ALDH5A1

ALDH5A1 is the gene that encodes for the enzyme delta-1-pyrroline-5-carboxylate synthetase (P5CS), which is involved in the biosynthesis of proline, an important amino acid. Proline is involved in various biological processes, including protein synthesis, cell signaling, and oxidative stress response.

Mutations in the ALDH5A1 gene are associated with a rare genetic disorder called pyrroline-5-carboxylate synthase deficiency (P5CS deficiency), which is characterized by elevated levels of pyrroline-5-carboxylate and a decrease in proline levels in the body. Symptoms of P5CS deficiency can vary but may include developmental delays, intellectual disability, seizures, and other neurological symptoms.

ALDH5A1 has also been implicated in the development of certain cancers, including breast cancer and glioblastoma. In breast cancer, ALDH5A1 has been shown to promote cancer cell growth and invasion, and targeting the enzyme may be a potential therapeutic strategy. In glioblastoma, ALDH5A1 has been suggested as a potential biomarker for predicting patient survival and response to treatment.

Research on ALDH5A1 and its role in various biological processes is ongoing, and further understanding of the enzyme may lead to the development of new treatments for genetic disorders and cancer.

Accumulating data shows that altered metabolic activity contributes to glioma development. Modulation of SSADH (succinic semialdehyde dehydrogenase) expression, implicated in the catabolism of GABA neurotransmitter, was shown to impact glioma cell properties, such as proliferation, self-renewal and tumorigenicity.

The purpose of a study by Piperi et al. was to investigate the clinical significance of SSADH expression in human gliomas. Using public single-cell RNA-sequencing data from glioma surgical resections, Piperi et al. initially grouped cancer cells according to ALDH5A1 (Aldehyde dehydrogenase 5 family member A1) expression, which encodes SSADH. Gene ontology enrichment analysis of genes differentially expressed between cancer cells expressing high or low levels of ALDH5A1, highlighted enrichment in genes implicated in the cell morphogenesis and motility. In glioblastoma cell lines, ALDH5A1 knockdown inhibited cell proliferation, induced apoptosis, and reduced their migratory potential. This was accompanied by a reduction in the mRNA levels of the adherens junction molecule ADAM-15 and deregulation in the expression of EMT biomarkers, with increased CDH1 and decreased vimentin mRNA levels. Evaluation of SSADH expression in a cohort of 95 gliomas using immunohistochemistry showed that SSADH expression was significantly elevated in cancer tissues compared to normal brain tissues, without any significant correlation with clinicopathological characteristics. In summary, data show that SSADH is upregulated in glioma irrespective of the histological grade, and its expression sustains glioma cell motility [1)]

1)

Piperi C, Saurty-Seerunghen MS, Levidou G, Sepsa A, Trigka EA, Klonou A, Markouli M, Strepkos D, Spyropoulou A, Kanakoglou DS, Lakiotaki E, Karatrasoglou EA, Boviatsis E, El-Habr EA, Korkolopoulou P. Glioma Cells Expressing High Levels of ALDH5A1 Exhibit Enhanced Migration Transcriptional Signature in Patient Tumors. Neurotherapeutics. 2023 Mar 28. doi: 10.1007/s13311-023-01354-8. Epub ahead of print. PMID: 36976494.