**Novel and rare variants identified in Hypogonadotropic Hypogonadism patients.**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient ID** | **Sex** | **Phenotype** | **Gene** | **Refseq** | **Variant identified (cDNA)** | **Variant identified (protein)** | **Genotype** | **Inheritance**  | **MAF (%) – gnomAD v2.1.1** | **Population Specific frequency (51 WES random samples)** | **Familial****Segregation** | **Variant Classification** | **Previously described** | **Additional Genetic variants** |
| 1 | M | CHH | *ANOS1* | NM\_000216.4:c.244C>T | c.244G>A | p.Gln82\* | p.Gln82\* | X-linked | Absent | Absent | YES | Pathogenic |  - |  - |
| 2 | M |  KS | *WDR11* | NM\_018117.12:c.731T>C | c.731T>C | p.Leu244Pro | p.Leu244Pro/WT | AD | Absent | Absent | NA | Probably Pathogenic |  - |   - |
| 3 | M |    CHH | *SRA1* | NM\_001035235.3:c.536T>C | c.536T>C | p.Ile179Thr | p.Ile179Thr/WT | AR  | 0.00081 | Absent | YES | Probably Pathogenic | ([67](#_ENREF_67), [71](#_ENREF_71)) | MC4R: p.Val103Ile/WT |
| *RNF216* | NM\_207111.3:c.2374G>A | c.2374G>A | p.Asp792Asn | p.Asp792Asn/WT | AR | Absent | Absent | Probably Pathogenic |  - |
| 4 | M |  CHH  | *CHD7* | NM\_017780.4:c.7198C>T | c.7198C>T | p.Arg2400Trp | p.Arg2400Trp/WT | AD | 0.0000154 | Absent | NA | Probably Pathogenic |  - | PROP1: p.Arg112Gln/WT (MAF: 0.000255%) MC4R: p.Val103Ile/WT |
| 5 | M |    CHH | *FGFR1* | NM\_023110.3:c.556C>G | c.556C>G | p.Pro186Ala | p.Pro186Ala/WT | AD | Absent | Absent | NA | Probably Pathogenic |  - |    -   - |
| *POLR3A* | NM\_007055.4:c.1681C>G | c.1681C>G | p.Arg561Gly | p.Arg561Gly/WT | AR | Absent | Absent | Probably Pathogenic |  - |
| 6 | M |    CHH | *FGFR1* | NM\_023110.3:c.2464C>T | c.2464C>T | p.Arg822Cys | p.Arg822Cys/WT | AD | 0.00026 | Absent | NA | Probably Pathogenic | ([143](#_ENREF_143)) |    - |
| 7 | F |    CHH | *SRA1* | NM\_001035235.3:c.536T>C | c.536T>C | p.Ile179Thr | p.Ile179Thr/p.Ile179Thr | AR | 0.00081 | Absent | NA | Probably Pathogenic | ([67](#_ENREF_67), [71](#_ENREF_71)) |   - |

KS, Kallman syndrome; CHH, Congenital Hypogonadotropic Hypogonadism; WT, Wild Type; AD, Autosomal Dominant; AR, Autosomal Recessive; MAF, Minor Allele Frequency; gnomAD, Genome Aggregation Database (https://gnomad.broadinstitute.org/); WES, Whole Exome Sequencing; NA, Not Available.