# Proactive Health Plus SINGLE-GENE RISK™ 151 GENES

## TEST CODE: PR21037

### Overview

MyOme Proactive Health Plus Single-Gene Risk™ report, 151 Genes uses a PCR-free whole-genome backbone that allows identification of a range of variant types. Whole-genome sequencing (WGS) allows MyOme to re-query a patient's genome as healthcare needs change and new information about the genome is discovered.

### Clinical Use

This test is intended for a wellness screening of germline heritable conditions in individuals from an asymptomatic population. MyOme annotates and interprets variants according to American College of Medical Genetics (ACMG) guidelines[1], and reports pathogenic or likely pathogenic variants. Genetic testing may provide information to assess individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy in conjunction with standard clinical assessment.

### Method

PCR-free library prep followed by 2x150 bp paired-end whole-genome sequencing is the backbone for this test. In-house pipeline analysis allows identification of single-nucleotide variants (SNVs), small insertions and deletions (indels) and copy number variants (CNVs). Variant interpretation is conducted by qualified scientists based on guidelines by the ACMG.

### Sample Types

- Blood (2 EDTA tubes)
- Saliva (2 tubes)
- Buccal (2 swabs)

### Turnaround Times

- From sample received, most results are delivered in 5-6 weeks.*
- Follow-up testing or re-requisitions are typically completed in under 2 weeks, often within just a few days.

### Included

- Analysis of SNVs, indels, and CNVs (deletions and duplications)
- Confirmation of Pathogenic/Likely Pathogenic variants by orthogonal method (e.g., Sanger sequencing)
- Cohesive report with actionable recommendations
- 151 genes included: *ABCD1, ACTA2, ACTC1, ACTN2, ACVRL1, APC, APOB, ATM, ATP7B, BAG3, BAP1, BARD1, BMPR1A, BMPR2, BRCA1, BRCA2, BRIP1, BTD, CACNA1C, CACNA1S, CALM1, CALM2, CALM3, CASQ2, CAV1, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2, COL3A1, COL5A1, COL5A2, CRYAB, CSRP3, DES, DICER1, DMD, DSC2, DSG2, DSP, EGFR, EMD, ENG, EPCAM, F2, F5, F9, FBN1, FH, FHL1, FLCN, FLNC, G6PD, GAA, GCH1, GDF2, GLA, GREM1, HAMP, HFE, HJV, HMBS, HNF1A, HNF1B, HOXB13, JUP, KCNE1, KCNH2, KCNJ2, KCNQ1, KIT, LAMP2, LDLR, LDLRAP1, LMNA, LZTR1, MAX, MEFV, MEN1, MET, MITF, MLH1, MSH2, MSH3, MSH6, MUTYH, MYBPC3, MYH11, MYH7, MYL2, MYL3, MYLK, NF1, NF2, NTHL1, OTC, PALB2, PCSK9, PDGFRA, PKP2, PLN, PMS2, POLD1, POLE, POT1, PRKAG2, PRKG1, PROC, PROS1, PTEN, RAD51C, RAD51D, RB1, RBM20, RET, RPE65, RYR1, RYR2, SCN5A, SDHAF2, SDHB, SDHC, SDHD, SERPINA1, SERPINC1, SLC40A1, SMAD3, SMAD4, SMAD9, STK11, TFR2, TGFB2, TGFB3, TGFBR1, TGFBR2, TMEM127, TMEM43, TNNC1, TNNI3, TNNT2, TP53, TPM1, TRDN, TSC1, TSC2, TTN, TTR, VCL, VHL, WT1*

### Test Performance[2]

- 30x average genome-wide coverage
- >99.5% of exonic regions at ≥10x depth
- >99.5% ClinVar P/LP variants covered by ≥10x depth
- >99% sensitivity for SNVs and indels
- 98% sensitivity for benchmark CNVs >1 kb in size

*Turnaround times are provided as estimates and begin once sample(s) are processed at MyOme. Turnaround times may be extended in cases outside of MyOme's control, including delays related to confirmation testing or other unforseen circumstances.

**1.** American College of Medical Genetics and Genomics. SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the ACMG. Genet Med. June22, 2023. doi: 10.1016/j.gim.2023.100866. **2.** MyOme Inc, Data on File

## CONDITION-GENE RELATIONSHIP

The genes listed below are analyzed in this report. MyOme selected them based on our Gene Inclusion Framework Guidelines. Genes are prioritized based on clinical validity, actionability, penetrance/prevalence, and feasibility.

| Cardiovascular | |
|---|---|
| **Condition** | **Gene(s)** |
| Arrhythmogenic right ventricular cardiomyopathy | *DES, DSC2, DSG2, DSP, JUP, PKP2, PLN, TMEM43* |
| Brugada syndrome | *SCN5A* |
| CACNA1C-related disorders | *CACNA1C* |
| Catecholaminergic polymorphic ventricular tachycardia | *CALM1, CALM2, CALM3, CASQ2, RYR2, TRDN* |
| Danon disease | *LAMP2* |
| Dilated cardiomyopathy | *ACTC1, BAG3, DES, FLNC, LMNA, MYH7, SCN5A, TNNC1, TNNI3, TNNT2, TPM1, TTN, VCL, RBM20* |
| Ehlers-Danlos syndrome, vascular type | *COL3A1* |
| Emery-Dreifuss muscular dystrophy | *EMD, FHL1, LMNA* |
| Fabry disease | *GLA* |
| Familial hypercholesterolemia | *APOB, LDLR, LDLRAP1, PCSK9* |
| Familial thoracic aortic aneurysm and dissection | *ACTA2, MYH11, MYLK, PRKG1, SMAD3, TGFB2, TGFB3* |
| Hereditary transthyretin-related amyloidosis | *TTR* |
| Hypertrophic cardiomyopathy | *ACTC1, CSRP3, MYBPC3, MYH7, MYL2, MYL3, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1* |
| Intrinsic Cardiomyopathy | *ACTN2, PLN* |
| Loeys-Dietz syndrome | *TGFB2, TGFB3, TGFBR1, TGFBR2, SMAD3* |
| Long QT syndrome | *CALM1, CALM2, CALM3, KCNH2, KCNQ1, SCN5A, TRDN* |
| Long QT syndrome, acquired | *KCNE1* |
| Marfan syndrome | *FBN1* |
| Myofibrillar myopathy | *BAG3, CRYAB, DES, FLNC* |
| Progressive muscular dystrophy | *DMD* |
| Short QT syndrome | *KCNH2, KCNJ2, KCNQ1* |

| Other | |
|---|---|
| **Condition** | **Gene(s)** |
| Acute intermittent porphyria | *HMBS* |
| Adrenoleukodystrophy | *ABCD1* |
| Alpha-1 antitrypsin defeciency | *SERPINA1* |
| Biotinidase deficiency | *BTD* |
| Ehlers-Danlos syndrome, classic type | *COL5A1, COL5A2* |
| Familial Mediterranean fever | *MEFV* |
| G6PD deficiency | *G6PD* |
| GTP cyclohydrolase I deficiency | *GCH1* |
| Hemophilia B | *F9* |
| Hereditary antithrombin deficiency | *SERPINC1* |
| Hereditary hemochromatosis | *HAMP, HFE, HJV, SLC40A1, TFR2* |
| Hereditary hemorrhagic telangiectasia | *ACVRL1, ENG, GDF2, SMAD4* |
| Hereditary thrombophilia due to congenital protein C deficiency | *PROC* |
| Hereditary thrombophilia due to congenital protein S deficiency | *PROS1* |
| Pompe disease | *GAA* |

| Other (Cont.) | |
|---|---|
| **Condition** | **Gene(s)** |
| Malignant hyperthemia | *CACNA1S, RYR1* |
| Monogenic diabetes | *HNF1A, HNF1B* |
| Ornithine transcarbamylase deficiency | *OTC* |
| Pompe disease | *GAA* |
| Pulmonary arterial hypertension | *BMPR2, CAV1,GDF2, SMAD9* |
| RPE65-related retinopathy | *RPE65* |
| Thrombophilia | *F2, F5* |
| Wilson disease | *ATP7B* |

| Cancer | |
|---|---|
| **Condition** | **Gene(s)** |
| BAP1-related tumor predisposition syndrome | *BAP1* |
| Birt-Hogg-Dube syndrome | *FLCN* |
| CDH1-related diffuse gastric and lobular breast cancer syndrome | *CDH1* |
| DICER1-related tumor predisposition | *DICER1* |
| Familial adenomatous polyposis | *APC, MSH3* |
| Familial ovarian cancer | *BRIP1, PALB2, RAD51C, RAD51D* |
| Gastrointestinal stromal tumor | *KIT, PDGFRA* |
| Hereditary breast cancer | *BARD1, ATM, CHEK2, PALB2* |
| Hereditary breast and ovarian cancer | *BRCA1, BRCA2* |
| Hereditary leiomyomatosis and renal cell cancer | *FH* |
| Hereditary Mixed Polyposis Syndrome (HMPS) | *GREM1* |
| Hereditary nonpolyposis colon cancer | *ATM* |
| Hereditary paraganglioma-pheochromocytoma syndrome | *MAX, SDHAF2, SDHB, SDHC, SDHD, TMEM127* |
| Juvenile polyposis syndrome | *BMPR1A* |
| Juvenile polyposis with hereditary hemorrhagic telangiectasia | *SMAD4* |
| Li-Fraumeni syndrome | *TP53* |
| Lynch syndrome | *EPCAM, MLH1, MSH2, MSH6,PMS2* |
| Melanoma | *CDK4 , MITF* |
| Melanoma-pancreatic cancer syndrome | *CDKN2A* |
| Multiple endocrine neoplasia | *CDKN1B, MEN1, RET* |
| MUTYH-associated polyposis | *MUTYH* |
| Neurofibromatosis type 1 | *NF1* |
| Neurofibromatosis type 2 | *NF2* |
| Non-small cell lung carcinoma | *EGFR* |
| NTHL1-deficiency tumor predisposition syndrome | *NTHL1* |
| Papillary renal cell carcinoma | *MET* |
| Peutz-Jeghers syndrome | *STK11* |
| Polyposis and colorectal cancer | *POLD1, POLE* |
| POT1 Tumor predisposition | *POT1* |
| Prostate cancer | *HOXB13* |
| PTEN hamartoma tumor syndrome | *PTEN* |
| Retinoblastoma | *RB1* |
| Schwannomatosis | *LZTR1* |
| Tuberous sclerosis complex | *TSC1, TSC2* |
| Von Hippel-Lindau syndrome | *VHL* |

 