Isocitrate dehydrogenase mutation

Isocitrate dehydrogenase (IDH) mutations are genetic alterations that occur in the isocitrate dehydrogenase enzymes, specifically the IDH1 and IDH2 genes. These mutations have been found in various types of cancer, including gliomas (a type of brain tumor), acute myeloid leukemia (AML), and chondrosarcoma (a type of bone cancer).

IDH enzymes are involved in cellular metabolism and play a role in the citric acid cycle (also known as the Krebs cycle) within the mitochondria of cells. They catalyze the conversion of isocitrate to alpha-ketoglutarate, generating nicotinamide adenine dinucleotide phosphate (NADPH) in the process. NADPH is important for cellular redox balance and providing reducing power for various cellular reactions.

When mutations occur in the IDH genes, the function of the enzyme is altered. IDH mutations result in a gain of function, leading to the production of an abnormal metabolite called 2-hydroxyglutarate (2-HG). Accumulation of 2-HG disrupts cellular processes, including epigenetic regulation and DNA repair mechanisms, which can contribute to the development and progression of cancer.

The presence of IDH mutations in cancer has clinical implications. In gliomas and AML, IDH mutations are considered diagnostic and prognostic markers. They are associated with specific tumor subtypes and have been linked to better overall survival and treatment response in certain cases. Additionally, IDH mutations have been targeted for therapeutic intervention in clinical trials, with drugs specifically designed to inhibit mutant IDH enzymes and reduce 2-HG levels.

It's important to note that while IDH mutations are commonly associated with certain cancers, not all cases of these cancers will have IDH mutations, and other genetic alterations or factors may also influence disease progression and treatment response. Therefore, genetic testing and comprehensive evaluation are necessary for accurate diagnosis and personalized treatment planning.

IDH-wildtype is a normal enzyme in the Krebs cycle, catalyzing isocitrate → α-ketoglutarate

● mutant IDH occurs in many tumors, but not in normal cells. IDH1 is the most common mutation. One metabolite is 2-hydroxyglutarate which may participate in tumorigenesis

● IDH mutations are found in 70–80% of secondary glioblastomas and its precursors (grade II & grade III glio- mas), but in only 5% of primary Glioblastomas

● prognosis in tumors with mutated IDH is better than those with IDH-wildtype

● WHO recommends testing for IDH mutations in all astrocytic tumors.

IDH-mutant glioma

see IDH-mutant glioma.

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