GENEReviews

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Camurati-Engelmann Disease

[*Progressive Diaphyseal Dysplasia*]

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Summary

Disease characteristics. Camurati-Engelmann disease (CED) is characterized by hyperostosis of the long bones and the skull, proximal muscle weakness, severe limb pain, a wide-based, waddling gait, and joint contractures. Facial features such as frontal bossing, enlargement of the mandible, proptosis, and cranial nerve impingement resulting in facial palsy are seen in severely affected individuals later in life.

Diagnosis/testing. Diagnosis of CED is based on physical examination and radiographic findings and can be confirmed by molecular genetic testing. Bone and muscle histology are nonspecific. *TGFB1* is the only gene known to be associated with CED. Sequence analysis identifies mutations in *TGFB1* in about 90% of affected individuals and is clinically available.

Management. Treatment of CED includes corticosteroids and losartan. Pain is managed with analgesics and non-pharmacologic methods. Bilateral myringotomy can improve conductive hearing loss resulting from serous otitis. Following initiation of corticosteroid treatment, blood pressure should be monitored monthly; when maintenance steroid dose is achieved, yearly evaluation includes complete neurologic examination, CBC count, blood pressure, and hearing screen.

Genetic counseling. CED is inherited in an autosomal dominant manner. Penetrance is reduced. The incidence of *de novo* mutations is unknown. Each child of an individual with CED has a 50% chance of inheriting the *TGFB1* mutation. Prenatal diagnosis may be available through laboratories offering custom prenatal mutation analysis for families in which the disease-causing mutation has been identified in an affected family member.

Diagnosis

Clinical Diagnosis

Features essential to the diagnosis of Camurati-Engelmann disease (CED) in a proband include the following:

- **Radiographic findings of hyperostosis** of one or more of the long bones. Periosteal and endosteal bony sclerosis of the diaphyses of the long bones results in uneven cortical thickening, increased bone diameter, and in some cases a narrowed medullary canal. Hyperostosis is usually restricted to the diaphyses but may progress to the

metaphyses. The epiphyses are rarely, if ever, involved. Hyperostosis is usually symmetric in the appendicular skeleton but may be asymmetric.

Other radiologic findings may include: (1) skull involvement beginning at the base of the anterior and middle fossae and often including the frontal bone [Wallace et al 2004]; (2) mild osteosclerosis in the posterior neural arch of the spine and parts of the flat bones that correspond to the diaphysis.

- **Proximal muscle weakness**

Testing

Changes in bone and muscle histology are nonspecific.

Molecular Genetic Testing

GeneReviews designates a molecular genetic test as clinically available only if the test is listed in the GeneTests Laboratory Directory *by either a US CLIA-licensed laboratory or a non-US clinical laboratory. GeneTests does not verify laboratory-submitted information or warrant any aspect of a laboratory's licensure or performance. Clinicians must communicate directly with the laboratories to verify information.*—ED.

Molecular Genetic Testing—Gene. *TGFB1* is the only gene known to be associated with CED.

Other loci. The affected members of one family with CED did not share marker haplotypes at the *TGFB1* locus and had no sequence alterations in *TGFB1* exons 1 through 7 [Hecht et al 2001], implying genetic locus heterogeneity.

Molecular genetic testing: Clinical uses

- Confirmatory diagnostic testing
- Clarification of genetic status in at-risk relatives

Molecular genetic testing: Clinical method

- **Sequence analysis.** More than 90% of individuals with CED have identifiable mutations in *TGFB1*. The majority of these mutations are missense mutations in exon 4 leading to single amino acid substitutions in the encoded protein. Mutations other than the three common alleles (R218C, R218H, C225R) include Y81H, L10-L12dup, R156C, H222D, C223S, C223R, and C223G [Janssens et al 2000, Kinoshita et al 2000, Campos-Xavier et al 2001, Hecht et al 2001, Mumm et al 2001, Janssens et al 2003, Kinoshita et al 2004, Wallace et al 2004, Janssens et al 2006].

Table 1 summarizes molecular genetic testing for this disorder.

Table 1. Molecular Genetic Testing Used in Camurati-Engelmann Disease

Test Method	Mutations Detected	Mutation Detection Rate	Test Availability
Sequence analysis	Sequence alterations of *TGFB1*	90%	Clinical Testing

Interpretation of test results. For issues to consider in interpretation of sequence analysis results, click here.

Testing Strategy for a Proband

- Molecular genetic testing of *TGFB1* should begin with sequencing of exon 4.

- If no mutation is found, the remaining exons should be sequenced.

Genetically Related (Allelic) Disorders

CED and Ribbing disease, representing phenotypic variations of the same disorder, are the only phenotypes currently known to be associated with mutations in *TGFB1*.

Clinical Description

Natural History

Individuals with Camurati-Engelmann disease (CED) present with limb pain, proximal muscle weakness, poor muscular development, a wide-based, waddling gait, easy fatigability, and headaches. The average age of onset of symptoms in the 199 reported individuals is 14 years, with a range of birth to age 76 years (see Literature Cited).

Extremities. Decreased muscle mass and weakness are most apparent in the proximal lower limbs, resulting in difficulty when rising from a sitting position. A wide-based, waddling gait is found in 64% of individuals. Joint contractures occur in 43% of individuals. Marfanoid body habitus is described in some affected individuals [Wallace et al 2004, Janssens et al 2006].

Bone pain is reported in 90% of affected individuals [Wallace et al 2004, Janssens et al 2006]. The pain is described as constant, aching, and most intense in the lower limbs. Pain often increases with activity, stress, and cold weather. Many individuals have intermittent episodes of severe pain and incapacitation. The enlarged bone shafts can also be palpable and tender on examination; 52% of affected individuals report bone tenderness with palpation [Wallace et al 2004]. Intermittent limb swelling, erythema, and warmth also occur.

Susceptibility to fracture may be reduced because of increased bone mineral density, but healing of fractures, when they occur, may be delayed [Wallace et al 2004].

Neurologic. Sclerosis of the cranial nerve foramina can lead to direct nerve compression or neurovascular compromise. Cranial nerve deficits occur in 38% of affected individuals. The most common deficits are hearing loss, vision problems, and facial paralysis.

Approximately 15% of individuals with CED have conductive and/or sensorineural hearing loss. Conductive loss can be caused by narrowing of the external auditory meatus, bony encroachment of the ossicles, or narrowing of the oval and round windows. Sensorineural hearing loss is caused by narrowing of the internal auditory canal and compression of the cochlear nerve and/or vasculature. Sensorineural loss can also occur with attempted decompression of the facial nerves.

Involvement of the orbit has led to proptosis, papilledema [Cohen & States 1956, Mottram & Hill 1965, Morse et al 1969, Wolf & Ford 1971, Tucker et al 1976], epiphora [Morse et al 1969], glaucoma, and subluxation of the globe [Brodrick 1977].

Rarely, clonus [Neuhauser et al 1948], sensory loss [Ramon & Buchner 1966], slurred speech, cerebellar ataxia [Kormas et al 1998], and bowel and bladder incontinence [Cockayne 1920] are reported.

Ribbing disease, an osteosclerotic disease of the long bones that is radiographically indistinguishable from CED and usually presents with bone pain after puberty [Makita et al 2000], is now known to be caused by mutations in *TGFB1* [Janssens et al 2006]. Thus, CED and Ribbing disease represent phenotypic variations of the same disorder.

Other. Musculoskeletal involvement can lead to varying degrees of lumbar lordosis, kyphosis, scoliosis, coxae valga, genua valga, flat feet, and frontal bossing.

Rare manifestations include anemia (hypothesized to be caused by a narrowed medullary cavity), anorexia, hepatosplenomegaly, decreased subcutaneous tissue, atrophic skin, hyperhidrosis of the hands and feet, delayed dentition, extensive caries, delayed puberty, and hypogonadism [Gupta & Cheikh 2005].

Pregnancy. One individual who experienced relief with steroids also experienced decreased bone pain and improved muscle strength while pregnant, which allowed discontinuation of her steroid therapy. Scintigraphic bone imaging with MDP a few hours after delivery of her second child showed decreased uptake compared to imaging prior to pregnancy and six weeks postpartum [De Vits et al 1994].

Genotype-Phenotype Correlations

No known correlation exists between the nature of the mutations and the severity of the clinical or radiographic manifestations [Campos-Xavier et al 2001].

Penetrance

Some obligate heterozygotes for CED with identified *TGFB1* mutations have had normal radiographs [Wallace et al 2004]; an exact penetrance figure is not known.

Anticipation

Earlier onset of symptoms and increased severity of symptoms and bone involvement in successive generations has been reported in several families [Saraiva 1997, Wallace et al 2004, Janssens et al 2006]. If these findings represent anticipation rather than ascertainment bias (the latter being more likely), the mechanism of anticipation is unknown. Although multiple copies of the amino acid leucine can be encoded by one observed mutation in exon 1, the mutation was not found in these families.

Nomenclature

Engelmann described the second reported occurrence of CED in 1929 as "osteopathic hyperostotica (sclerotisans) multiplex infantilis."

The terms Engelmann disease and diaphyseal dysplasia were commonly used until Neuhauser et al (1948) coined the term progressive diaphyseal dysplasia.

Gulledge and White (1951) suggested the term progressive diaphyseal hyperostosis, which was not widely used.

Prevalence

The prevalence is unknown. At least 200 individuals have been reported.

The disorder is pan ethnic.

Differential Diagnosis

For current information on availability of genetic testing for disorders included in this section, see GeneTests Laboratory Directory. —ED.

Few disorders share the clinical and radiographic findings of Camurati-Engelmann disease (CED). The correct diagnosis is made by physical examination and skeletal survey.

- **Craniodiaphyseal dysplasia** [OMIM 218300] has progressive and marked enlargement of the midline cranial bones causing a distinct facial deformity including nasal bridge widening and ocular hypertelorism. Cranial involvement in CED is milder and only on occasion results in frontal bossing and proptosis. The sclerosis of the long bones in craniodiaphyseal dysplasia is restricted to the diaphyses, which helps differentiate it from CED, in which the metaphyses can be affected as well.
- **Kenny-Caffey syndrome type 2** [OMIM 127000] is characterized by dwarfism, cortical thickening of the long bones, delayed fontanel closure, craniofacial anomalies, hypocalcemia, and hypoparathyroidism. Neither laboratory abnormalities nor delayed fontanel closure occur in CED.
- **Juvenile Paget disease** [OMIM 239000] is characterized by a predisposition to fractures, coarse trabeculations, and bowing of the long bones. There is no predisposition to fractures or bowing of the long bones in CED.
- **Diaphyseal dysplasia with anemia** [OMIM 231095] results in severe anemia and an increased susceptibility to infections. Diaphyseal dysplasia with anemia comprises endosteal bone formation with no evidence of subperiosteal bone formation. The presence of endosteal and subperiosteal bone deposition present in CED help distinguish it from the endosteal hyperostoses as well.
- **Hyperostosis corticalis generalisata, Worth type** [OMIM 144750] has endosteal thickening without widening of the diaphyseal shaft. There is also a characteristic wide deep mandible with an increased gonial angle, which is distinct from the enlarged mandible found only on occasion in CED.
- ***SOST*-related sclerosing bone dysplasias** include sclerosteosis (SCL) and van Buchem disease. A distinguishing clinical feature of SCL is variable syndactyly, usually of the second (index) and third (middle) fingers. The manifestations of van Buchem disease are generally milder than SCL, and syndactyly is absent. The *SOST*-related sclerosing bone dysplasias are inherited in an autosomal recessive manner, while CED is inherited in an autosomal dominant manner. Individuals with SCL and van Buchem disease have endosteal hyperostosis with smooth periosteal surfaces, whereas individuals with CED have periosteal thickening and an uneven, rough cortex.

Management

Evaluations at Initial Diagnosis to Establish the Extent of Disease

The initial evaluation should include neurologic examination, measurement of blood pressure, complete skeletal survey, ESR (erythrocyte sedimentation rate), CBC count, hearing screen, and ophthalmologic evaluation.

If acute bone pain is present, ESR and bone scan may be helpful as baseline measures of disease activity.

Treatment of Manifestations

Corticosteroids may relieve many of the symptoms of Camurati-Engelmann disease (CED). Several investigators report success with corticosteroid treatment in reducing pain and weakness, improving gait, exercise tolerance, and flexion contractures, and correcting anemia and hepatosplenomegaly [Allen et al 1970, Lindstrom 1974, Minford et al 1981, Crisp & Brenton 1982, Low et al 1985, Naveh et al 1985, Bourantas et al 1995, Schapira et al 1995, Saraiva 1997, Heymans et al 1998, Bas et al 1999, Wallace et al 2004]. Unsuccessful steroid therapy was reported in one adult [Smith et al 1977].

Individuals with severe symptoms can be treated with a bolus of prednisolone 1.0-2.0 mg/kg/day followed by rapid tapering to the lowest alternate-day dose tolerated. Less symptomatic individuals can be started on 0.5-1.0 mg/kg every other day. Some individuals may be able to discontinue steroid therapy during quiescent periods.

Higher-dose steroids may help with acute pain crises.

Losartan. Although no outcome data are available, losartan can be tried in symptomatic individuals who do not tolerate corticosteroids or who have concomitant hypertension. Losartan has an anti-TGFβ effect and is being tested in Marfan syndrome.

Other analgesics, and non-pharmacologic methods are frequently used for alleviation of pain.

Hearing loss evaluation by an otolaryngologist should include a BAER and a CT with fine cuts through the inner ear. Reports of successful treatment of hearing loss in CED are rare. Surgical decompression of the internal auditory canals can improve hearing. However, the skull hyperostosis is progressive, and cranial nerve compression often recurs [Miyamoto et al 1980].

Corticosteroids may delay skull hyperostosis and cranial nerve impingement. Lindstrom (1974) reported no change in conductive hearing loss with steroid therapy. A 30-year-old woman with a 75-dB neurosensory hearing loss on the right and a 65-dB neurosensory hearing loss of the left experienced some improvement in hearing with prednisone. Her hearing stabilized after decompression of the right internal auditory canal [Miyamoto et al 1980].

Bilateral myringotomy can improve conductive hearing loss resulting from serous otitis in individuals with CED [Mottram & Hill 1965].

A 71-year-old woman with bilateral conductive hearing loss and patent internal auditory canals underwent a cochlear implantation, and speech detection improved from 75 dB to 45 dB [Friedland et al 2000]. General contraindications for cochlear implants include a narrowed internal auditory canal and absence of a functioning eighth nerve, both of which can be found in individuals with CED. (See also Hereditary Deafness and Hearing Loss Overview)

Prevention of Primary Manifestations

Initiation of steroids prior to the onset of proximal muscle weakness and/or sclerotic bone changes has not been reported. Because of the variable symptomatology and decreased penetrance, treatment of asymptomatic individuals cannot be recommended.

Prevention of Secondary Complications

Steroids may delay bone hyperostosis and prevent or delay the onset of skull involvement. Histologic studies following steroid therapy showed increased bone resorption and secondary remodeling with increased osteoblastic activity and decreased lamellar bone deposition [Allen et al 1970]. However, several authors reported no regression of sclerosis on radiographic evaluation [Allen et al 1970, Naveh et al 1985, Verbruggen et al 1985] or on scintigraphic evaluation [Heymans et al 1998, Bas et al 1999]. Lindstrom (1974) and Bas et al (1999) reported diminished sclerosis on radiographs following steroid therapy. Verbruggen et al (1985) and Inaoka et al (2001) reported reduced radioactivity on bone scintigraphy. Long-term follow-up studies should be conducted to evaluate the success of corticosteroid therapy in preventing anemia, hepatosplenomegaly, headaches, and cranial nerve impingement.

Surveillance

After initiating corticosteroids, affected individuals should be followed monthly, with efforts to taper the steroids to the lowest tolerated dose. Blood pressure should be monitored at each visit, as hypertension can develop following the initiation of steroid therapy [Crisp & Brenton 1982].

When a maintenance steroid dose is achieved, yearly evaluations should include a complete neurologic exam, CBC count, blood pressure, and hearing screen.

Testing of Relatives at Risk

Testing of at-risk asymptomatic relatives is helpful to avoid potential misdiagnosis and unnecessary extremity pain later in life.

Therapies Under Investigation

Search ClinicalTrials.gov for access to information on clinical studies for a wide range of diseases and conditions.

Other

The following therapies have proven ineffective:

- **NSAIDs**
- **Biophosphonates.** Bone pain and uptake of 99mTc methylene diphosphonate by scintigraphy increased with pamidronate in a 27-year-old woman with CED [Inaoka et al 2001]. Clodronate infusion caused increased bone pain in one individual with CED and no improvement in another individual reported by Castro et al (2005).
- **Excess phosphate.** Treatment with cellulose phosphate led to worsening hypocalcemia and proximal myopathy in another individual [Crisp & Brenton 1982].

Genetics clinics are a source of information for individuals and families regarding the natural history, treatment, mode of inheritance, and genetic risks to other family members as well as information about available consumer-oriented resources. See the GeneTests Clinic Directory.

Support groups have been established for individuals and families to provide information, support, and contact with other affected individuals. The Resources section (below) may include disease-specific and/or umbrella support organizations.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, 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. This section is not meant to address all personal, cultural, or ethical issues that individuals may face or to substitute for consultation with a genetics professional. To find a genetics or prenatal diagnosis clinic, see the GeneTests Clinic Directory.

Mode of Inheritance

Camurati-Engelmann disease (CED) is inherited in an autosomal dominant manner.

Risk to Family Members

Parents of a proband

- Many individuals diagnosed with CED have an affected parent.
- A proband with CED may have the disorder as the result of a new gene mutation. The proportion of cases caused by *de novo* mutations is unknown.
- Recommendations for the evaluation of parents of a proband with an apparent *de novo* mutation include a complete skeletal survey or AP radiographs of the extremities and a lateral skull film. If the radiographs are normal, molecular genetic testing should be performed because of the possibility of reduced penetrance (i.e., individuals with a disease-causing mutation may have no clinical manifestations).

Note: Although many individuals diagnosed with CED have an affected parent, the family history may appear to be negative because of failure to recognize the disorder in family members.

Sibs of a proband

- The risk to the sibs of the proband depends upon the genetic status of the proband's parents.
- If a parent of the proband is affected or has an identified mutation in *TGFB1*, the risk to the sibs is 50%.
- When the parents are clinically unaffected, molecular genetic testing can be used to identify individuals who have a disease-causing mutation but no clinical manifestations.
- If the disease-causing mutation found in the proband cannot be detected in the DNA of either parent, the two possible genetic explanations are germline mosaicism in a parent or a *de novo* mutation in the proband. Although no instances of germline mosaicism have been reported, it remains a possibility.

Offspring of a proband. Each child of an individual with CED has a 50% chance of inheriting the mutation.

Other family members of a proband. The risk to other family members depends upon the genetic status of the proband's parents. If a parent is found to be affected or has an identified mutation in *TGFB1*, his or her family members are at risk.

Related Genetic Counseling Issues

Considerations in families with an apparent *de novo* mutation. When neither parent of a proband with an autosomal dominant condition has the disease-causing mutation or clinical evidence of the disorder, it is likely that the proband has a *de novo* mutation. However, possible non-medical explanations including alternate paternity or undisclosed adoption could also be explored.

Family planning. The optimal time for determination of genetic risk is before pregnancy.

DNA banking. DNA banking is the storage of DNA (typically extracted from white blood cells) for possible future use. Because it is likely that testing methodology and our understanding of genes, mutations, and diseases will improve in the future, consideration should be given to banking DNA of affected individuals. DNA banking is particularly relevant in situations in which the sensitivity of currently available testing is less than 100%. See DNA Banking for a list of laboratories offering this service.

Prenatal Testing

No laboratories offering molecular genetic testing for prenatal diagnosis of CED are listed in the GeneTests Laboratory Directory. However, prenatal testing may be available for families in which the disease-causing mutations have been identified in an affected family member in a research or clinical laboratory. For laboratories offering custom prenatal testing, see Testing.

Preimplantation genetic diagnosis (PGD) may be available for families in which the disease-causing mutation has been identified in an affected family member. For laboratories offering PGD, see Testing.

Molecular Genetics

Information in the Molecular Genetics tables is current as of initial posting or most recent update. —ED.

Table A. Molecular Genetics of Camurati-Engelmann Disease

Gene Symbol	Chromosomal Locus	Protein Name
TGFB1	19q13.1	Transforming growth factor beta-1

Data are compiled from the following standard references: Gene symbol from HUGO; chromosomal locus, locus name, critical region, complementation group from OMIM; protein name from Swiss-Prot.

Table B. OMIM Entries for Camurati-Engelmann Disease

131300	CAMURATI-ENGELMANN DISEASE
190180	TRANSFORMING GROWTH FACTOR, BETA-1; TGFB1

Table C. Genomic Databases for Camurati-Engelmann Disease

Gene Symbol	Entrez Gene	HGMD
TGFB1	7040 (MIM No. 190180)	TGFB1

For a description of the genomic databases listed, click here.

Normal allelic variants:*TGFB1* has seven exons. Several polymorphisms in *TGFB1* have been investigated for their effect on plasma *TGFB1* levels and bone mineral density. These include -1638G>A in a consensus CREB halfsite, -1347 C>T, 29T>C in the signaling peptide resulting in an L10P amino acid substitution, 11007delC in intron 4, and 20744T>C in intron 5. Several other polymorphisms have been identified including -1826C>A, 75G>C in exon 1 resulting in an R25P substitution, a 4426(TAAA)10-11 tetranucleotide repeat in intron 1, and 11935C>T in exon 5 resulting in a T263I substitution [Langdahl et al 1997, Grainger et al 1999, Yamada et al 2001, Hinke et al 2001, Keen et al 2001, Ziv et al 2003]. None of these polymorphisms have been found to be associated with disease severity in families with Camurati-Engelmann disease (CED) [Campos-Xavier et al 2001, Wallace et al 2004]. Watanabe et al (2002) catalogued nine additional single-base substitution polymorphisms, four in intron 1 (1511C>T, 1546A>G, 2064T>G, 3435C>T), three in intron 2 (6835A>G, 7234T>C, 7441G>T), and two in intron 5 (18381C>G, 19319A>G). Shah et al (2006) identified a distal promoter segment (-2665 to -2005) and ten novel polymorphisms.

Pathologic allelic variants: Three mutations in exon 4 of the *TGFB1* gene account for approximately 80% of the mutations observed in CED [Janssens et al 2000, Kinoshita et al 2000, Campos-Xavier et al 2001, Hecht et al 2001, Mumm et al 2001, Janssens et al 2003, Kinoshita et al 2004, Wallace et al 2004, Janssens et al 2006]:

- A g.10815C>T (c.652C>T) transition causing an R218C substitution is found in about 40% of individuals.
- A 10816G>A (c.653G>A) transition causing an R218H substitution or a 10830T>C (c.673T>C) transition causing a C225R substitution are found in an additional 35% of individuals.
- Other mutations include 30_38dup (L10-L12dup), 241T>C (Y81H), c.466C>T (R156C), c.664C>G (H222D), C223S, c.667T>C (C223R), and c.667T>G (C223G).

For more information, see Genomic Databases table above.

Normal gene product: Transforming growth factor beta-1 (TGF-β1) is synthesized as a large precursor molecule. TGF-β1 preprotein contains a signal peptide of 29 amino acids that is proteolytically cleaved. TGF-β1 is further cleaved after amino acid 278 to form latency-associated peptide (LAP) and active TGF-β1 [Dubois et al 1995]. LAP dimerizes with interchain disulfide links at Cys223 and Cys225. TGF-β1 can be secreted as an inactive small latent complex that consists of a mature TGF-β1 homodimer non-covalently associated with an LAP homodimer [Gentry et al 1988]. Most cells secrete TGF-β1 as a large latent complex of TGF-β1/LAP bound to latent TGFB-binding proteins (LTBP) [Kanzaki et al 1990]. LTBPs facilitate TGF-β1 folding, secretion, and possibly targeting to the TGFB matrix [Miyazono & Heldin 1992].

Abnormal gene product: The majority of mutations in individuals with CED lead to single amino acid substitutions in the carboxy terminus of TGF-β1 latency-associated peptide (LAP). The substitutions are near the site of interchain disulfide bonds between the LAP homodimers. These mutations may disrupt dimerization of LAP and binding to active TGF-β1, leading to increased active TGF-β1 release from the cell. R218H mutant fibroblasts from individuals with CED showed increased active TGF-β1 in the cell media compared to normal fibroblasts [Saito et al 2001]. R218C, H222D, and C225R mutant constructs also showed increased active TGF-β1 in the medium of transfected cells. In contrast, the L10-L12dup and Y81H mutations caused a decrease in the amount of TGF-β1 secreted. However, in a luciferase reporter assay specific for TGF-β1-induced transcriptional response, the mutant cells showed increased luciferase activity, suggesting intracellular activation of the receptor [Janssens et al 2003].

Resources

GeneReviews provides information about selected national organizations and resources for the benefit of the reader. GeneReviews is not responsible for information provided by other organizations. Information that appears in the Resources section of a GeneReview is current as of initial posting or most recent update of the GeneReview. Search GeneTests*for this disorder and select* Resources *for the most up-to-date Resources information.*—ED.

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Phone: 800-942-2732 (parent hotline); 717-703-0073 (business V/TTY)
Fax: 717-909-5599
Email: asdc@deafchildren.org
www.deafchildren.org

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International Skeletal Dysplasia Registry
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www.csmc.edu

References

Medical Genetic Searches: A specialized PubMed search designed for clinicians that is located on the PubMed Clinical Queries page. PubMed

Published Statements and Policies Regarding Genetic Testing

No specific guidelines regarding genetic testing for this disorder have been developed.

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Suggested Readings

Chapter Notes

Revision History

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