

Gene Section

Short Communication

AMBN (ameloblastin (enamel matrix protein))

Marina Gonçalves Diniz, Ricardo Santiago Gomez, Carolina Cavalieri Gomes, André Luiz Sena Guimarães

Department of Oral Surgery and Pathology, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Belo Horizonte-MG CEP 31270, Brazil (MGD, RSG), Department of Pathology, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Belo Horizonte-MG CEP 31270, Brazil (CCG), Department of Dentistry, Universidade Estadual de Montes Claros, Montes Claros, Brazil (ALSG)

Published in Atlas Database: December 2011

Online updated version : <http://AtlasGeneticsOncology.org/Genes/AMBNID51161ch4q13.html>
DOI: 10.4267/2042/47320

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2012 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

HGNC (Hugo): AMBN

Location: 4q13.3

Local order: AMBN is between the sequence tagged site markers D4S409 and D4S1558 (Karrman et al., 1997).

DNA/RNA

Note

The putative start codon location and exon-intron sizes differs among reports in literature.

Description

13 exons and 12 introns (Toyosawa et al., 2000; Macdougall et al., 2000) encompassing approximately 15005 bp.

Until 2011, 44 SNP were described (NCBI dbSNP).

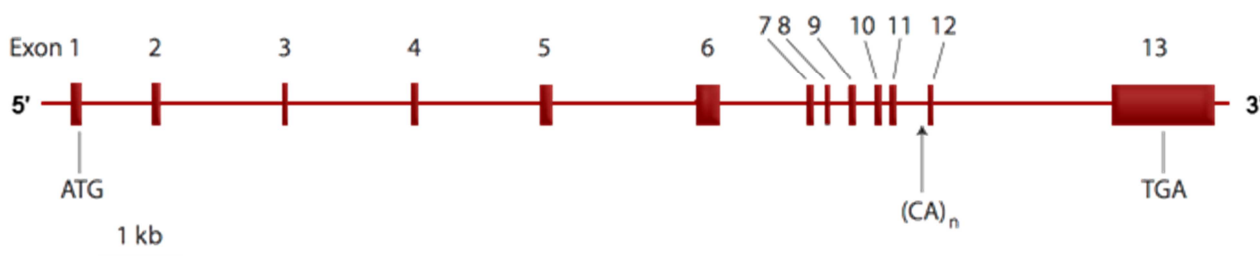
Transcription

Alternatively spliced. Exon 6 can be excluded by the use of an alternative splice site (Macdougall et al., 2000). There are 2 validated alternative polyadenylation sites.

Protein

Description

The predicted protein has 447 aa (48,3 kDa). There are 3 protein isoforms. The human precursor protein contains a phosphorylation site for tyrosine kinase, a SH3 binding region, an O-linked glycosylation, and a heparin binding domain (Kobayashi et al., 2007; Krebsbach et al., 1996; Yamakoshi et al., 2001; Sonoda et al., 2009). Ameloblastin is cleaved after secretion into several lower-molecular-mass proteins that are developmentally expressed (Ravindranath et al., 2007).



The genomic organization of the human ameloblastin gene according to Mardh et al., 2001. The map is drawn to scale. Filled boxes represent exons and the thin lines indicate introns. Sequencing of AMBN intron 11 revealed an interrupted dinucleotide repeat (CA)_n.

Expression

Tomes processes of secretory ameloblasts (Krebsbach et al., 1996; Cerny et al., 1996; Fong et al., 1996), odontoblasts and pre-odontoblasts (Fong et al., 1996; Nagano et al., 2003). Outer enamel, and sheath space between rod and interrod enamel (Uchida et al., 1995; Macdougall et al., 2000). Early bone and cartilage extracellular matrices during embryogenesis (Spahr et al., 2006).

Localisation

Extracellular matrix.

Function

Tooth enamel biomineralization (Uchida et al., 1997). Interactions between the ameloblasts and the enamel extracellular matrix (Fukumoto et al., 2004). Dental epithelium cell adhesion (Sonoda et al., 2009). Early bone formation and repair (Iizuza et al., 2011; Tamburstuen et al., 2011).

Homology

Pig (sheathlin), cattle, rat, and mouse AMBN sequences showed a high amino acid sequence similarity.

Mutations

Somatic

AMBN gene mutations have been observed in several epithelial odontogenic tumor entities: unicystic ameloblastoma, solid ameloblastoma, adenomatoid odontogenic tumor, squamous odontogenic tumor, and calcifying epithelial odontogenic tumor (Toyosawa et al., 2000; Perdigão et al., 2004; Perdigão et al., 2009).

Implicated in

Odontogenic tumors

Disease

Odontogenic tumours arise from the residues of odontogenic epithelium and/or ectomesenchyme, as a result of disturbances in the development of teeth and associated structures.

Oncogenesis

AMBN gene is mutated in ameloblastomas and others odontogenic tumors (Toyosawa et al., 2000; Perdigão et al., 2004; Perdigão et al., 2009). Ambn-null mice develop odontogenic tumors of dental epithelium origin (Fukumoto et al., 2004). AMBN expression prevents odontogenic tumor development by suppressing cell proliferation and maintaining differentiation phenotype through Msx2, p21, and p27 (Sonoda et al., 2009). The absence of ameloblastin in epithelial odontogenic tumors has been considered a useful marker for the functional differentiation of secretory ameloblast (Takata et al., 2000).

Amelogenesis imperfecta

Disease

Amelogenesis imperfect is a common group of inherited defects such as hypoplastic or hypomineralized enamel. Autosomal dominant, autosomal recessive, and X-linked forms of amelogenesis imperfect are recognized.

Oncogenesis

Amelogenin and ameloblastin have an impaired secretion in ameloblasts of phenocopies human X-linked amelogenesis imperfect mice, which results in severe enamel bio-mineralization defects, loss of ameloblast phenotype, increased ameloblast apoptosis, and formation of multi-cellular masses (Barron et al., 2010). AMBN mutations in the coding region or splice sites were discarded to be responsible for autosomal dominant amelogenesis imperfecta (Mardh et al., 2001).

References

- Uchida T, Fukae M, Tanabe T, Yamakoshi Y, Satoda T, Murakami C, et al.. Immunochemical and immunocytochemical study of a 15 kDa non-amelogenin and related proteins in the porcine immature enamel: proposal of a new group of enamel proteins sheath proteins. *Biomed Res.* 1995; 16:131-140.
- Cerny R, Slaby I, Hammarstrom L, Wurtz T.. A novel gene expressed in rat ameloblasts codes for proteins with cell binding domains. *J Bone Miner Res.* 1996 Jul;11(7):883-91.
- Fong CD, Slaby I, Hammarstrom L.. Amelin: an enamel-related protein, transcribed in the cells of epithelial root sheath. *J Bone Miner Res.* 1996 Jul;11(7):892-8.
- Krebsbach PH, Lee SK, Matsuki Y, Kozak CA, Yamada KM, Yamada Y.. Full-length sequence, localization, and chromosomal mapping of ameloblastin. A novel tooth-specific gene. *J Biol Chem.* 1996 Feb 23;271(8):4431-5.
- Uchida T, Murakami C, Dohi N, Wakida K, Satoda T, Takahashi O.. Synthesis, secretion, degradation, and fate of ameloblastin during the matrix formation stage of the rat incisor as shown by immunocytochemistry and immunocytochemistry using region-specific antibodies. *J Histochem Cytochem.* 1997 Oct;45(10):1329-40.
- MacDougall M, Simmons D, Gu TT, Forsman-Semb K, Mardh CK, Mesbah M, Forest N, Krebsbach PH, Yamada Y, Berdal A.. Cloning, characterization and immunolocalization of human ameloblastin. *Eur J Oral Sci.* 2000 Aug;108(4):303-10.
- Takata T, Zhao M, Uchida T, Kudo Y, Sato S, Nikai H.. Immunohistochemical demonstration of an enamel sheath protein, sheathlin, in odontogenic tumors. *Virchows Arch.* 2000 Apr;436(4):324-9.
- Toyosawa S, Fujiwara T, Ooshima T, Shintani S, Sato A, Ogawa Y, Sobue S, Ijuhin N.. Cloning and characterization of the human ameloblastin gene. *Gene.* 2000 Oct 3;256(1-2):1-11.
- Mardh CK, Backman B, Simmons D, Golovleva I, Gu TT, Holmgren G, MacDougall M, Forsman-Semb K.. Human ameloblastin gene: genomic organization and mutation analysis in amelogenesis imperfecta patients. *Eur J Oral Sci.* 2001 Feb;109(1):8-13.

Yamakoshi Y, Tanabe T, Oida S, Hu CC, Simmer JP, Fukae M.. Calcium binding of enamel proteins and their derivatives with emphasis on the calcium-binding domain of porcine sheathlin. *Arch Oral Biol.* 2001 Nov;46(11):1005-14.

Nagano T, Oida S, Ando H, Gomi K, Arai T, Fukae M.. Relative levels of mRNA encoding enamel proteins in enamel organ epithelia and odontoblasts. *J Dent Res.* 2003 Dec;82(12):982-6.

Fukumoto S, Kiba T, Hall B, Iehara N, Nakamura T, Longenecker G, Krebsbach PH, Nanci A, Kulkarni AB, Yamada Y.. Ameloblastin is a cell adhesion molecule required for maintaining the differentiation state of ameloblasts. *J Cell Biol.* 2004 Dec 6;167(5):973-83.

Perdigao PF, Gomez RS, Pimenta FJ, De Marco L.. Ameloblastin gene (AMBN) mutations associated with epithelial odontogenic tumors. *Oral Oncol.* 2004 Sep;40(8):841-6.

Spahr A, Lyngstadaas SP, Slaby I, Pezeshki G.. Ameloblastin expression during craniofacial bone formation in rats. *Eur J Oral Sci.* 2006 Dec;114(6):504-11.

Kobayashi K, Yamakoshi Y, Hu JC, Gomi K, Arai T, Fukae M, Krebsbach PH, Simmer JP.. Splicing determines the glycosylation state of ameloblastin. *J Dent Res.* 2007 Oct;86(10):962-7.

Ravindranath RM, Devarajan A, Uchida T.. Spatiotemporal expression of ameloblastin isoforms during murine tooth development. *J Biol Chem.* 2007 Dec 14;282(50):36370-6. Epub 2007 Oct 5.

Perdigao PF, Carvalho VM, DE Marco L, Gomez RS.. Mutation of ameloblastin gene in calcifying epithelial odontogenic tumor. *Anticancer Res.* 2009 Aug;29(8):3065-7.

Sonoda A, Iwamoto T, Nakamura T, Fukumoto E, Yoshizaki K, Yamada A, Arakaki M, Harada H, Nonaka K, Nakamura S, Yamada Y, Fukumoto S.. Critical role of heparin binding domains of ameloblastin for dental epithelium cell adhesion and ameloblastoma proliferation. *J Biol Chem.* 2009 Oct 2;284(40):27176-84. Epub 2009 Jul 31.

Barron MJ, Brookes SJ, Kirkham J, Shore RC, Hunt C, Mironov A, Kingswell NJ, Maycock J, Shuttleworth CA, Dixon MJ.. A mutation in the mouse Amelx tri-tyrosyl domain results in impaired secretion of amelogenin and phenocopies human X-linked amelogenesis imperfecta. *Hum Mol Genet.* 2010 Apr 1;19(7):1230-47. Epub 2010 Jan 12.

Iizuka S, Kudo Y, Yoshida M, Tsunematsu T, Yoshiko Y, Uchida T, Ogawa I, Miyauchi M, Takata T.. Ameloblastin regulates osteogenic differentiation by inhibiting Src kinase via cross talk between integrin beta1 and CD63. *Mol Cell Biol.* 2011 Feb;31(4):783-92. Epub 2010 Dec 13.

Tamburstuen MV, Reseland JE, Spahr A, Brookes SJ, Kvalheim G, Slaby I, Snead ML, Lyngstadaas SP.. Ameloblastin expression and putative autoregulation in mesenchymal cells suggest a role in early bone formation and repair. *Bone.* 2011 Feb;48(2):406-13. Epub 2010 Sep 18.

This article should be referenced as such:

Diniz MG, Gomez RS, Gomes CC, Guimarães ALS. AMBN (ameloblastin (enamel matrix protein)). *Atlas Genet Cytogenet Oncol Haematol.* 2012; 16(5):326-328.
