Isocitrate dehydrogenase-1 (IDH1)

Isocitrate dehydrogenase-1 (IDH1) is an enzyme that plays a crucial role in cellular metabolism. It is involved in the citric acid cycle, also known as the tricarboxylic acid cycle or Krebs cycle, which is a series of biochemical reactions that occur in the mitochondria of cells to generate energy.

The primary function of IDH1 is to catalyze the oxidative decarboxylation of isocitrate, a molecule derived from the breakdown of glucose, to produce alpha-ketoglutarate (α-KG), carbon dioxide, and nicotinamide adenine dinucleotide phosphate (NADPH). This reaction involves the removal of a carboxyl group from isocitrate and the transfer of electrons to NADP+, resulting in the production of NADPH, which is an important reducing agent used in various cellular processes.

The conversion of isocitrate to alpha-ketoglutarate by IDH1 is a key step in the citric acid cycle, as alpha-ketoglutarate serves as an intermediate that can be further metabolized to generate energy or be used in other metabolic pathways. Additionally, alpha-ketoglutarate is involved in various cellular processes, such as amino acid metabolism and the regulation of gene expression through epigenetic modifications.

Mutations in the IDH1 gene can result in altered forms of the IDH1 enzyme with neomorphic enzymatic activity. These mutations, particularly at a specific amino acid position called R132, lead to a gain of function where the mutant IDH1 enzyme produces an abnormal metabolite called D-2-hydroxyglutarate (D-2-HG) instead of alpha-ketoglutarate. The accumulation of D-2-HG can disrupt cellular processes and has been associated with the development and progression of certain types of cancer, including gliomas (a type of brain tumor) and acute myeloid leukemia (AML).

The presence of IDH1 mutations, especially the IDH1-R132H mutation, can serve as a diagnostic and prognostic marker for certain cancers. Furthermore, targeted therapies are being developed to specifically inhibit mutant IDH1 enzymes and reduce the levels of D-2-HG as a potential treatment strategy for IDH1-mutant cancers.

Understanding the function and regulation of IDH1 is essential in the fields of cancer research, metabolism, and drug development, as it provides insights into cellular metabolism and the role of IDH1 mutations in disease pathogenesis.

see IDH1 gene.

see IDH1 gene mutation.