

NOVEL GENES DISCOVERED IN NORMOSMIC HYPOGONADOTROPIC HYPOGONADISM (NHH)

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Characterized by delayed or absent sexual development, idiopathic hypogonadotropic hypogonadism (IHH) is a disorder that includes the deficient production, secretion, or action of gonadotropin-releasing hormone (GnRH). Producing neurons in the brain, GnRH directly controls sexual development during puberty. Misplacement of the GnRH producing neurons leads to hypogonadotropic hypogonadism, which is divided into two categories: Kallmann syndrome (KS) and normosmic IHH (nHH). While both KS and nHH, defined as the absence or delay of puberty, low gonadotropins and sex steroids, are similar, KS also includes the absence or impairment of smell. Whole exome sequencing (WES) is used to examine protein-coding regions of the human genome in order to detect genetic variants that could be causative. Sanger sequencing is used to confirm variants identified by WES. Using WES and Sanger sequencing, we were able to identify new genetic variants within the nHH and KS patient populations. In this study, our goal was to identify pathogenic variants in known and novel nHH/KS genes, focusing efforts on rare, loss-of-function variants in: WDR11, GLI2, CTNNA1, ANKHD1, SEMA6A, PRRC2C, EHBP1, and RIF1 genes. This study broadens our understanding of pathogenic variants in known and novel IHH genes that may contribute to the disease phenotype.