

NF2 – Neurofibromatosis type 2

NIHR BioResource – Rare Diseases study project

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Summary

Type 2 neurofibromatosis (NF2) is an autosomal dominant disorder caused by mutations in the NF2 tumour suppressor gene NF2 on chromosome 22.



Prof. Gareth Evans, NF2 project Lead

Around 1 in 25-33,000 people are born with an NF2 germline variant although more than one-third of the 60% of *de novo* cases are not conceived with the mutation but this develops later in embryogenesis (mosaics). NF2 has a substantial effect on life expectancy and individuals with a constitutional truncating variant in exons 2-13 have the worst prognosis.

The vast majority of people with NF2 will develop bilateral vestibular schwannomas (benign nerve sheath tumours of the 8th cranial nerve) that cause deafness and balance problems. Most also develop additional schwannomas on other cranial, spinal and peripheral nerves. Cranial and spinal meningiomas and intraspinal low grade indolent ependymomas are the other major tumour features.

Cutaneous features can be subtle with only 70% having evidence of intracutaneous plaque-like schwannomas or subcutaneous lesions on peripheral nerves. A diagnosis can be made when the Manchester criteria modifications to NIH criteria are fulfilled. Café-au-lait patches are more frequent than in the general population but in only around 1-2% will meet NIH criteria for NF1. Although there are fairly strong genotype-phenotype correlations there is still considerable variation recorded even amongst identical twins as such other genetic and environmental modifiers are likely. Samples for DNA analysis for genome wide association studies and plasma for biomarkers is advised.

Recruitment Criteria

Inclusion

Patients can be recruited to the NIHR BioResource if they meet diagnostic criteria or have an identified pathogenic variant in *NF2*.

By the modified NIH consensus diagnostic (Manchester) criteria*, NF2 is diagnosed in individuals with **ONE** of the following:

- Bilateral vestibular schwannomas
- A first-degree relative with NF2 AND
 - unilateral vestibular schwannoma OR
 - ANY TWO** of the following: meningioma, schwannoma, glioma, neurofibroma, cataract in the form of posterior subcapsular lenticular opacities or cortical wedge cataract
- Unilateral vestibular schwannoma AND ANY TWO** of the following: meningioma, schwannoma, glioma, neurofibroma, cataract in the form of posterior subcapsular lenticular opacities or cortical wedge cataract
- Multiple meningiomas AND
 - Unilateral vestibular schwannoma OR
 - ANY TWO** of the following: schwannoma, glioma, neurofibroma, cataract in the form of posterior subcapsular lenticular opacities or cortical wedge cataract

*Baser *et al* 2002; <https://www.ncbi.nlm.nih.gov/books/NBK1201/>

** "Any two of" includes two of any tumour type, such as 2 schwannomas.