THE UNIVERSITY OF CHICAGO | Genetic Services Laboratories

Next Generation Sequencing Panel for Hypospadias

Clinical Features:

Hypospadias is a common malformation in which defective development results in abnormal placement of the urethral opening of the penis[1, 2, 3]. Estimates of the incidence of hypospadias range from 4 to 40 in 10,000 male births; it is most frequently observed in Caucasians and least frequently observed in Asians and Hispanics[3]. The majority of genes identified in conjunction with hypospadias are syndromic, although they may also cause isolated hypospadias when mutated[1, 2]. Few genes are associated solely with isolated hypospadias[1, 2, 3]. Syndromes associated with hypospadias include WAGR syndrome, Opitz GBBB syndrome, and Smith-Lemli-Opitz syndrome[1].

Our Hypospadias Panel includes sequencing of the 61 genes listed below.

Hypospadias Sequencing Panel						
Autosomal Dominant			**Autosomal Recessive**			**X-linked**
BMP4	IRF6	SPECC1L	B3GALTL	FBXL4	PEX1	AR
CDKN1C	MAP3K1	TP63	CUL7	FIG4	RBBP8	ARX
CREBBP	MID1	WT1	CYP11A1	FRAS1	SRD5A2	ATRX
FGF10	PDE4D	ZEB2	DHCR7	FREM2	TMEM70	BCOR
FGFR1	PITX2		DNMT3B	GRIP1	UBR1	EFNB1
FGFR2	PTDSS1		EPG5	HBA1	WDR35	FLNA
FGFR3	PTPN11		ESCO2	HSD3B2	WNT7A	GPC3
GLI3	SALL1		EVC	MKKS		HCCS
HNF1B	SETBP1		EVC2	NR5A1		MAMLD1
HOXA13	SOX2		FAT4	PCNT		MED12

Hypospadias Sequencing Panel (61 genes sequencing)

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$2000
CPT codes:	81407
Turn-around time:	8 weeks

Note: We cannot bill insurance for the above test.

Test methods:

Comprehensive sequence coverage of the coding regions and splice junctions of all genes in this panel is performed. Targets of interest are enriched and prepared for sequencing using the Agilent SureSelect system. Sequencing is performed using Illumina technology and reads are aligned to the reference sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic and likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20 bp. Deletion/duplication analysis of the panel genes is performed by oligonucleotide array-CGH. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by array-CGH. Array-CGH will not detect low-level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of this assay may be reduced when DNA is extracted by an outside laboratory.

Results:

Results, along with an interpretive report, will be faxed to the referring physician. Additional reports will be provided as requested. All abnormal results will be reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References:

1. George M, Schneuer FJ, Jamieson SE, Holland AJ. Genetic and environmental factors in the aetiology of hypospadias. *Pediatr Surg Int* 2015, **31**(6)**:** 519-527.
2. Marrocco G, Grammatico P, Vallasciani S, Gulia C, Zangari A, Marrocco F*, et al.* Environmental, parental and gestational factors that influence the occurrence of hypospadias in male patients. *J Pediatr Urol* 2015, **11**(1)**:** 12-19.
3. van der Zanden LF, van Rooij IA, Feitz WF, Franke B, Knoers NV, Roeleveld N. Aetiology of hypospadias: a systematic review of genes and environment. *Hum Reprod Update* 2012, **18**(3)**:** 260-283.

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