Soft tissue tumors: Dermatofibrosarcoma protuberans

Kayuri Patel, Dolores Lopez-Terrada

Department of Pathology at Texas Children's Hospital and Baylor College of Medicine, Houston, TX 77030, USA (KP, DLT)

Published in Atlas Database: August 2008
Online updated version: http://AtlasGeneticsOncology.org/Tumors/DermFibroSarcProtID5059.html
DOI: 10.4267/2042/44544

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2009 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Alias
Dermatofibrosarcoma Protuberans
Darier Ferrand tumor
Darier-Hoffmann tumor

Note
t(17;22)(q22;q13) is found in most if not all Dermatofibrosarcoma Protuberans cases.

Clinics and pathology

Disease
Neoplasm of the deep dermis with extension to the subcutis, characterized by locally aggressive growth. Dermatofibrosarcoma Protuberans (DFSP) is primarily associated with the trunk, limbs, head, neck and vulva.

Epidemiology
Rare soft tissue tumor, accounts for up to 1% of all soft tissue sarcomas.

Clinics
Typically diagnosed in young to middle-aged adults and affects either sex and all races, however numerous pediatric and congenital cases have been reported. The duration of the lesions prior to diagnosis is commonly more than 5 years, and decades in some cases.
Soft tissue tumors: Dermatofibrosarcoma protuberans

Patel K, Lopez-Terrada D

Atlas Genet Cytogenet Oncol Haematol. 2009; 13(8)

601

From top to bottom: a), b) Strong CD34 immunoreactivity (CD34, 40x).

Pathology
Monotonous storiform pattern of uniform, cytologically bland spindle cells, with a characteristic honeycomb pattern of infiltration into the subcutaneous fat. Immunohistochemical staining demonstrates strong positivity for vimentin and CD34 and negativity for factor XIIIa staining. Apolipoprotein has also been described as a marker for DFSP.

Treatment
Preferred treatment for DFSP is wide surgical excision with pathologically negative margins. Recently Imatinib mesylate therapy has been documented to induce extensive regression of primary and metastatic lesions.

Prognosis
Despite the local invasiveness, DFSP rarely metastasizes. The risk for development of metastatic disease is only 5%. The extent of surgical excision determines the prognosis of the patient. To reduce the local recurrence rate, a wide surgical excision with adequate margins is used.

Cytogenetics

Cytogenetics Morphological
Cytogenetically, DFSP is characterized by the presence of the recurrent t(17;22)(q22;q13) translocation or, more commonly, supernumerary ring chromosomes containing material from chromosomal regions 17q22 and 22q13 accompanied by simple chromosome trisomies. The translocation results in the fusion of the alpha chain type 1 of collagen (COL1A1) gene with the platelet-derived growth factor Beta (PDGFbeta) gene.

Cytogenetics Molecular
Fluorescence in situ hybridization based approaches can be used to demonstrate the t(17;22), using gene specific probes to demonstrate PDGFbeta gene rearrangements as well as genetic gains and losses.

Genes involved and proteins

COL1A1
Location
17q21.31-q22

Note
Molecular location: from base pairs 45,616,456 to 45,633,999.

DNA / RNA
COL1A1 is transcribed from centromere to telomere at 17q21.31-q22. The mRNA sequence contains 5927 bp, comprising 52 exons and spans approximately 18 kb. Exons 5 to 49 encode the alpha helical domain.

Protein
The COL1A1 gene produces a component of type I collagen called the pro-a1(I) chain. The Alpha1 (I)
chains of the type I collagen are synthesized as procollagen molecules containing amino and carboxy-terminal propeptides, which are removed by site-specific endopeptidase synthesizing the 1464 amino acid protein.

**PDGFbeta**

**Location**
22q12.3-q13.1

**Note**
Molecular location: from base pairs 37,949,665 to 37,970,936.

**DNA / RNA**
The PDGFbeta mRNA sequence contains 3373 bp, comprising 7 exons and spans approximately 22 kb. Exon 7 and most part of the exon 1 are non-coding sequences.

**Protein**
The PDGFbeta chains are synthesized as 240 amino acids precursors molecules containing amino and carboxy-terminal propeptides, which are removed by site-specific endopeptidases. Two PDGFbeta precursor chains associate in dimers to form the mature PDGFB after proteolysis.

**Result of the chromosomal anomaly**

**Fusion Protein**

**Note**
COL1A1 and PDGFbeta both encoded as pro-peptides are processed by proteolytic cleavage at N and C-terminus to give mature proteins. Sequences analyses of the chimerical COL1A1/PDGFBeta fusion transcripts has shown that the COL1A1/PDGFBeta putative proteins exhibit a pro-peptide structure, with a preserved N-terminus COL1A1 pro-peptide containing the signal peptide and the N and C-terminus PDGFbeta maturation cleavage sites. The result of this characteristic rearrangement of COL1A1 and PDGFbeta is the transcriptional up-regulation of the PDGFB gene. The associated COL1A1-PDGFBeta fusion protein is posttranslationally processed to a functional PDGFBeta and results in PDGFBeta-mediated autocrine and/or paracrine activation of platelet-derived growth factor receptor-beta (PDGFBB).

**References**

Naeem R, Lux ML, Huang SF, Naber SP, Corson JM, Fletcher JA. Ring chromosomes in dermatofibrosarcoma protuberans are composed of interspersed sequences from chromosomes 17 and 22. Am J Pathol. 1995 Dec;147(6):1553-8


Fletcher C., Mesenchymal Tumors Diagnostic Histopathology of Tumors. 2007; Churchill Livingstone 3rd Ed.; vol 2: 1489-1491.

Patel KU, Szabo SS, Hernandez VS, Prieto VG, Abruzzo LV, Lazar AJ, López-Terrada D. Dermatofibrosarcoma protuberans COL1A1-PDGF fusion is identified in virtually all dermatofibrosarcoma protuberans cases when investigated by newly developed multiplex reverse transcription polymerase chain reaction and fluorescence in situ hybridization assays. Hum Pathol. 2008 Feb;39(2):184-93

| This article should be referenced as such: |