Male Infertility Panel

The Male Infertility Panel is a comprehensive next-generation sequencing (NGS) panel that analyzes genes associated with increased risks for male infertility, including Y chromosome microdeletions, congenital absence of the vas deferens, sex chromosome aneuploidy, and other causes of male factor infertility.

INDICATIONS FOR TESTING

• Molecular confirmation of a clinical diagnosis
• Personal history of oligospermia or azoospermia, absence of the vas deferens or other male infertility causes
• A family history suggestive of a hereditary infertility syndrome
• Risk assessment for asymptomatic family members of proband with a molecular diagnosis

Y Chromosome Microdeletions

Y chromosome microdeletions are deletions of the region of the Y chromosome, called the azoospermia factor (AZF), which encode genes that are important for male fertility. A deletion in these regions can cause severely reduced sperm production (oligospermia) or absent sperm production (azoospermia). Y chromosome microdeletions are one of the most common causes of infertility in men, and are identified in approximately 3-15% of men with nonobstructive azoospermia and approximately 10% of men with severe oligospermia (Stahl et al, 2012; Stahl et al, 2010). Overall, Y chromosome microdeletions occur in 1 in 2000 to 1 in 3000 males (Silber et al, 2012).

INCLUDED DISORDERS:

This panel includes genes associated with:
• Y chromosome microdeletions

INHERITANCE:

Y chromosome microdeletions typically occur de novo (for the first time) in affected individuals. Since Y chromosome microdeletions typically cause male infertility, they are usually not passed down to next generations. However, any males conceived via assisted reproductive technology using the sperm of an affected man will also carry the same Y chromosome microdeletion.

REGION ASSAYED:

AZF region of the Y chromosome

REFERENCES:

Biallelic pathogenic variants in the CFTR gene are associated with a spectrum of disorders, including classic cystic fibrosis, atypical cystic fibrosis, and congenital absence of the vas deferens (CAVD). Congenital absence of the vas deferens typically occurs when an individual has one severe pathogenic variant, and one mild pathogenic variant in the CFTR gene.

Congenital absence of the vas deferens occurs when an individual is born without the vas deferens, which transports sperm from the epididymis to the ejaculatory ducts. CAVD accounts for 25% of obstructive azoospermia (Wosnitzer and Goldstein, 2014), and approximately 80% of men with obstructive azoospermia carry at least one pathogenic CFTR variant (Chillon et al, 1995; Yu et al, 2012).

**INCLUDED DISORDERS:**
This panel includes genes associated with:
- Congenital absence of the vas deferens (CAVD)
- Cystic fibrosis (CF)

**INHERITANCE:**
CFTR-related disorders, including cystic fibrosis and congenital absence of the vas deferens are inherited in an autosomal recessive fashion.

**INCLUDED GENE:**
CFTR

**REFERENCES:**

**Sex Chromosome Aneuploidy**

Sex chromosome aneuploidy is the presence of an abnormal number of sex chromosomes. Male individuals typically have 46 chromosomes, including one X chromosome and one Y chromosome, while females typically have 46 chromosomes, including two X chromosomes. The most common sex chromosome aneuploidy identified in males is Klinefelter syndrome, which occurs in approximately 1 in 500 males (Nielsen and Wohlert, 1991) and is the most common genetic cause of non-obstructive azoospermia identified in infertile males (Bojesen and Gravholt, 2007). Males with Klinefelter may have delayed or incomplete puberty, gynecomastia, reduced facial and body, and reduced fertility.

**INCLUDED DISORDERS:**
This panel assesses the following disorders:
- Klinefelter syndrome
- Other sex chromosome abnormalities

**INHERITANCE:**
Sex chromosome aneuploidies are typically not inherited but rather occur as random errors that occur during cell division in the formation of sperm and egg cells in a parent.

**ASSAYED REGIONS:**
- X and Y chromosomes

**REFERENCES:**
Other Male Factor Infertility

Male factor infertility may be caused by disorders of male sexual development, spermatogenic failure, or hormonal problems. A variety of syndromic and nonsyndromic forms of oligospermia and azoospermia are caused by genetic disorders. This panel tests for genetic disorders resulting in male infertility that is not caused by other genetic causes (sex chromosome aneuploidy, y chromosome microdeletions, CBAVD).

**INCLUDED DISORDERS:**
- Azoospermia
- 46,XY sex reversal
- Oligospermia
- Androgen insensitivity syndrome
- Hypogonadotropic hypogonadism

**INHERITANCE:**
The disorders included in this panel are inherited in autosomal dominant, autosomal recessive, X-linked, and Y-linked manners.

**INCLUDED GENE(S) (9):**

| AR | AURKC | CATSPER1 | DYP19L2 | FSHB | FSHR | LHCGR | SRY | USP9Y |

**EMERGING EVIDENCE GENES (10):**
Emerging evidence genes can also be included. These genes do not have a clear association with male factor infertility, but emerging evidence suggests that they may play a role in disease pathogenesis.

| CATSPER2 | DDX25 | LHB | PRDM9 |
| NRSA1 | PRM1 | USP26 | DAZL |