IDH1 Mutations Are Early Events in the Development of Astrocytomas and Oligodendrogliomas.

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IDH1 encodes isocitrate dehydrogenase 1, which participates in the citric acid cycle and was recently reported to be mutated in 12% of glioblastomas. We assessed IDH1 mutations in 321 gliomas of various histological types and biological behaviors. A total of 130 IDH1 mutations was detected, and all were located at amino acid residue 132. Of these, 91% were G-->A mutations (Arg-->His). IDH1 mutations were frequent in low-grade diffuse astrocytomas (88%) and in secondary glioblastomas that developed through progression from low-grade diffuse or anaplastic astrocytoma (82%). Similarly, high frequencies of IDH1 mutations were found in oligodendrogliomas (79%) and oligoastrocytomas (94%). Analyses of multiple biopsies from the same patient (51 cases) showed that there were no cases in which an IDH1 mutation occurred after the acquisition of either a TP53 mutation or loss of 1p/19q, suggesting that IDH1 mutations are very early events in gliomagenesis and may affect a common glial precursor cell population. IDH1 mutations were co-present with TP53 mutations in 63% of low-grade diffuse astrocytomas and with loss of heterozygosity 1p/19q in 64% of oligodendrogliomas; they were rare in pilocytic astrocytomas (10%) and primary glioblastomas (5%) and absent in ependymomas. The frequent presence of IDH1 mutations in secondary glioblastomas and their near-complete absence in primary glioblastomas reinforce the concept that despite their histological similarities, these subtypes are genetically and clinically distinct entities.

PMID: 19246647 [PubMed - as supplied by publisher]