Noonan Spectrum Disorders and RASopathies

Precision Panel

Overview

Noonan Syndrome is a genetic disorder that impairs normal development of several parts of the body. The main features of Noonan Syndrome include unusual fascies (hypertelorism, down-slanting eyes, webbed neck), congenital heart disease, short stature and chest deformity. Mental retardation can be seen in approximately 25% of individuals affected by Noonan syndrome. Other findings present to varying degrees include skeletal, neurologic, genitourinary, lymphatic, eye and skin manifestations. Gene mutations identified in individuals with Noonan Syndrome phenotype are involved in the RAS/MAPK (mitogen-activated protein kinase) signal transduction pathway, also known as RASopathy. RASopathies are developmental syndromes caused by germline mutations in genes that alter the RAS subfamily and MAPK that control signal transduction and that present overlapping clinical features. Some of the diseases belonging to this category include Noonan syndrome, Costello syndrome, Neurofibromatosis type 1, cardio-facio-cutaneous syndrome and others. The most common mode of inheritance for these diseases is autosomal dominant.

The Igenomix Noonan Spectrum Disorders and RASopathies Precision Panel can be used to make a directed and accurate differential diagnosis of Noonan syndrome and RASopathies ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Indications

The Igenomix Noonan Spectrum Disorders and RASopathies Precision Panel is indicated for those patients with a clinical diagnosis presenting with the following manifestations:

- Facial features: triangular-shaped face, hypertelorism, down-slanting palpebral fissures, ptosis, low set ears etc
- Ocular abnormalities: amblyopia, myopia, astigmatism, strabismus etc
- Sensorineural hearing loss
- Pectus carinatum or excavatum
- Cardiac abnormalities: pulmonary stenosis, hypertrophic cardiomyopathy
- Skeletal features: joint laxity, short stature etc
- Skin abnormalities

- Genitourinary abnormalities

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.
- Early initiation of treatment with a multidisciplinary team to perform appropriate medical care, early surveillance of malignancy and surgical repair of anatomic abnormalities.
- Risk assessment of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

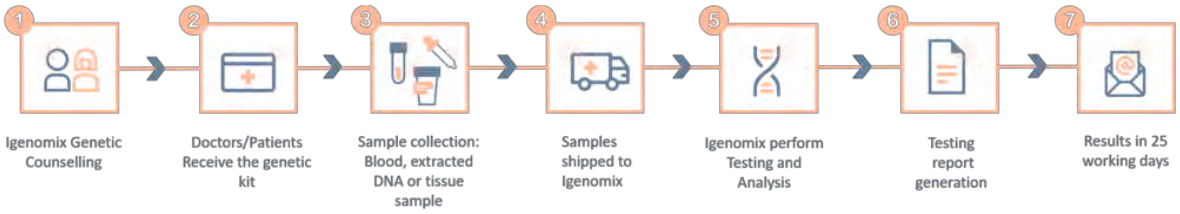
Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
A2ML1	Noonan Syndrome	AD,MU,P	100	23 of 23
ACTB	Baraitser-Winter Syndrome, Developmental Malformations-Deafness-Dystonia Syndrome	AD	100	40 of 40
ACTG1	Baraitser-Winter Syndrome	AD	98.59	55 of 55
BRAF	Cardiofaciocutaneous Syndrome, Leopard Syndrome, Noonan Syndrome, Cardiofaciocutaneous Syndrome	AD	100	80 of 80
CBL	Noonan Syndrome-like Disorder With Or Without Juvenile Myelomonocytic Leukemia	AD	100	46 of 47
CCNK	Intellectual Developmental Disorder With Hypertelorism And Distinctive Facies	AD	96.69	1 of 1
CDC42	Takenouchi-Kosaki Syndrome, Macrothrombocytopenia-Lymphedema-Developmental Delay-Facial Dysmorphism-Camptodactyly Syndrome	AD	99.97	10 of 10
EPHB4	Nonimmune Hydrops Fetalis And/Or Atrial Septal Defect	AD	100	65 of 65
FGD1	Aarskog-Scott Syndrome	X,XR,G	98.95	NA of NA
HRAS	Costello Syndrome, Schimmelpenning-Feuerstein-Mims Syndrome, Linear Nevus Sebaceus Syndrome	AD	100	34 of 34
KAT6B	Genitopatellar Syndrome, Ohdo Syndrome, Blepharophimosis-Intellectual Disability Syndrome	AD	99.97	80 of 80
KRAS	Aplasia Cutis Congenita With Epibulbar Dermoids , Cardiofaciocutaneous Syndrome, Noonan Syndrome, Ras-Associated Autoimmune Lymphoproliferative Syndrome Type IV, Schimmelpenning-Feuerstein-Mims Syndrome, Cardiofaciocutaneous Syndrome, Encephalocraniocutaneous Lipomatosis, Toriello-Lacassie-Droste Syndrome	AD	100	38 of 38
LZTR1	Noonan Syndrome	AD	99.99	136 of 136
MAP2K1	Cardiofaciocutaneous Syndrome, Noonan Syndrome	AD	100	31 of 31
MAP2K2	Cardiofaciocutaneous Syndrome, Neurofibromatosis-Noonan Syndrome	AD	100	37 of 37
MAP3K8	Susceptibility To Lung Cancer	AD	99.91	1 of 1
MRAS	Noonan Syndrome	AD	100	3 of 3
NF1	Neurofibromatosis-Noonan Syndrome, Neurofibromatosis Type I, Watson Syndrome, Deletion	AD	97.97	3082 of 3166

NRAS	Neurocutaneous Melanosis, Noonan Syndrome, Ras-Associated Autoimmune Lymphoproliferative Syndrome Type IV, Schimmelpenning-Feuerstein-Mims Syndrome	AD	100	15 of 15
PPP1CB	Noonan Syndrome-Like Disorder With Loose Anagen Hair	AD	99.87	12 of 12
PTPN11	Leopard Syndrome, Metachondromatosis, Noonan Syndrome	AD	100	150 of 151
RAF1	Cardiomyopathy Dilated Cardiomyopathy, Leopard Syndrome, Noonan Syndrome	AD	100	64 of 64
RASA1	Capillary Malformation-Arteriovenous Malformation, Parkes Weber Syndrome	AD	99.56	169 of 169
RASA2	Noonan Syndrome		99.82	5 of 5
RIT1	Noonan Syndrome	AD	99.85	27 of 27
RRAS	Noonan Syndrome		95.86	3 of 3
RRAS2	Noonan Syndrome	AD	99.8	6 of 6
SASH1	Pigment Dyscrasia, Onychodystrophy, And Keratoderma, Dyschromatosis Universalis Hereditaria	AD,AR	99.86	15 of 15
SHOC2	Noonan Syndrome-Like Disorder With Loose Anagen Hair	AD	99.98	8 of 8
SOS1	Hereditary Gingival Fibromatosis, Noonan Syndrome	AD	100	103 of 104
SOS2	Noonan Syndrome	AD	99.48	6 of 7
SPRED1	Legius Syndrome	AD	100	84 of 84

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



Contact us

Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

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

References

1. Romano, A. A., Allanson, J. E., Dahlgren, J., Gelb, B. D., Hall, B., Pierpont, M. E., Roberts, A. E., Robinson, W., Takemoto, C. M., & Noonan, J. A. (2010). Noonan syndrome: clinical features, diagnosis, and management guidelines. *Pediatrics*, *126*(4), 746–759. https://doi.org/10.1542/peds.2009-3207
2. Turner, A. (2011). Noonan syndrome. *Journal Of Paediatrics And Child Health*, *50*(10), E14-E20. doi: 10.1111/j.1440-1754.2010.01970.x
3. Cessans, C., Ehlinger, V., Arnaud, C., Yart, A., Capri, Y., & Barat, P. et al. (2016). Growth patterns of patients with Noonan syndrome: correlation with age and genotype. *European Journal Of Endocrinology*, *174*(5), 641-650. doi: 10.1530/eje-15-0922

4. Turner A. M. (2014). Noonan syndrome. *Journal of paediatrics and child health*, *50*(10), E14–E20. https://doi.org/10.1111/j.1440-1754.2010.01970.x
5. Allanson, J., Bohring, A., Dörr, H., Dufke, A., Gillessen-Kaesbach, G., & Horn, D. et al. (2010). The face of Noonan syndrome: Does phenotype predict genotype. *American Journal Of Medical Genetics Part A*, *152A*(8), 1960-1966. doi: 10.1002/ajmg.a.33518
6. Liao, J., & Mehta, L. (2019). Molecular Genetics of Noonan Syndrome and RASopathies. *Pediatric endocrinology reviews : PER*, *16*(Suppl 2), 435–446. https://doi.org/10.17458/per.vol16.2019.lm.molecularnoonan
7. Rauen K. A. (2013). The RASopathies. *Annual review of genomics and human genetics*, *14*, 355–369. https://doi.org/10.1146/annurev-genom-091212-153523
8. Aoki, Y., Niihori, T., Inoue, S., & Matsubara, Y. (2016). Recent advances in RASopathies. *Journal of human genetics*, *61*(1), 33–39. https://doi.org/10.1038/jhg.2015.114