Neurofibromatosis

Precision Panel

Overview

Neurofibromatosis type 1 (NF1) and type 2 (NF2) are neurocutaneous congenital disorders that can affect organs of ectodermal origin including skin, central nervous system, and eyes. Both are inherited in an autosomal dominant pattern and are characterised by a high *de novo* mutation rate as well as variable expression. NF1 and NF2 differ with regards to their age of onset, clinical manifestations, gene loci, and gene protein products. However, in both conditions, the altered gene products have a crucial role in the dysregulation of tumour suppression. NF1, also known as von Recklinghausen syndrome, includes effects on multiple systems of the body and is characterised by benign tumours of nerves and skin (neurofibromas) as well as areas of abnormal skin colour (pigmentation) which are referred to as café au lait spots. In addition, clinical manifestations include bone dysplasia, learning disabilities, and increased risk of malignancy. Clinical features of NF2 include schwannomas of multiple cranial and spinal nerves, among others.

The Igenomix Neurofibromatosis Precision Panel can serve as a diagnostic tool potentially leading to better management and prognosis. It provides a comprehensive analysis of the genes involved in these disorders using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved, and their high or intermediate penetrance.

Indications

The Igenomix Neurofibromatosis Precision Panel is indicated in patients with a clinical suspicion or diagnosis of Neurofibromatosis type 1 or type 2 presenting with the following manifestations:

- Multiple neurofibromas
- Café au lait spots
- Lisch nodules (pigmented iris hamartomas)
- Seizures and/or focal neurologic signs
- Intellectual disability
- Bone involvement: scoliosis, short stature, fractures, cortical thinning, etc.
- Other relevant tumours including pheochromocytoma, Wilms tumour, meningiomas, ependymomas
- Bilateral vestibular schwannomas (acoustic neuroma)
- Early-onset cataracts

Clinical Utility

The clinical utility of this panel is:

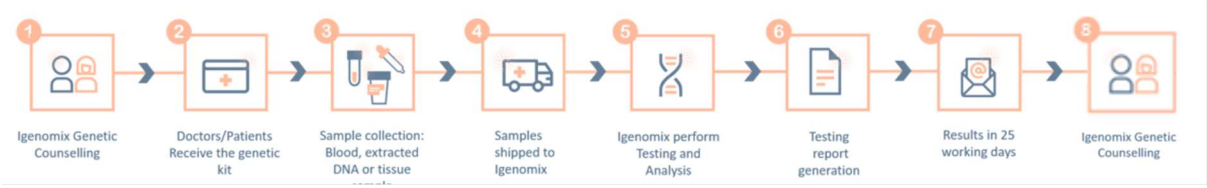
- A genetic and molecular diagnosis for a patient with a confirmed or suspected clinical diagnosis of NF1 or NF2.
- Early initiation of treatment with a multidisciplinary team for appropriate surveillance of malignancy, appropriate laser treatment and/or chemotherapy, surgical resection of tumours, as well as orthopaedic intervention.
- Risk assessment of asymptomatic family members.
- Improved pathways from diagnosis to treatment in susceptible populations.

Genes & Diseases

GENE	OMIM DISEASE	INHERITANCE*	% GENE COVERAGE (20X)	CLINVAR**	HGMD**
KIT	Piebaldism	AD	100	86 of 86	112 of 112
KITLG	Familial progressive hyperpigmentation	AD	99.93	6 of 6	10 of 10
LZTR1	Noonan 10 syndrome, Schwannomatosis 2	AD,AR	99.99	59 of 59	136 of 136
MAP2K2	Neurofibromatosis-Noonan syndrome	AD	100	24 of 24	37 of 37
NF1	Neurofibromatosis 1, Neurofibromatosis-Noonan syndrome, Familial spinal neurofibromatosis	AD	97.97	1613 of 1618	3082 of 3166
NF2	Neurofibromatosis 2	AD	100	83 of 83	359 of 362
PTPN11	Noonan syndrome with multiple lentigines	AD	100	136 of 136	150 of 151
RAF1	Noonan 5 syndrome	AD	100	46 of 46	64 of 64
SMARCB1	Schwannomatosis 1	AD	100	35 of 35	97 of 99
SPRED1	Legius syndrome	AD	100	48 of 48	84 of 84

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive.
**Number of clinically relevant mutations according to HGMD

Methodology



Contact us

Call +44 (0)20 8068 8176 or send an email to info.uk@igenomix.com for any of the following:

- Get more information about the test.
- Request your kit.
- Request a pick-up of the kit after collecting the sample.

References

1. Plotkin, S. R., & Wick, A. (2018). Neurofibromatosis and Schwannomatosis. *Seminars in neurology*, *38*(1), 73–85. https://doi.org/10.1055/s-0038-1627471
2. Korf B. R. (2013). Neurofibromatosis. *Handbook of clinical neurology*, *111*, 333–340. https://doi.org/10.1016/B978-0-444-52891-9.00039-7
3. Spyk, S., Thomas, N., Cooper, D., & Upadhyaya, M. (2011). Neurofibromatosis type 1-associated tumours: Their somatic mutational spectrum and pathogenesis. *Human Genomics*, *5*(6), 623. doi: 10.1186/1479-7364-5-6-623
4. Pemov, A., Dewan, R., Hansen, N., Chandrasekharappa, S., Ray-Chaudhury, A., & Jones, K. et al. (2020). Comparative clinical and genomic analysis of neurofibromatosis type 2-associated cranial and spinal meningiomas. *Scientific Reports*, *10*(1). doi: 10.1038/s41598-020-69074-z
5. Farschtschi, S., Mautner, V. F., McLean, A., Schulz, A., Friedrich, R. E., & Rosahl, S. K. (2020). The Neurofibromatoses. *Deutsches Arzteblatt international*, *117*(20), 354–360. https://doi.org/10.3238/arztebl.2020.0354
6. Cimino, P. J., & Gutmann, D. H. (2018). Neurofibromatosis type 1. *Handbook of clinical neurology*, *148*, 799–811. https://doi.org/10.1016/B978-0-444-64076-5.00051-X