

# PREMATURE OVARIAN INSUFFICIENCY PANEL DG-5.1.0 (55 GENES)

| Gene     | Twist X2 covered 10x | Twist X2 covered 20x | srWGS covered 10x | srWGS covered 15x | srWGS covered 20x | Associated Phenotype description and OMIM disease ID                                                                    |
|----------|----------------------|----------------------|-------------------|-------------------|-------------------|-------------------------------------------------------------------------------------------------------------------------|
| AARS2    | 100%                 | 100%                 | 100%              | 100%              | 99.5%             | Leukoencephalopathy, progressive, with ovarian failure, 615889; Combined oxidative phosphorylation deficiency 8, 614096 |
| ANKRD31  | 100%                 | 100%                 | 100%              | 99.9%             | 99.8%             |                                                                                                                         |
| BMP15    | 100%                 | 100%                 | 98.6%             | 90.2%             | 70.4%             | Premature ovarian failure 4, 300510; Ovarian dysgenesis 2, 300510                                                       |
| BNC1     | 100%                 | 100%                 | 100%              | 100%              | 99.8%             | ?Premature ovarian failure 16, 618723                                                                                   |
| C14orf39 | 100%                 | 100%                 | 100%              | 100%              | 99.7%             | Spermatogenic failure 52, 619202; Premature ovarian failure 18, 619203                                                  |
| CLPP     | 100%                 | 100%                 | 100%              | 100%              | 98.9%             | Perrault syndrome 3, 614129                                                                                             |
| CYP17A1  | 100%                 | 100%                 | 100%              | 100%              | 99.5%             | 17,20-lyase deficiency, isolated, 202110; 17-alpha-hydroxylase/17,20-lyase deficiency, 202110                           |
| CYP19A1  | 100%                 | 100%                 | 100%              | 100%              | 99.8%             | Aromatase deficiency, 613546                                                                                            |
| DAP3     | 91.7%                | 90.8%                | 100%              | 100%              | 99.6%             | Perrault syndrome 7, 621101                                                                                             |
| DCAF17   | 96.5%                | 96.5%                | 100%              | 99.9%             | 99.7%             | Woodhouse-Sakati syndrome, 241080                                                                                       |

|           |      |      |      |       |       |                                                                                                                                                                                                                                                                                                       |
|-----------|------|------|------|-------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EIF2B5    | 100% | 100% | 100% | 100%  | 99.6% | Leukoencephalopathy with vanishing white matter 5, with or without ovarian failure, 620315                                                                                                                                                                                                            |
| EIF4ENIF1 | 100% | 100% | 100% | 100%  | 99.7% |                                                                                                                                                                                                                                                                                                       |
| ERAL1     | 100% | 100% | 100% | 99.9% | 99.3% | Perrault syndrome 6, 617565                                                                                                                                                                                                                                                                           |
| ERCC6     | 100% | 100% | 100% | 100%  | 99.6% | UV-sensitive syndrome 1, 600630;Cerebrooculofacioskeletal syndrome 1, 214150;?De Sanctis-Cacchione syndrome, 278800;Cockayne syndrome, type B, 133540;{Macular degeneration, age-related, susceptibility to, 5}, 613761;Premature ovarian failure 11, 616946;{Lung cancer, susceptibility to}, 211980 |
| ESR1      | 100% | 100% | 100% | 100%  | 99.7% | Breast cancer, somatic, 114480;{Migraine, susceptibility to}, 157300;Estrogen resistance, 615363;{Myocardial infarction, susceptibility to}, 608446                                                                                                                                                   |
| ESR2      | 100% | 100% | 100% | 100%  | 99.8% | ?Ovarian dysgenesis 8, 618187                                                                                                                                                                                                                                                                         |
| FANCM     | 100% | 100% | 100% | 100%  | 99.8% | Premature ovarian failure 15, 618096;Spermatogenic failure 28, 618086                                                                                                                                                                                                                                 |
| FIGLA     | 100% | 100% | 100% | 100%  | 99.3% | Premature ovarian failure 6, 612310                                                                                                                                                                                                                                                                   |
| FIGNL1    | 100% | 100% | 100% | 100%  | 99.9% |                                                                                                                                                                                                                                                                                                       |

|         |       |       |       |       |       |                                                                                                              |
|---------|-------|-------|-------|-------|-------|--------------------------------------------------------------------------------------------------------------|
| FOXL2   | 100%  | 100%  | 99.9% | 99.4% | 96.8% | Premature ovarian failure 3, 608996;Blepharophimosis, epicanthus inversus, and ptosis, types 1 and 2, 110100 |
| FSHB    | 100%  | 100%  | 100%  | 100%  | 99.6% | Hypogonadotropic hypogonadism 24 without anosmia, 229070                                                     |
| FSHR    | 100%  | 100%  | 100%  | 100%  | 99.8% | Ovarian hyperstimulation syndrome, 608115;Ovarian dysgenesis 1, 233300                                       |
| GALT    | 100%  | 100%  | 100%  | 100%  | 99.5% | Galactosemia, 230400                                                                                         |
| GDF9    | 100%  | 100%  | 100%  | 100%  | 99.9% | Premature ovarian failure 14, 618014                                                                         |
| GGPS1   | 100%  | 100%  | 100%  | 100%  | 99.9% | Muscular dystrophy, congenital hearing loss, and ovarian insufficiency syndrome, 619518                      |
| HARS2   | 100%  | 100%  | 100%  | 99.9% | 98.9% | Perrault syndrome 2, 614926                                                                                  |
| HFM1    | 100%  | 100%  | 100%  | 100%  | 99.7% | Premature ovarian failure 9, 615724                                                                          |
| HROB    | 95.2% | 95.2% | 100%  | 100%  | 99.4% | Ovarian dysgenesis 11, 620897                                                                                |
| HSD17B4 | 100%  | 100%  | 100%  | 100%  | 99.9% | D-bifunctional protein deficiency, 261515;Perrault syndrome 1, 233400                                        |
| HSF2BP  | 100%  | 100%  | 100%  | 100%  | 99.9% | Premature ovarian failure 19, 619245                                                                         |
| KASH5   | 100%  | 100%  | 100%  | 100%  | 99.5% | Spermatogenic failure 88, 620547;Premature ovarian failure 22, 620548                                        |

|       |       |       |      |       |       |                                                                                                                                                                                                                                                                            |
|-------|-------|-------|------|-------|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LARS2 | 96.2% | 96.2% | 100% | 100%  | 99.8% | Perrault syndrome 4, 615300;Hydrops, lactic acidosis, and sideroblastic anemia, 617021                                                                                                                                                                                     |
| LHCGR | 100%  | 100%  | 100% | 100%  | 99.7% | Leydig cell adenoma, somatic, with precocious puberty, 176410;Leydig cell hypoplasia with pseudohermaphroditism, 238320;Leydig cell hypoplasia with hypergonadotropic hypogonadism, 238320;Luteinizing hormone resistance, female, 238320;Precocious puberty, male, 176410 |
| MCM8  | 94.4% | 94.4% | 100% | 100%  | 99.8% | ?Premature ovarian failure 10, 612885                                                                                                                                                                                                                                      |
| MCM9  | 100%  | 100%  | 100% | 100%  | 99.8% | Ovarian dysgenesis 4, 616185                                                                                                                                                                                                                                               |
| MEI4  | 100%  | 100%  | 100% | 100%  | 99.9% |                                                                                                                                                                                                                                                                            |
| MSH4  | 100%  | 100%  | 100% | 100%  | 99.8% | Premature ovarian failure 20, 619938;Spermatogenic failure 2, 108420                                                                                                                                                                                                       |
| NOBOX | 100%  | 100%  | 100% | 99.9% | 99.1% | Premature ovarian failure 5, 611548                                                                                                                                                                                                                                        |
| NR5A1 | 98.7% | 95%   | 100% | 100%  | 99.5% | 46XX sex reversal 4, 617480;Premature ovarian failure 7, 612964;46XY sex reversal 3, 612965;Adrenocortical insufficiency, 612964;Spermatogenic failure 8, 613957                                                                                                           |
| PMM2  | 94.6% | 94.6% | 100% | 100%  | 99.7% | Congenital disorder of glycosylation, type Ia, 212065                                                                                                                                                                                                                      |

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|---------|-------|-------|------|-------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| POLG    | 100%  | 100%  | 100% | 100%  | 99.8% | 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 |
| PSMC3IP | 100%  | 100%  | 100% | 100%  | 99.5% | Ovarian dysgenesis 3, 614324                                                                                                                                                                                                                                                                                                                |
| RNF111  | 97.5% | 97.5% | 100% | 100%  | 99.6% |                                                                                                                                                                                                                                                                                                                                             |
| SOHLH1  | 100%  | 100%  | 100% | 100%  | 99.5% | Ovarian dysgenesis 5, 617690;Spermatogenic failure 32, 618115                                                                                                                                                                                                                                                                               |
| SOX11   | 100%  | 100%  | 100% | 99.7% | 96%   | Intellectual developmental disorder with microcephaly and with or without ocular malformations or hypogonadotropic hypogonadism, 615866                                                                                                                                                                                                     |
| SPATA22 | 100%  | 100%  | 100% | 100%  | 99.6% | Premature ovarian failure 25, 621002;Spermatogenic failure 96, 621001                                                                                                                                                                                                                                                                       |
| SPIDR   | 100%  | 100%  | 100% | 100%  | 99.7% | Ovarian dysgenesis 9, 619665                                                                                                                                                                                                                                                                                                                |
| STAG3   | 100%  | 100%  | 100% | 100%  | 99.3% | Spermatogenic failure 61, 619672;Premature ovarian failure 8, 615723                                                                                                                                                                                                                                                                        |
| SWSAP1  | 100%  | 100%  | 100% | 100%  | 99.1% |                                                                                                                                                                                                                                                                                                                                             |

|        |       |       |      |      |       |                                                                                                                                                                                                                                                                                                 |
|--------|-------|-------|------|------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SYCE1  | 100%  | 100%  | 100% | 100% | 99.3% | Premature ovarian failure 12, 616947;Spermatogenic failure 15, 616950                                                                                                                                                                                                                           |
| SYCP2L | 100%  | 100%  | 100% | 100% | 99.7% | Premature ovarian failure 24, 620840                                                                                                                                                                                                                                                            |
| TP63   | 100%  | 100%  | 100% | 100% | 99.6% | Premature ovarian failure 21, 620311;Ectrodactyly, ectodermal dysplasia, and cleft lip/palate syndrome 3, 604292;Hay-Wells syndrome, 106260;Split-hand/foot malformation 4, 605289;Orofacial cleft 8, 618149;Rapp-Hodgkin syndrome, 129400;ADULT syndrome, 103285;Limb-mammary syndrome, 603543 |
| TWINK  | 100%  | 100%  | 100% | 100% | 99.6% | Mitochondrial DNA depletion syndrome 7 (hepatocerebral type), 271245;Progressive external ophthalmoplegia with mitochondrial DNA deletions, autosomal dominant 3, 609286;Perrault syndrome 5, 616138                                                                                            |
| ZNF541 | 100%  | 100%  | 100% | 100% | 99.5% |                                                                                                                                                                                                                                                                                                 |
| ZSWIM7 | 91.9% | 85.2% | 100% | 100% | 99.6% | Spermatogenic failure 71, 619831;?Ovarian dysgenesis 10, 619834                                                                                                                                                                                                                                 |

Gene symbols used follow HGNC guidelines: Gray KA, Yates B, Seal RL, Wright MW, Bruford EA. Nucleic Acids Res. 2015 Jan 43(Database issue):D1079-85.

*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 mapped against GRCh38.*

*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 mapped against GRCh38.*

*srWGS 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 covered 15x describes the percentage of a gene's coding sequence that is covered at least 15x when analyzed by WGS mapped against GRCh38.*

*srWGS 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 : November 25th, 2024.*

*This list is accurate for panel version DG 5.1.0*

*Ad 1. Blank field signifies a gene without a current OMIM association Ad 2. OMIM phenotype descriptions between {} signify risk factors*