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## ARIH1

ARIH1, also known as HHARI (Happy Associated RING Finger E3 Ubiguitin Ligase), is a gene that encodes a protein with E3 ubiquitin ligase activity. Ubiquitin ligases are enzymes that play a crucial role in the ubiquitin-proteasome pathway, which is responsible for targeting specific proteins for degradation within the cell.

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The ARIH1/HHARI protein is involved in regulating protein turnover and degradation by attaching ubiquitin molecules to target proteins, marking them for degradation by the proteasome. This process is essential for maintaining proper cellular function and ensuring that damaged or unnecessary proteins are removed from the cell.

ARIH1/HHARI has been studied in various contexts, including its potential role in the regulation of cell cycle progression and DNA damage response. Dysregulation of ubiquitin ligases like ARIH1 can contribute to the development of various diseases, including cancer, as they can lead to the accumulation of proteins that should be degraded.

When ARIH1 and BRAF genes fuse together, the resulting fusion protein can have novel properties that may drive the growth and survival of cancer cells. The specific effects of this fusion would depend on the breakpoints within the genes and the functional domains retained in the fusion protein.

It's important to note that the discovery of novel fusion genes like ARIH1:BRAF is a significant finding in cancer research. Understanding the molecular alterations that drive gliomas and other cancers is crucial for developing targeted therapies that can potentially disrupt these cancer-promoting pathways.

Treatment options for gliomas often depend on the specific genetic alterations present in the tumor, so further research and characterization of this fusion are necessary to determine its clinical significance and potential implications for treatment. Physicians and researchers may explore targeted therapies designed to inhibit the abnormal signaling caused by the ARIH1:BRAF fusion if it is found to be a driver of glioma  $^{1)}$ .

## Xu E, Stone SL, Zhong Y, Golenberg N, Qiu L, Abdullaev Z, Aldape K, Bagley L, Halpern CH, Amankulor N, Nasrallah MP. A novel ARIH1::BRAF fusion in a glioma. J Neuropathol Exp Neurol. 2023 Sep 23:nlad074. doi: 10.1093/jnen/nlad074. Epub ahead of print. PMID: 37742132.

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