IDH1-mutant refers to a specific genetic mutation found in the IDH1 gene. The IDH1 gene provides instructions for producing the IDH1 enzyme (isocitrate dehydrogenase 1), which is involved in cellular metabolism.

Mutations in the IDH1 gene result in a change in the DNA sequence, leading to an altered form of the IDH1 enzyme. This mutation is most commonly associated with a single amino acid substitution at position 132 of the IDH1 protein, where the amino acid arginine is replaced by histidine (R132H).

IDH1-mutant enzymes acquire a new enzymatic activity known as neomorphic activity. Instead of catalyzing the conversion of isocitrate to alpha-ketoglutarate (α-KG) in a normal cellular metabolic pathway, mutant IDH1 enzymes convert isocitrate to an oncometabolite called D-2-hydroxyglutarate (D-2-HG). D-2-HG is an abnormal metabolite that accumulates in cells and disrupts various cellular processes, including epigenetic regulation and cellular differentiation. This accumulation is believed to contribute to the development and progression of certain cancers.

IDH1 mutations, particularly the IDH1-R132H mutation, are frequently found in certain types of cancers, such as gliomas (a type of brain tumor) and chondrosarcomas (a type of bone cancer). The presence of IDH1 mutations, including IDH1-R132H, can serve as a diagnostic and prognostic marker for these cancers. Additionally, targeted therapies are being developed to specifically inhibit mutant IDH1 enzymes and reduce the levels of D-2-HG in order to disrupt the cancer-promoting effects of the mutation.