

## Hereditary Desmoid Disease.

### Identity

Other names Familial Infiltrative Fibromatosis.

**Inheritance** Autosomal dominant disorder; frequency is less than  $1/10^5$  newborns; unknown new mutation rate; variable disease expression; penetrance is unknown. Hereditary desmoid disease occurs primarily in association with [familial adenomatous polyposis](#).

### Clinics

**Phenotype and clinics** Normally, presence of multiple desmoid tumours especially in the mesentery. Desmoid tumours can develop elsewhere and are often initiated after trauma. Micro-adenomas in the lower gastrointestinal tract, often not reported. Upper GI polyps are often observed.

**Neoplastic risk** Strictly speaking desmoid tumours are not neoplastic but they are locally invasive and highly destructive. Often associated with extreme pain and respond poorly to treatment. Usually they occur in association with familial adenomatous polyposis. Desmoid tumours usually occur in the abdominal cavity and have been associated with traumatic events that include surgery and childbirth. They have been reported at other anatomical sites.

**Treatment** There is no defined treatment that is affective in all cases. Nevertheless, the use of non-steroidal anti-inflammatory drugs (NSAIDs) in combination with tamoxifen has been suggested but there is no firm evidence to indicate its benefit.

**Evolution** Disease development involves the loss of APC and appears to be associated with 3<sup>1</sup> APC germline mutations. Little is known about downstream events in the evolution of the disease.

**Prognosis** Patients with hereditary desmoid disease fall into three categories; those that develop disease, which spontaneously regresses (very rarely reported); patients with stabile disease that does not progress: and patients with severe progressive and fatal disease.

### Genes involved and Proteins

**Gene Name** [APC \(Adenomatous Polyposis Coli\)](#)

**Location** 5q21-q22

#### Protein

**Description** Tumour suppressor gene with multiple functions; Normal APC gene product interacts with adherens junction proteins a-catenin and [b-catenin](#).

**Expression** APC expression is present in all cells but at varying levels.

**Localisation** Mainly in the cytoplasm but there is a nuclear localization signal and it is observed in the nucleus.

**Function** Primary function appears to be the regulation of b-catenin in association with GSK-b via the ubiquitin degradation pathway. It has also been shown to help orientate the

mitotic spindle during cell replication.  
Homology Partial homology with , where it is about 76% homologous in the first half of the protein.

### Mutations

**Germinal** Many mutations have been described in the APC gene, most of which result in premature termination codons. With respect to familial desmoid disease two sites have been described that occur in the sparsely mutated 3'- region of the gene. Germline mutations at codon 1924 and 1860 have been reported in rare families with desmoid disease.

**Somatic** There appears to be a mutation cluster region in the APC gene that is centered around codon 1309. These mutations have only been described in [colorectal tumours](#) and there is little information with respect to desmoid disease.

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## Contributor(s)

**Written** 08-2006 Rodney J Scott.

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