Kallmann Syndrome

Precision Panel

Overview

Kallmann Syndrome (KS) is a rare genetic disorder that belongs to the spectrum of isolated hypogonadotropic hypogonadism. This decrease in gonadal function is due to a failure in differentiation or migration of neurons that embryologically arise in the olfactory mucosa and travel to the hypothalamus. Thus, a particular feature of Kallman Syndrome is the presence of either anosmia (lack of sense of smell) or severe hyposmia. Some non-reproductive, non-olfactory symptoms can also be present, depending on the genetic form of disease which include cranial anomalies, missing teeth, optic problems and/or congenital heart disease. Inability to attain puberty or failure to fully complete it is one of the main forms of presentation and an early interventional replacement therapy could prevent further complications derived from a delay in treatment. It is inherited typically in an autosomal dominant fashion.

The Igenomix Kallmann Syndrome Precision Panel can be used to make a directed and accurate diagnosis as well as a differential diagnosis of hypogonadotropic hypogonadism 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 Kallmann Syndrome Precision Panel is indicated for those patients with a clinical diagnosis or suspicion with or without the following manifestations:

- Amenorrhea
- Dyspareunia
- Infertility
- Decreased muscle strength and diminished aggressiveness and drive in men
- Osteoporosis
- Anosmia or hyposmia (decreased or absent sense of smell)
- Fatigue
- Difficulty breathing
- Palpitations
- Syncope
- Color blindness
- Epilepsy
- Deafness
- Paraplegia
- Skeletal 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 gonadal steroid replacement therapy, assisted reproduction technology (ARTs), psychological counselling and surveillance and prevention of complications such as osteoporosis, adrenocortical insufficiency and neurologic disorders.
- Early planification of surgical care for congenital heart disease and cleft lip or palate.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.

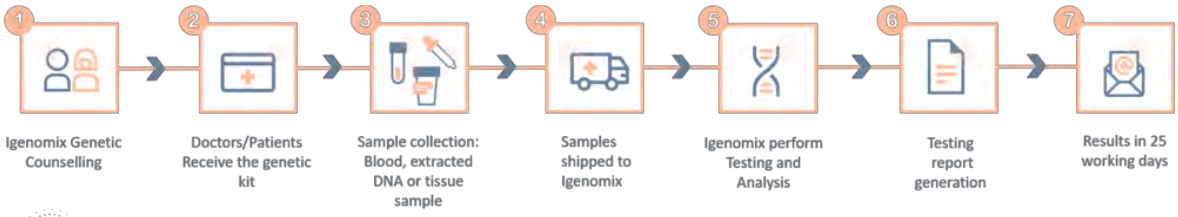
Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
ANOS1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	X,XR,G	96.86	-
CCDC141	Hypogonadotropic Hypogonadism Without Anosmia, Kallmann Syndrome	AR	99.7	1 of 1
CHD7	Charge Syndrome, Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Omenn Syndrome	AD	96.25	823 of 896
DCC	Familial Horizontal Gaze Palsy, With Progressive Scoliosis, With Impaired Intellectual Development, Familial Congenital Mirror Movements, Kallmann Syndrome	AD,AR	94	39 of 39
DUSP6	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD,AR	99.36	4 of 4
FEZF1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AR	99.95	3 of 3
FGF17	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD,AR	99.98	8 of 8
FGF8	Hypogonadotropic Hypogonadism With Or Without Anosmia, Alobar Holoprosencephaly, Kallmann Syndrome, Lobar Holoprosencephaly, Microform Holoprosencephaly, Midline Interhemispheric Variant Of Holoprosencephaly, Normosmic Congenital Hypogonadotropic Hypogonadism	AD	98.36	38 of 38
FGFR1	Encephalocraniocutaneous Lipomatosis, Hartsfield Syndrome, Jackson-Weiss Syndrome, Kallmann Syndrome, Osteoglophonic Dysplasia, Pfeiffer Syndrome, Isolated Trigonocephaly, Lobar Holoprosencephaly, Microform Holoprosencephaly, Normosmic Congenital Hypogonadotropic Hypogonadism, Oligodontia, Osteoglosphonic Dysplasia, Septo-Optic Dysplasia Spectrum	AD	100	279 of 280
FLRT3	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AD	99.98	7 of 7
GNRH1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100	12 of 12
GNRHR	Hypogonadotropic Hypogonadism Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100	59 of 59
HESX1	Septooptic Dysplasia, Combined Pituitary Hormone Deficiencies, Kallmann Syndrome, Pituitary Stalk Interruption Syndrome, Septo-Optic Dysplasia Spectrum	AD,AR	100	26 of 26
HS6ST1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD	99.97	8 of 8
IL17RD	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AD,AR	99.95	17 of 17
KISS1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100	9 of 10

KISS1R	Hypogonadotropic Hypogonadism With Or Without Anosmia, Central Precocious Puberty, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD,AR	99.41	42 of 43
NDNF	Hypogonadotropic Hypogonadism With Anosmia, Kallmann Syndrome	AD	99.33	-
NSMF	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD	99.69	11 of 11
PROK2	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD	100	20 of 20
PROKR2	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Pituitary Stalk Interruption Syndrome, Septo-Optic Dysplasia Spectrum	AD	100	64 of 64
SEMA3A	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AD	100	29 of 29
SOX10	Peripheral Demyelinating Neuropathy, Waardenburg Syndrome, Kallmann Syndrome, Waardenburg-Shah Syndrome	AD	99.74	139 of 147
SPRY4	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD,AR	99.72	13 of 13
TAC3	Hypogonadotropic Hypogonadism With Or Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100	10 of 10
TACR3	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	99.97	40 of 40
WDR11	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Pituitary Stalk Interruption Syndrome	AD,AR	100	19 of 19

*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



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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. Stamou, M. I., & Georgopoulos, N. A. (2018). Kallmann syndrome: phenotype and genotype of hypogonadotropic hypogonadism. *Metabolism: clinical and experimental*, *86*, 124–134. https://doi.org/10.1016/j.metabol.2017.10.012
2. Meczekalski, B., Podfigurna-Stopa, A., Smolarczyk, R., Katulski, K., & Genazzani, A. R. (2013). Kallmann syndrome in women: from genes to diagnosis and treatment. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*, *29*(4), 296–300. https://doi.org/10.3109/09513590.2012.752459
3. Bonomi, M., Libri, D., Guizzardi, F., Guarducci, E., Maiolo, E., & Pignatti, E. et al. (2011). New understandings of the genetic basis of isolated idiopathic central hypogonadism. *Asian Journal Of Andrology*, *14*(1), 49-56. doi: 10.1038/aja.2011.68

4. Dodé, C., Teixeira, L., Levilliers, J., Fouveaut, C., Bouchard, P., Kottler, M. L., Lespinasse, J., Lienhardt-Roussie, A., Mathieu, M., Moerman, A., Morgan, G., Murat, A., Toublanc, J. E., Wolczynski, S., Delpech, M., Petit, C., Young, J., & Hardelin, J. P. (2006). Kallmann syndrome: mutations in the genes encoding prokineticin-2 and prokineticin receptor-2. *PLoS genetics*, *2*(10), e175. https://doi.org/10.1371/journal.pgen.0020175
5. Pingault, V., Bodereau, V., Baral, V., Marcos, S., Watanabe, Y., & Chaoui, A. et al. (2013). Loss-of-Function Mutations in SOX10 Cause Kallmann Syndrome with Deafness. *The American Journal Of Human Genetics*, *92*(5), 707-724. doi: 10.1016/j.ajhg.2013.03.024
6. Sonne, J., & Lopez-Ojeda, W. (2020). Kallmann Syndrome. In *StatPearls*. StatPearls Publishing.