BRAF fusion

BRAF Fusions refer to genetic alterations in the BRAF gene that result in fusion proteins involving BRAF and another gene. BRAF, a protein kinase, is a critical component of the RAS-RAF-MEK-ERK signaling pathway, which regulates cell growth, proliferation, and differentiation. Mutations or fusions involving the BRAF gene can lead to aberrant signaling and contribute to the development of cancer.

In the context of cancer, BRAF fusions typically involve the fusion of the BRAF gene with another gene, often resulting in a hybrid or chimera protein. These fusion proteins can have unique properties that drive tumor growth, making them important targets for cancer research and potential therapeutic interventions. The specific fusion partner and the structure of the fusion protein can vary between different cases of BRAF fusions.

Here are a few key points regarding BRAF fusions:

Fusion Partners: BRAF can fuse with various partner genes, and the resulting fusion protein can have different functional consequences. Some common fusion partners include KIAA1549, FAM131B, and AGK, among others.

Oncogenic Potential: BRAF fusions are considered oncogenic because they can lead to uncontrolled activation of the RAS-RAF-MEK-ERK signaling pathway, which promotes cell proliferation and survival. This pathway is often dysregulated in cancer.

Cancer Types: BRAF fusions have been identified in various cancer types, including certain types of pediatric brain tumors (e.g., pilocytic astrocytomas), lung cancer, colorectal cancer, and more. The presence of a BRAF fusion can have implications for prognosis and treatment selection.

Targeted Therapy: Some BRAF fusions respond to targeted therapies designed to inhibit the abnormal signaling caused by the fusion protein. For example, drugs like vemurafenib and dabrafenib, which target mutant BRAF proteins, have shown efficacy in some BRAF fusion-positive tumors.

Research and Diagnosis: The identification of specific BRAF fusions is important for accurate cancer diagnosis and can guide treatment decisions. Molecular testing techniques, such as DNA sequencing or fluorescence in situ hybridization (FISH), are used to detect these genetic alterations.

It's important to note that the presence of a BRAF fusion may not be the same in all cases of a given cancer type, and the clinical significance and response to therapy can vary. Therefore, precise molecular characterization of the fusion and its functional consequences is crucial for understanding its role in cancer and for tailoring treatment strategies.

Research into BRAF fusions and their role in cancer is ongoing, and new discoveries continue to shape our understanding of these genetic alterations and their therapeutic implications.

BRAF fusion in neurosurgery

- ALK-rearranged papillary thyroid carcinoma with a germline MEN1 mutation
- Real-life implementation of molecular criteria for diagnosing gliomas according to 2021 WHO Classification: a national survey from the Italian Association of Neuro-Oncology and Society of Neurosurgery

- 38-Year Delayed Spinal Leptomeningeal Dissemination of a Paediatric Pilocytic Astrocytoma: A Case Report
- Comprehensive transcriptomic profiling of fusions and abnormal variant transcripts in pilocytic astrocytoma using NanoString nCounter technology
- Unveiling the BRAF fusion structure variations through DNA and RNA sequencing
- VOPP1::EGFR fusion is associated with NFkappaB pathway activation in a glioneural tumor with histological features of ganglioglioma
- Imaging Clusters of Pediatric Low-Grade Glioma are Associated with Distinct Molecular Characteristics
- Performance of Machine Learning Models in Predicting BRAF Alterations Using Imaging Data in Low-Grade Glioma: A Systematic Review and Meta-Analysis

---

Like many other neoplasms, brain tumors, especially the ones originating from glia of white and grey matter, can harbor v-RAF murine sarcoma viral oncogene homolog B1 (BRAF) gene alterations. Early animal models with Ras-1-induced glioma formation and experimental blocking of the BRAF hotspot mutation in brain tumor cell cultures suggest that tumor growth is similarly regulated via mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) as seen in non-CNS-tumors [1) 2)].

Pediatric low-grade gliomas (PLGGs) are commonly associated with BRAF gene fusions that aberrantly activate the mitogen-activated protein kinase (MAPK) signaling pathway.

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 [3)].

1)
Ahn J.H., Lee Y.W., Ahn S.K., Lee M. Oncogenic BRAF inhibitor UAI-201 induces cell cycle arrest and autophagy in BRAF mutant glioma cells. Life Sci. 2014;104:38–46. doi: 10.1016/j.lfs.2014.03.026.
2)
Lyustikman Y., Momota H., Pao W., Holland E.C. Constitutive activation of Raf-1 induces glioma formation in mice. Neoplasia (New York, NY) 2008;10:501–510. doi: 10.1593/neo.08206.
3)
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.