NF2 alteration

NF2 alteration any abnormal change affecting the NF2 gene, such as:

Point mutations (→ “NF2 mutation”)

Deletions (e.g., loss of part or all of the gene)

Copy number variations (e.g., monosomy 22)

Epigenetic silencing (e.g., promoter methylation)

Structural rearrangements (e.g., gene fusions)

NF2 alteration is the most commonly-found genetic abnormality in meningiomas and is known to initiate events for aggressive meningiomas. Whereas the meningioma outcomes differs depending on their epigenomics/transcriptomics profile, the effect of NF2 alteration on the prognosis of benign meningiomas is not fully elucidated. This study aimed to probe the importance of NF2 alteration in prognosis of World Health Organization grade 1 meningioma. A long-term retrospective follow-up (5.3 ± 4.5 years) study involving 281 consecutive WHO grade I meningioma patients was performed.

Teranishi et al. assessed tumor recurrence in correlation with extent of resection (EOR), histopathological findings, tumour location, and NF2 alteration. “NF2 meningioma” was defined as meningiomas with presence of NF2 mutation and/or chromosome 22q loss. Overall, NF2 meningioma per se was not a predictor of prognosis in the whole cohort; however, it was a predictor of meningioma recurrence in supratentorial meningiomas, together with EOR and Ki-67. In a striking contrast, NF2 meningioma showed a better prognosis than non-NF2 meningioma in infratentorial meningioma. Supratentorial NF2 meningiomas had higher Ki-67 and FOXM1 than those of others, possibly explaining the worse prognosis in this subtype. The combination of NF2 alteration, high Ki-67 and supratentorial location defines subgroup with the worst prognosis among WHO grade I meningiomas. Clinical connotation of NF2 alteration in terms of prognosis of WHO grade I meningioma differs in an opposite way between supratentorial and infratentorial tumors. Integrated anatomical, histopathological, and genomic classifications will provide the best follow-up schedule and proactive measures [1)].

NF2 mutation

NF2 mutation refers to a specific alteration in the DNA sequence of the *NF2* gene, which encodes the tumor suppressor protein **Merlin** (also known as **schwannomin**). Mutations in this gene are commonly associated with **neurofibromatosis type 2**, as well as several sporadic tumors of the nervous system.

Gene Information

- **Gene**: NF2 (Neurofibromin 2)
- **Chromosomal location**: 22q12.2
- **Protein product**: Merlin (moesin-ezrin-radixin-like protein)
- **Function**: Tumor suppressor; regulates contact-dependent inhibition of proliferation

Types of Mutations

- **Nonsense mutations** → Premature stop codon → truncated protein
- **Frameshift mutations** → Alter reading frame → dysfunctional protein
- **Missense mutations** → Amino acid change → variable effect on function
- **Splice-site mutations** → Aberrant mRNA splicing
- **Large deletions** → Loss of one or more exons

Associated Conditions

- **Neurofibromatosis type 2 (NF2)**
  - Bilateral vestibular schwannomas
  - Meningiomas (multiple)
  - Ependymomas (especially spinal)
- **Sporadic tumors**
  - Schwannomas
  - Meningiomas (particularly grade I and II)
  - Mesotheliomas (less commonly)

Diagnostic Techniques

- **Next-Generation Sequencing (NGS)**
- **Sanger sequencing**
- **MLPA (for large deletions)**
- **FISH or array-CGH (for copy number changes)**

Clinical Relevance

- Loss of **Merlin** function leads to **deregulation of contact inhibition**, promoting tumorigenesis.
- **Germline NF2 mutations** cause inherited **NF2 syndrome**.
- **Somatic NF2 mutations** are frequently found in sporadic **meningiomas** and **schwannomas**.
- May be used for **molecular subclassification** of CNS tumors (e.g., **NF2-altered meningioma**).

Related Pages

- nf2_alteration
- merlin_protein

- neurofibromatosis_type_2
- meningioma
- schwannoma

1)
Teranishi Y, Okano A, Miyawaki S, Ohara K, Ishigami D, Hongo H, Dofuku S, Takami H, Mitsui J, Ikemura M, Komura D, Katoh H, Ushiku T, Ishikawa S, Shin M, Nakatomi H, Saito N. Clinical significance of NF2 alteration in grade I meningiomas revisited; prognostic impact integrated with extent of resection, tumour location, and Ki-67 index. Acta Neuropathol Commun. 2022 May 15;10(1):76. doi: 10.1186/s40478-022-01377-w. PMID: 35570314.