evalIncl assessment of gross & fine motor skills, speech/language, cognitive abilities, & vocational skills w/special attn to speech delay & anomaliesConsultation w/clinical geneticist &/or genetic counselorTreatment of ManifestationsTreatment includes the following:Early intervention programs, special education, and vocational training to address developmental disabilitiesCommunication rehabilitation with sign language or alternative means of communicationBehavior management strategies including referral to a behavioral specialist/psychologist and consideration of medication if neededReferral of the family to support groups and other resourcesStandard treatment for any of the following if identified:Refractive errors and strabismusHearing lossSeizuresRenal diseaseCryptorchidismOrthopedic complicationsDental problemsReferral to an endocrinologist for consideration of human growth hormone (HGH) therapy. HGH therapy with modest response has been reported in three children with FHS. Caution is

indicated as limited information about HGH therapy in FHS is available.Investigation for celiac disease if indicated by clinical featuresSurveillanceTable 4. Recommended Surveillance for Individuals with Floating-Harbor SyndromeView in own windowSystem/ConcernEvaluationFrequency

Constitutional

Eval of growthClose monitoring w/each visit, esp in 1st yr of life

Bone age examEval for signs of early puberty

Especially in persons treated w/growth hormone

Eyes

Ophthalmologic evalAnnually

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Audiology evalAnnually; more frequent eval if history of multiple episodes of otitis media

Renal

Blood pressure measurementAnnuallyAssessment of renal function incl plasma BUN & creatinineAnnuallyStandard monitoring for renal anomaliesFollow-up renal ultrasound if symptomaticSonographic eval for renal cystsIn teenage/adult yrs as indicated by abnormalities on renal function tests &/or blood pressure measurementEvaluation of Relatives at RiskSee Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.Pregnancy ManagementNo specific pregnancy complications for the mother or the fetus have been observed in the two women with SRCAP pathogenic variants who had children with FHS.Therapies Under InvestigationSearch ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

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Treatment of ManifestationsTreatment includes the following:Early intervention programs, special education, and vocational training to address developmental disabilitiesCommunication rehabilitation with sign language or alternative means of communicationBehavior management strategies including referral to a behavioral specialist/psychologist and consideration of medication if neededReferral of the family to support groups and other resourcesStandard treatment for any of the following if identified:Refractive errors and strabismusHearing lossSeizuresRenal diseaseCryptorchidismOrthopedic complicationsDental problemsReferral to an endocrinologist for consideration of human growth hormone (HGH) therapy. HGH therapy with modest response has been reported in three children with FHS. Caution is indicated as limited information about HGH therapy in FHS is available.Investigation for celiac disease if indicated by clinical features

Early intervention programs, special education, and vocational training to address developmental disabilities

Communication rehabilitation with sign language or alternative means of communication

Behavior management strategies including referral to a behavioral specialist/psychologist and consideration of medication if needed

Referral of the family to support groups and other resources

Standard treatment for any of the following if identified:

Refractive errors and strabismus

Hearing loss

Seizures

Renal disease

Cryptorchidism

Orthopedic complications

Dental problems

Referral to an endocrinologist for consideration of human growth hormone (HGH) therapy. HGH therapy with modest response has been reported in three children with FHS. Caution is indicated as limited information about HGH therapy in FHS is available.

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SurveillanceTable 4. Recommended Surveillance for Individuals with Floating-Harbor SyndromeView in own windowSystem/ConcernEvaluationFrequency

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Evaluation of Relatives at RiskSee Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Pregnancy ManagementNo specific pregnancy complications for the mother or the fetus have been observed in the two women with SRCAP pathogenic variants who had children with FHS.

Therapies Under InvestigationSearch ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.Mode of InheritanceFloating-Harbor syndrome (FHS) is inherited in an autosomal dominant manner.Risk to Family Members

Parents of a proband

Most individuals with FHS have the disorder as the result of a de novo SRCAP pathogenic variant and therefore represent simplex cases (i.e., a single occurrence in the family).Transmission of an SRCAP pathogenic variant from an affected mother to her child has been reported in two families to date [Nikkel et al 2013].Molecular genetic testing and clinical evaluation for signs of FHS are recommended for the parents of a proband with an apparent de novo pathogenic variant.If the pathogenic variant found in the proband cannot be detected in the leukocyte DNA of either parent,

the proband most likely has a de novo pathogenic variant; another possible explanation is germline mosaicism in a parent. Though theoretically possible, no instances of germline mosaicism have been reported.The family history of some individuals diagnosed with FHS may appear to be negative because of failure to recognize the disorder in a family member with a milder phenotype. Therefore, an apparently negative family history cannot be confirmed unless appropriate clinical evaluation and/or molecular genetic testing has been performed on the parents of the proband.An advanced paternal age effect is suggested. In their series of 13 individuals with a heterozygous SRCAP pathogenic variant, Hood et al [2012] reported a mean paternal age of 36.9 years (range 29-44 years).Sibs of a proband. The risk to the sibs of the proband depends on the clinical/genetic status of the proband's parents:In the rare case of a parent being affected and/or known to have the pathogenic variant identified in the proband, the risk to sibs is 50%.If the proband has a known SRCAP pathogenic variant that cannot be detected in the leukocyte DNA of either parent, the recurrence risk to sibs is estimated to be 1% because of the theoretic possibility of parental germline mosaicism [Rahbari et al 2016].Offspring of a proband. Each child of an individual with FHS has a 50% chance of inheriting the SRCAP pathogenic variant.Other family members. The risk to other family members depends on the status of the proband's parents: if a parent has the FHS-causing pathogenic variant, the parent's family members may be at risk.Related Genetic Counseling IssuesConsiderations in families with an apparent de novo pathogenic variant. When neither parent of a proband with an autosomal dominant condition has the pathogenic variant identified in the proband or clinical evidence of the disorder, the pathogenic variant is likely de novo. However, non-medical explanations including alternate paternity or maternity (e.g., with assisted reproduction) and undisclosed adoption could also be explored.

Family planning

The optimal time for determination of genetic risk and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to the parents of an affected child and to young adults who are affected.Prenatal Testing and

Preimplantation Genetic TestingOnce the SRCAP pathogenic variant has been identified in an affected family member, prenatal testing for a pregnancy at increased risk for FHS and preimplantation genetic testing are possible.Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Mode of InheritanceFloating-Harbor syndrome (FHS) is inherited in an autosomal dominant manner.

Risk to Family Members

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Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

Human Growth Foundation

www.hgfound.org

MAGIC Foundation

Phone: 800-362-4423Email: contactus@magicfoundation.org

www.magicfoundation.org

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Molecular GeneticsInformation in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.Table A.Floating-Harbor Syndrome: Genes and DatabasesView in own windowGeneChromosome LocusProteinLocus-Specific DatabasesHGMDClinVar

SRCAP

16p11.2

Helicase SRCAP

SRCAP @ LOVD

SRCAP

SRCAP

Data are compiled from the following standard references: gene from

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For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.Table B.OMIM Entries for Floating-Harbor Syndrome (View All in OMIM) View in own window

136140FLOATING-HARBOR SYNDROME; FLHS

611421SNF2-RELATED CBP ACTIVATOR PROTEIN; SRCAPMolecular PathogenesisIntroduction. Helicase SRCAP is a nuclear protein that mediates different intracellular signaling pathways as well as chromatin remodeling. The encoded protein is an ATPase that is necessary for the incorporation of a histone variant into nucleosomes.SRCAP functions as a transcriptional activator for CREB and CBP-mediated transcription, along with Notch-mediated and steroid receptor-mediated transcription [Hood et al 2016]. Alteration in SRCAP has the potential for producing widespread target-gene dysregulation.Mechanism of disease causation. Unknown. However, the non-random clustering of pathogenic variants (see Genotype-Phenotype Correlations) that predict truncated SRCAP strongly suggests a dominant-negative disease mechanism due to loss of one or more critical domain(s) – for instance, the three C-terminal AT-hook DNA-binding motifs (see Hood et al [2016] for details of SRCAP domains).Table 5. Notable SRCAP Pathogenic VariantsView in own windowReference SequencesDNA Nucleotide ChangePredicted Protein ChangeComment [Reference]

NM_006662.2

NP_006653.2

c.7303C>Tp.Arg2435TerRecurrent pathogenic variants [Hood et al 2012, Nikkel et al 2013]c.7330C>Tp.Arg2444TerVariants listed in the table have been provided by the authors. GeneReviews staff have not independently verified the classification of variants.GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.Cancer and Benign TumorsThe Cancer Genome Atlas summarizes somatic pathogenic variants in genes

(including SRCAP) involved in chromatin remodeling which may have a role in regulating genes in human malignancies. SRCAP is frequently mutated in numerous cancers including melanomas, lung cancers, stomach adenocarcinoma, and colorectal adenocarcinoma [Chen et al 2016].

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Notable SRCAP Pathogenic Variants

Reference SequencesDNA Nucleotide ChangePredicted Protein ChangeComment

[Reference]

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NP_006653.2

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