TMCO1

Transmembrane and coiled-coil domains 1 (TMCO1) is a recently discovered transmembrane protein of endoplasmic reticulum (ER), which plays a critical role in maintaining calcium homeostasis. TMCO1 dysfunction has been proved to be closely related to a variety of human diseases, including glaucoma, deformities, mental retardation, and tumorigenesis.

Xin et al. identified an autosomal recessive condition in 11 individuals in the Old Order Amish of northeastern Ohio. The syndrome was characterized by distinctive craniofacial dysmorphism, skeletal anomalies, and mental retardation. The typical craniofacial dysmorphism included brachycephaly, highly arched bushy eyebrows, synophrys, long eyelashes, low-set ears, microdontism of primary teeth, and generalized gingival hyperplasia, whereas Sprengel deformity of scapula, the fusion of the spine, rib abnormities, pectus excavatum, and pes planus represented skeletal anomalies. The genome-wide homozygosity mapping using six affected individuals localized the disease gene to a 3.3-Mb region on chromosome 1q23.3-q24.1. Candidate gene sequencing identified a homozygous frameshift mutation, c.139_140delAG, in the transmembrane and coiled-coil domains 1 (TMCO1) gene, as the pathogenic change in all affected members of the extended pedigree. This mutation is predicted to result in a severely truncated protein (p.Ser47Ter) of only one-fourth the original length. The TMCO1 gene product is a member of DUF841 superfamily of several eukaryotic proteins with unknown function. The gene has highly conserved amino acid sequence and is universally expressed in all human tissues examined. The high degree of conservation and the ubiquitous expression pattern in human adult and fetal tissues suggest a critical role for TMCO1. This report shows a TMCO1 sequence variant being associated with a genetic disorder in human. We propose “TMCO1 defect syndrome” as the name of this condition [1)].

The role of TMCO1 in gliomas remains unclear. The purpose of this study was to detect the role of TMCO1 in the pathogenesis and progression of gliomas. This study demonstrated that TMCO1 was upregulated in gliomas and its overexpression predicted poor prognosis. We also revealed that the expression of TMCO1 was associated with the World Health Organization (WHO) grade of gliomas. Knockdown of TMCO1 inhibited the proliferation and induced apoptosis of U87 and U251 cells. In addition, TMCO1 induced Glioblastoma cell migration and invasion by promoting epithelial-mesenchymal transition (EMT). This date collectively proved the crucial role of TMCO1 as a novel prognostic factor and underlying therapeutic target for glioma patients [2)].

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Xin B, Puffenberger EG, Turben S, Tan H, Zhou A, Wang H. Homozygous frameshift mutation in TMCO1 causes a syndrome with craniofacial dysmorphism, skeletal anomalies, and mental retardation. Proc Natl Acad Sci U S A. 2010 Jan 5;107(1):258-63. doi: 10.1073/pnas.0908457107. Epub 2009 Dec 14. PMID: 20018682; PMCID: PMC2806776.

2)
Gao L, Ye Z, Liu JH, Yang JA, Li Y, Cai JY, Wang YX, Tong SA, Deng G, Zhang S, Chen QX. TMCO1 expression promotes cell proliferation and induces epithelial-mesenchymal transformation in human gliomas. Med Oncol. 2022 May 15;39(5):90. doi: 10.1007/s12032-022-01687-y. PMID: 35568751.