

Gene Section

Mini Review

SLC4A1 (solute carrier family 4, anion exchanger, member 1 (erythrocyte membrane protein band 3, Diego blood group))

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Identity

Other names: AE1, BND3, CD233, DI, EMPB3, EPB3, FR, MGC116750, MGC116753, MGC126619, MGC126623, RTA1A, SW, WD, WD1, WR

HGNC (Hugo): SLC4A1

Location: 17q21.31

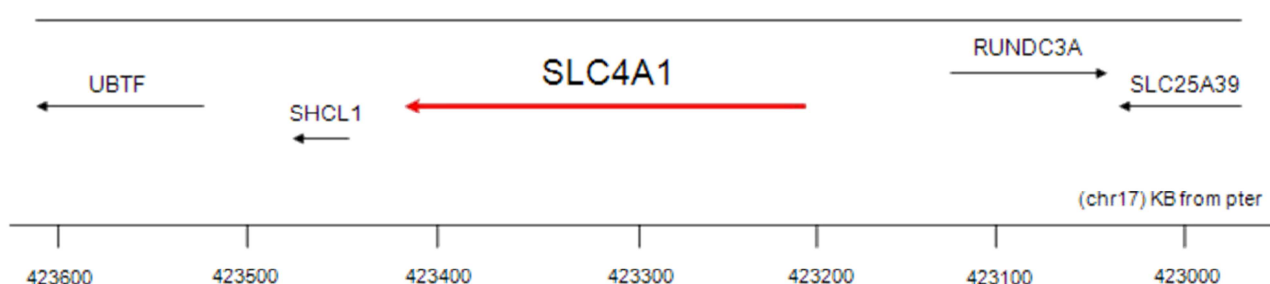
Local order: 17q21-q22, chromosome 17: 42325753-42345509.

DNA/RNA

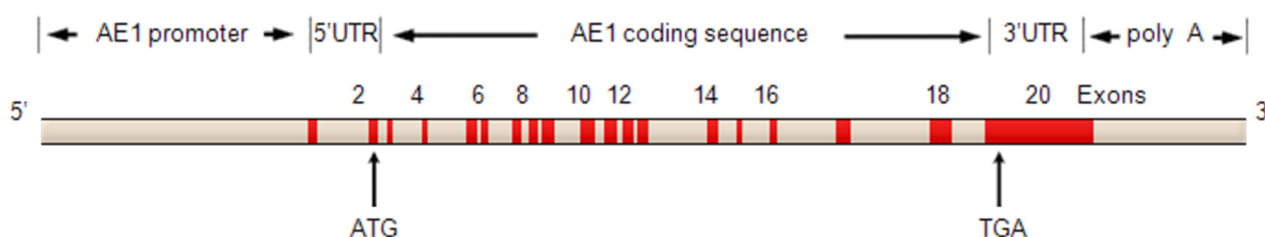
Description

SLC4A1 is a gene that spans 19.757 kb of genomic DNA on the long arm of chromosome 17, in the telomere-to-centromere orientation. The gene consists of twenty exons of which the first exon is non-coding. The start codon is located at the beginning of exon 2 and the stop codon in the beginning of exon 20.

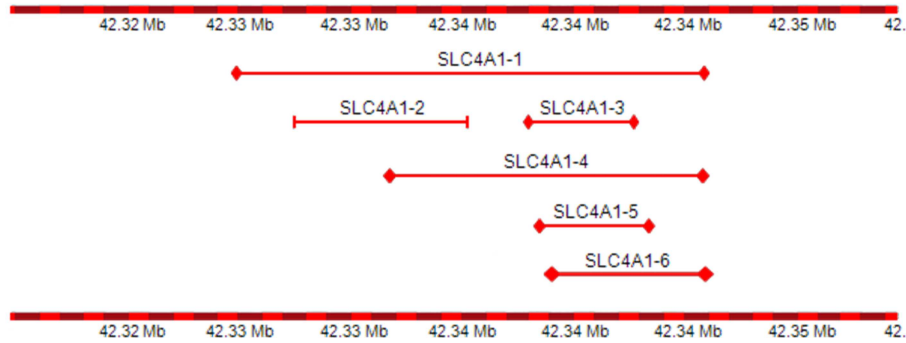
A.



B.

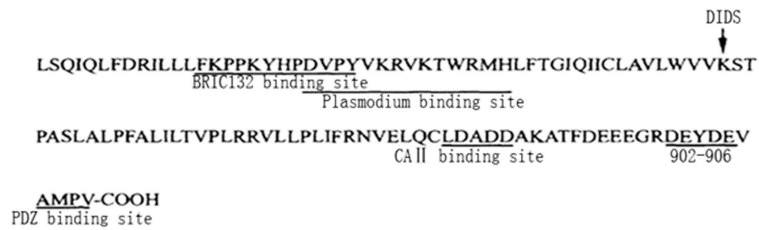


C.

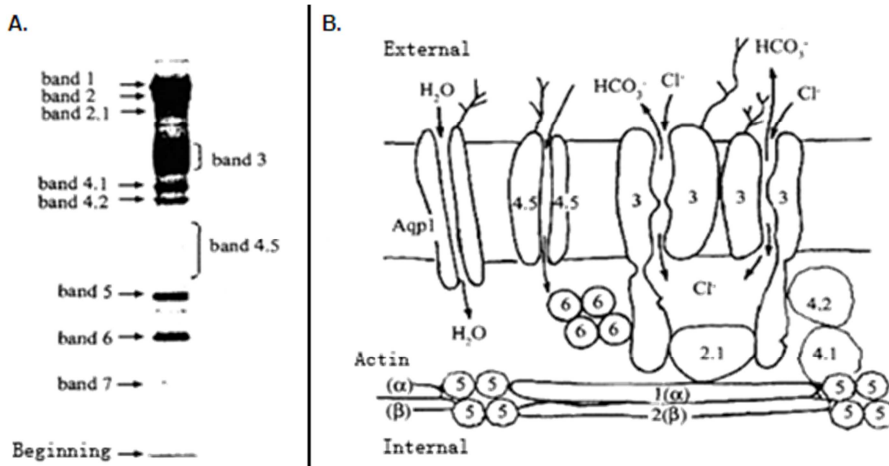


Transcript	Length (bp)	Protein	Biotype	Length (aa)
SLC4A1-1	4965	YES	Protein coding	911
SLC4A1-2	393	YES	Protein coding	131
SLC4A1-3	462	YES	Protein coding	86
SLC4A1-4	419	NO	Processed transcript	N/A
SLC4A1-5	1922	NO	Retained intron	N/A
SLC4A1-6	460	NO	Retained intron	N/A

A. SLC4A1 chromosome 17: bp 42325753-42345509, strand+ (UCSC). B. SLC4A1 genomic DNA (20 exons). C. Transcripts.



The C-terminal structure of AE1.



A. SDS-PAGE of erythrocyte membrane protein. B. Schematic diagram of membrane skeleton proteins.

Transcription

The SLC4A1 mRNA is 4.953 kb long. In the Ensembl database, its mRNA is 4.965 kb long. Compared with NCBI database, the beginning additional bases are GCTGTCA; the stop bases are GTGGC. However the coding sequences of them are the same. There are also five other transcripts: 419 bp, 1922 bp and 460 bp, that encode no protein, and 393 bp 462 bp, that encode other proteins.

Protein

Description

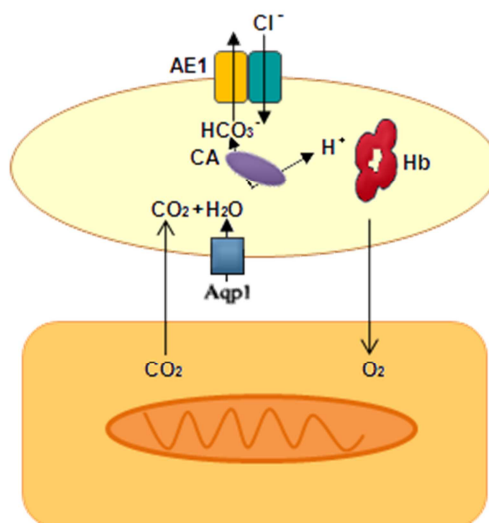
911 amino acids; 95 kDa.

Function

Anion exchanger protein 1 (AE1), is a classical cell membrane transporter, also called band 3, that participates in the regulation of intracellular pH and ion homeostasis in vivo by transmembrane $\text{Cl}^-/\text{HCO}_3^-$ exchange.

The C-terminal region of AE1 directly interacts with tumor suppressor p16, and then, it sequesters p16 protein in the cytoplasm and causes gastric cancer. The transmembrane of AE2 interfered with AE1. They can form heterodimers. AE2 was degraded through ubiquitination by APC in the cytoplasm.

Clinical data analysis showed that abnormal expression of AE1 with p16 is correlated with occurrence and development of gastric cancer.



The model of erythrocyte $\text{Cl}^-/\text{HCO}_3^-$ exchange.

Homology

Anion exchanger.

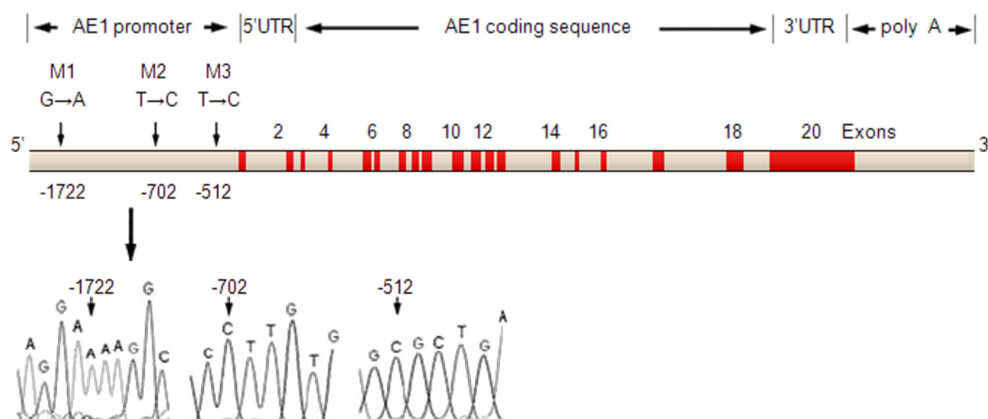
Mutations

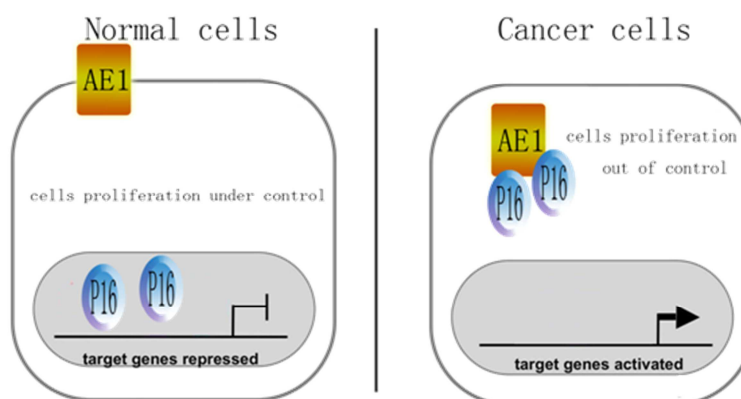
Germinal

Point mutations in promoter of AE1 gene were detected in AE1 positive gastric and colon cancer cells.

Somatic

These mutations were only detected in cancer, not in normal cells.





Implicated in

Gastric and colon cancer

Disease

Gastric cancer is the most common gastrointestinal cancer; it has a high incidence area in China. In China, multiple gastric cancers patients were more than 40 years old; during all of the gastric cancers, two-third of the patients were 40-60 years old, and the ratio of male to female is 3.6:1.

Prognosis

In China, 5-year survival rate of gastric cancer: I a was 99%~100%; I b was 81%~89%; II was 65%~73%; III a was 43%~50%; III b was 25%; V was 13%. With the increase of the staging of the trend rate of 5-year survival gradually decreased. The 5-year survival rate was closely negatively related to the expression of SLC4A1.

Cytogenetics

AE1 immunoreactivity was negative in normal gastric tissue. Positive immunostaining of AE1 was detected in gastric carcinoma regardless of the location. AE1 was most frequently expressed in the gastric antrum carcinoma compared with gastric body cancer ($P=0.034$). Expression of AE1 was significantly associated with bigger tumor size, deeper invasion, shorter survival period, and non-lymph metastasis. In para-cancer tissues of intestinal type gastric cancer, the expression frequency of AE1 was higher than that in diffuse-type ($P=0.011$) (Xu et al., 2009; Liu et al., 2009).

Hybrid/Mutated gene

During the process of gastric cancer, AE1 was translated accompanied by the abnormal expression of P16 protein.

Oncogenesis

p16INK4A (p16) binds to cyclin-dependent kinase 4/cyclin-dependent kinase 6 and negatively regulates cell growth. During the process of gastric and colon cancer and in gastric and colon cancer cell lines, forced expression of AE1 in the cytoplasm interacted with p16, and sequestered the protein in the cytoplasm (Fu

et al., 2005). So, AE1 plays a crucial role in the pathogenesis of gastric and colon adenocarcinoma (Shen et al., 2007; Wu et al., 2010).

To be noted

Note

Most of our information was obtained from National Center for Biotechnology Information (NCBI). Tables and diagrams were designed after the databases of Ensembl.

References

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