Neurofibromatosis type 2 (NF2)
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Identity

Other names: Central neurofibromatosis; Bilateral acoustic neurofibromatosis; Bilateral acoustic neurinoma; Bilateral acoustic schwannomas

Inheritance: autosomal dominant with almost complete penetrance; frequency is 3/10^5 newborns; neomutation represent 50% of cases; variable expressivity from mild disease through life (Gardner type) to severe condition at young age (Wishart type: with more than 3 tumours).

Clinics

NF2 is an hamartoneoplastic syndrome; hamartomas are localized tissue proliferations with faulty differenciacion and mixture of component tissues; they are heritable malformations that have a potential towards neoplasia.

Phenotype and clinics

Bilateral vestibular (8th cranial pair) schwannomas; other central or peripheral nerve schwannomas; meningiomas; ependymomas.

Hearing loss (average age 20 yrs), tinnitus, imbalance, headache, cataract in 50%, facial paralysis.

Café-au-lait spots and cutaneous and peripheral neurofibromas may be present, but far less extensively than in neurofibromatosis type 1.

Neoplastic risk

NF2 cases represent about 5% of schwannomas and meningiomas (i.e. risk increased by 2000), appearing at the age of 20, while they are found in the general population at the age of 50 and over.

Prognosis

These tumours are usually benign, but their location within the central nervous system gives them a grave prognosis; patients with the Wishart severe form usually do not survive past 50 yrs.

Cytogenetics

Inborn condition

Normal.

Cancer cytogenetics

Chromosome 22 loss is very frequent both in sporadic and in NF2 schwannomas and meningiomas.

Genes involved and Proteins

SCH

Location: 22q12.1-12.2 junction, (incidentally not far from EWS (Ewing tumour))

DNA/RNA

Description: 16 exons; 120 kb.

Transcription: alternate splicing after exon 15.

Protein

Protein has been called schwannomin or SCH.

Description: 590 or 595 amino acids; 66 kDa; domains: NH2 -- membrane binding -- a helix binding to actin of the cytoskeleton -- COOH.

Expression: in lung, kidney, ovary, breast, placenta, neuroblasts.

Function: membrane- cytoskeleton anchor (as APC also appears to be); has characteristics of a tumour suppressor, as has been found in sporadic as well as NF2 induced schwannomas and meningiomas (accordingly to the Rb model).

Homology ezrin, radixin, moesin, members of the erythrocytes band 4.1 family, especially so in the N-term.

Mutations

Germinal: (inborn condition of NF2 patients): protein truncations due to various frameshift deletions or insertions or nonsense mutations; splice-site or missense mutations are also found; phenotype-genotype correlations are observed (i.e. that severe
phenotypes are found in cases with protein truncations rather than those with amino acid substitution).

**Somatic:** tumourigenesis in NF2 patients.

### References


*This article should be referenced as such:*