

## Familial liver adenomatosis

### Identity

**Note** Liver adenomatosis is a rare disease defined by the presence of multiple adenomas within an otherwise normal hepatic parenchyma. In 2002, frequent bi-allelic inactivation of [TCF1/HNF-1alpha](#), was identified in [hepatocellular adenomas](#). In 80% of the cases both mutations were of somatic origin. However, in the remaining cases, one heterozygous germline mutation has been found in patients revealing a relation between liver adenomatosis and maturity-onset diabetes of the young (MODY3). MODY3 is a rare dominantly inherited subtype of non-insulin-dependent diabetes mellitus characterized by early onset, usually before the age of 25, and a primary defect in insulin secretion. In 1996, heterozygous germline mutations of TCF1/HNF1a have been linked to the occurrence of MODY3 in humans.

Other names Familial hepatic adenomas

**Inheritance** autosomal dominant disorder with low penetrance

### Clinics

Phenotype and clinics To date, all familial liver adenomatosis cases described are related to TCF1/HNF1a constitutional mutation. Genotype-phenotype correlation analysis showed that TCF1/HNF1a benign lesions were steatotic.

Neoplastic risk Among MODY3 patients only a very small minority will develop liver adenomatosis. Cases of malignant transformation are uncommon.

Evolution Patients presenting TCF1/HNF1a mutated adenomatosis are at risk of tumor hemorrhagic rupture.

### Genes involved and Proteins

**Note** HNF1a is a homeodomain containing transcription factor that is implicated in hepatocyte differentiation and is required for the liver-specific expression of several genes, including  $\beta$ -fibrinogen, albumin and a1-antitrypsin.

**Gene Name** [TCF1](#)

Location 12q24.31

#### DNA/RNA

Description 10 coding exons

#### Protein

Description hepatocyte nuclear factor 1 alpha, HNF1A

Function transcription factor  
Homology homeodomain, pou family

### **Mutations**

Germinal at least 6 different mutations were found in familial adenomatosis:  
R229X, R272S, P291fs (2 cases), G55fs, IVS2 +1 G>T  
Somatic inactivation of the second allele in adenoma tumors is by gene deletion  
or mutation.

### **Bibliography**

#### **Familial liver-cell adenomas and diabetes mellitus.**

Foster JH, Donohue TA, Berman MM.  
N Engl J Med 1978; 299: 239-241.  
Medline [207987](#)

#### **Mutations in the hepatocyte nuclear factor-1alpha gene in maturity-onset diabetes of the young (MODY3).**

Yamagata K, Oda N, Kaisaki PJ, Menzel S, Furuta H, Vaxillaire M, Southam L, Cox RD, Lathrop GM, Boriraj VV, Chen X, Cox NJ, Oda Y, Yano H, Le Beau MM, Yamada S, Nishigori H, Takeda J, Fajans SS, Hattersley AT, Iwasaki N, Hansen T, Pedersen O, Polonsky KS, Bell GI, et al.  
Nature 1996 Dec 5; 384(6608): 455-458.  
Medline [8945470](#)

#### **Liver adenomatosis: reappraisal, diagnosis, and surgical management: eight new cases and review of the literature.**

Chiche L, Dao T, Salame E, Galais MP, Bouvard N, Schmutz G, Rousselot P, Bioulac-Sage P, Segol P, Gignoux M.  
Ann Surg 2000; 231: 74-81.  
Medline [10636105](#)

#### **Bi-allelic inactivation of TCF1 in hepatic adenomas.**

Bluteau O, Jeannot E, Bioulac-Sage P, Marques JM, Blanc JF, Bui H, Beaudoin JC, Franco D, Balabaud C, Laurent-Puig P, Zucman-Rossi J.  
Nat Genet 2002; 32: 312-315.  
Medline [12355088](#)

#### **Familial liver adenomatosis associated with hepatocyte nuclear factor 1alpha inactivation.**

Bacq Y, Jacquemin E, Balabaud C, Jeannot E, Scotto B, Branchereau S, Laurent C, Bourlier P, Pariente D, de Muret A, Fabre M, Bioulac-Sage P, Zucman-Rossi J.  
Gastroenterology 2003; 125: 1470-1475.  
Medline [14598263](#)

**Hepatocyte nuclear factor-1 alpha gene inactivation: cosegregation between liver adenomatosis and diabetes phenotypes in two maturity-onset diabetes of the young (MODY)3 families.**

Reznik Y, Dao T, Coutant R, Chiche L, Jeannot E, Clauin S, Rousselot P, Fabre M, Oberti F, Fatome A, Zucman-Rossi J, Bellanne-Chantelot C.

J Clin Endocrinol Metab 2004; 89: 1476-1480.

Medline [15001650](#)

**Genotype-phenotype correlation in hepatocellular adenoma: New classification and relationship with HCC.**

Zucman-Rossi J, Jeannot E, Van Nhieu JT, Scoazec JY, Guettier C, Rebouissou S, Bacq Y, Leteurtre E, Paradis V, Michalak S, Wendum D, Chiche L, Fabre M, Mellottee L, Laurent C, Partensky C, Castaing D, Zafrani ES, Laurent-Puig P, Balabaud C, Bioulac-Sage P.

Hepatology 2006 Feb 22; 43(3): 515-524

Medline [16496320](#)

[REVIEW articles](#)      *automatic search in PubMed*

[Last year publications](#)      *automatic search in PubMed*

**Contributor(s)**

Written      03-      Jessica Zucman-Rossi  
                 2006

**Citation**

*This paper should be referenced as such :*

**Zucman-Rossi J** . Familial liver adenomatosis. Atlas Genet Cytogenet Oncol Haematol. March 2006 .

URL : <http://AtlasGeneticsOncology.org/Kprones/FamLiverAdenomID10130.html>

© Atlas of Genetics and Cytogenetics in Oncology and Haematology

---