

HYPOGONADOTROPIC HYPOGONADISM (KALLMANN)

PANEL DG-4.0.0 (58 GENES)

| <i>Gene</i> | <i>Twist X2 covered >10x</i> | <i>Twist X2 covered >20x</i> | <i>WGS covered >10x</i> | <i>WGS covered >20x</i> | <i>Associated Phenotype description and OMIM disease ID</i> |
|-------------|---------------------------------|---------------------------------|----------------------------|----------------------------|---|
| ADCY3 | 100.0% | 100.0% | 100.0% | 98.7% | {Obesity, susceptibility to, BMIQ19}, 617885 |
| ANOS1 | 100.0% | 99.8% | 97.6% | 68.8% | Hypogonadotropic hypogonadism 1 with or without anosmia (Kallmann syndrome 1), 308700 |
| ARHGAP35 | 100.0% | 100.0% | 100.0% | 99.0% | |
| AXL | 100.0% | 100.0% | 100.0% | 98.7% | |
| CCDC141 | 99.5% | 98.9% | 100.0% | 98.0% | |
| CHD7 | 100.0% | 100.0% | 100.0% | 98.6% | Hypogonadotropic hypogonadism 5 with or without anosmia, 612370;CHARGE syndrome, 214800 |
| CNGA2 | 99.9% | 99.7% | 97.1% | 68.6% | |
| CUL4B | 96.7% | 96.6% | 97.1% | 66.8% | Intellectual developmental disorder, X-linked syndromic, Cabezas type, 300354 |

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|--------|--------|--------|--------|-------|---|
| DCAF17 | 100.0% | 100.0% | 99.9% | 98.3% | Woodhouse-Sakati syndrome, 241080 |
| DCC | 100.0% | 100.0% | 100.0% | 98.6% | Mirror movements 1 and/or agenesis of the corpus callosum, 157600;Esophageal carcinoma, somatic, 133239;Colorectal cancer, somatic, 114500;Gaze palsy, familial horizontal, with progressive scoliosis, 2, 617542 |
| DUSP6 | 100.0% | 100.0% | 100.0% | 98.2% | Hypogonadotropic hypogonadism 19 with or without anosmia, 615269 |
| FEZF1 | 100.0% | 100.0% | 100.0% | 97.4% | Hypogonadotropic hypogonadism 22, with or without anosmia, 616030 |
| FGF17 | 100.0% | 100.0% | 100.0% | 99.6% | Hypogonadotropic hypogonadism 20 with or without anosmia, 615270 |
| FGF8 | 100.0% | 100.0% | 99.9% | 96.8% | Hypogonadotropic hypogonadism 6 with or without anosmia, 612702 |

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|-------|--------|--------|--------|-------|---|
| FGFR1 | 99.7% | 98.5% | 100.0% | 99.1% | Pfeiffer syndrome, 101600;Hypogonadotropic hypogonadism 2 with or without anosmia, 147950;Jackson-Weiss syndrome, 123150;Hartsfield syndrome, 615465;Trigonocephaly 1, 190440;Osteoglophonic dysplasia, 166250;Encephalocraniocutaneous lipomatosis, somatic mosaic, 613001 |
| FLRT3 | 100.0% | 99.7% | 100.0% | 99.5% | Hypogonadotropic hypogonadism 21 with anosmia, 615271 |
| FSHB | 98.7% | 98.0% | 100.0% | 99.8% | Hypogonadotropic hypogonadism 24 without anosmia, 229070 |
| GLI2 | 100.0% | 100.0% | 100.0% | 99.7% | Culler-Jones syndrome, 615849;Holoprosencephaly 9, 610829 |
| GNRH1 | 100.0% | 100.0% | 100.0% | 96.8% | ?Hypogonadotropic hypogonadism 12 with or without anosmia, 614841 |
| GNRHR | 100.0% | 100.0% | 100.0% | 98.9% | Hypogonadotropic hypogonadism 7 without anosmia, 146110 |

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| HESX1 | 100.0% | 100.0% | 100.0% | 95.2% | Pituitary hormone deficiency, combined, 5, 182230;Septo-optic dysplasia, 182230;Growth hormone deficiency with pituitary anomalies, 182230 |
| HS6ST1 | 100.0% | 100.0% | 100.0% | 92.1% | {Hypogonadotropic hypogonadism 15 with or without anosmia}, 614880 |
| IGSF10 | 100.0% | 100.0% | 100.0% | 99.0% | |
| IL17RD | 100.0% | 100.0% | 100.0% | 99.1% | Hypogonadotropic hypogonadism 18 with or without anosmia, 615267 |
| KISS1 | 100.0% | 100.0% | 100.0% | 96.5% | ?Hypogonadotropic hypogonadism 13 with or without anosmia, 614842 |
| KISS1R | 100.0% | 100.0% | 100.0% | 98.6% | Hypogonadotropic hypogonadism 8 with or without anosmia, 614837;?Precocious puberty, central, 1, 176400 |
| KLB | 100.0% | 100.0% | 100.0% | 99.2% | |
| LEP | 100.0% | 100.0% | 100.0% | 99.5% | Obesity, morbid, due to leptin deficiency, 614962 |
| LEPR | 94.6% | 94.6% | 100.0% | 98.2% | Obesity, morbid, due to leptin receptor deficiency, 614963 |
| LHB | 100.0% | 100.0% | 100.0% | 99.9% | Hypogonadotropic hypogonadism 23 with or without anosmia, 228300 |

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|--------|--------|--------|--------|-------|---|
| LHX3 | 100.0% | 100.0% | 100.0% | 97.3% | Pituitary hormone deficiency, combined, 3, 221750 |
| NDNF | 100.0% | 100.0% | 100.0% | 98.2% | Hypogonadotropic hypogonadism 25 with anosmia, 618841 |
| NOS1 | 100.0% | 100.0% | 100.0% | 99.2% | |
| NR0B1 | 100.0% | 99.8% | 98.5% | 73.1% | Adrenal hypoplasia, congenital, 300200;46XY sex reversal 2, dosage-sensitive, 300018 |
| NSMF | 100.0% | 100.0% | 100.0% | 98.1% | Hypogonadotropic hypogonadism 9 with or without anosmia, 614838 |
| NTN1 | 100.0% | 100.0% | 100.0% | 97.0% | Mirror movements 4, 618264 |
| PCSK1 | 100.0% | 100.0% | 100.0% | 98.8% | {Obesity, susceptibility to, BMIQ12}, 612362;Endocrinopathy due to proprotein convertase 1/3 deficiency, 600955 |
| PHF6 | 100.0% | 100.0% | 98.0% | 73.9% | Borjeson-Forssman-Lehmann syndrome, 301900 |
| PLXNA1 | 100.0% | 100.0% | 100.0% | 99.9% | Dworschak-Punetha neurodevelopmental syndrome, 619955 |

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| PNPLA6 | 100.0% | 100.0% | 100.0% | 99.7% | Spastic paraplegia 39, autosomal recessive, 612020;Oliver-McFarlane syndrome, 275400;?Laurence-Moon syndrome, 245800;Boucher-Neuhauser syndrome, 215470 |
| POLG | 100.0% | 100.0% | 100.0% | 99.4% | Mitochondrial recessive ataxia syndrome (includes SANDO and SCAE), 607459;Mitochondrial DNA depletion syndrome 4B (MNGIE type), 613662;Mitochondrial DNA depletion syndrome 4A (Alpers type), 203700;Progressive external ophthalmoplegia, autosomal dominant 1, 157640;Progressive external ophthalmoplegia, autosomal recessive 1, 258450 |
| POLR3A | 100.0% | 100.0% | 100.0% | 98.8% | Wiedemann-Rautenstrauch syndrome, 264090;Leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism, 607694 |

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|---------|--------|--------|--------|-------|--|
| POLR3B | 100.0% | 99.9% | 100.0% | 98.3% | Leukodystrophy, hypomyelinating, 8, with or without oligodontia and/or hypogonadotropic hypogonadism, 614381;Charcot-Marie-Tooth disease, demyelinating, type 1l, 619742 |
| POLR3GL | 100.0% | 100.0% | 100.0% | 99.0% | Short stature, oligodontia, dysmorphic facies, and motor delay, 619234 |
| PROK2 | 100.0% | 100.0% | 100.0% | 98.3% | Hypogonadotropic hypogonadism 4 with or without anosmia, 610628 |
| PROKR2 | 100.0% | 100.0% | 100.0% | 99.6% | Hypogonadotropic hypogonadism 3 with or without anosmia, 244200 |
| PROP1 | 100.0% | 100.0% | 100.0% | 95.7% | Pituitary hormone deficiency, combined, 2, 262600 |
| SEMA3A | 100.0% | 100.0% | 100.0% | 99.1% | {Hypogonadotropic hypogonadism 16 with or without anosmia}, 614897 |
| SEMA3E | 100.0% | 100.0% | 100.0% | 98.3% | |
| SOX10 | 97.8% | 97.8% | 100.0% | 97.9% | Waardenburg syndrome, type 4C, 613266;PCWH syndrome, 609136;Waardenburg syndrome, type 2E, with or without neurologic involvement, 611584 |

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| SOX11 | 100.0% | 100.0% | 100.0% | 90.9% | Intellectual developmental disorder with microcephaly and with or without ocular malformations or hypogonadotropic hypogonadism, 615866 |
| SOX2 | 100.0% | 100.0% | 99.9% | 95.2% | Optic nerve hypoplasia and abnormalities of the central nervous system, 206900;Microphthalmia, syndromic 3, 206900 |
| SPRY4 | 100.0% | 100.0% | 100.0% | 99.8% | Hypogonadotropic hypogonadism 17 with or without anosmia, 615266 |
| TAC3 | 100.0% | 100.0% | 100.0% | 99.9% | Hypogonadotropic hypogonadism 10 with or without anosmia, 614839 |
| TACR3 | 100.0% | 99.8% | 100.0% | 98.8% | Hypogonadotropic hypogonadism 11 with or without anosmia, 614840 |
| TCF12 | 100.0% | 100.0% | 100.0% | 98.5% | Craniosynostosis 3, 615314;Hypogonadotropic hypogonadism 26 with or without anosmia, 619718 |
| TENM1 | 99.9% | 99.5% | 98.7% | 73.1% | |
| WDR11 | 100.0% | 100.0% | 100.0% | 98.6% | Intellectual developmental disorder, autosomal recessive 78, 620237;Hypogonadotropic hypogonadism 14 with or without anosmia, 614858 |

TWIST X2 Covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x when analyzed by WES using TWIST X2 chemistry.

TWIST X2 Covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x when analyzed by WES using TWIST X2 chemistry.

srWGS GRCh38 Covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x when analyzed by WGS mapped against GRCh38.

srWGS GRCh38 Covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x when analyzed by WGS mapped against GRCh38.

non-protein coding genes are covered, but as coverage statistics are based on protein coding regions, statistics could not be generated.

OMIM release used for OMIM disease identifiers and descriptions : March 17th, 2023.

This list is accurate for panel version DG 4.0.0

Ad 1. "No OMIM phenotype" signifies a gene without a current OMIM association Ad 2. OMIM phenotype descriptions between {} signify risk factors