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| --- | --- | --- | --- | --- | --- | --- |
| **Supplemental Table 1.** Actionable gene list | | | | | | |
|  | | **Phenotype** | | | **Gene/genes** | |
| **Cardiovascular** | | Ehlers-Danlos syndrome, vascular type | | | *COL3A1, COL5A1* | |
|  | | Marfan syndrome, Loeys-Dietz syndromes, familial thoracic aortic aneurysms & dissections | | | *FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH1, MYLK* | |
|  | | Hypertrophic cardiomyopathy | | | *MYBPC3, MYH7, TNNT2, TNNI3, TPM, MYL3, ACTC1, PRKAG2,*  *GLA* | |
|  | | Dilated cardiomyopathy | | | *MYL2, LMNA* | |
|  | | Catecholaminergic polymorphic ventricular tachycardia | | | *RYR2* | |
|  | | Arrhythmogenic right ventricular cardiomyopathy | | | *PKP2, DSP ,DSC2,*  *TMEM43, DSG2* | |
|  | | Romano-Ward long-QT syndrome types 1, 2, and 3, Brugada syndrome | | | *KCNQ1, KCNH2, SCN5A,*  *KCNJ2, KCNE1* | |
|  | | Familial hypercholesterolemia | | | *LDLR, APOB, PCSK9* | |
|  | | Diabetes | | | *HNF1A, HNF1B* | |
| **Cancer** | | Hereditary breast and ovarian cancer | | | *BRCA1, BRCA2,* | |
|  | | Li-Fraumeni syndrome | | | *TP53* | |
|  | | Peutz-Jeghers syndrome | | | *STK11* | |
|  | | Lynch syndrome | | | *MLH1, MSH2, MSH6,*  *PMS2, POLD1, POLE* | |
|  | | Familial adenomatous polyposis | | | *APC* | |
|  | | *MYH*-associated polyposis; adenomas, multiple colorectal, *FAP* type 2; colorectal adenomatous polyposis, autosomal recessive, with pilomatricomas | | | *MUTYH* | |
|  | | Juvenile polyposis | | | *BMPR1A, SMAD4* | |
|  | | Von Hippel–Lindau syndrome | | | *VHL* | |
|  | | Multiple endocrine neoplasia type 1 | | | *MEN1* | |
|  | | Multiple endocrine neoplasia type 2 | | | *RET* | |
|  | | Familial medullary thyroid cancerd | | | *RET* | |
|  | | *PTEN* hamartoma tumor syndrome | | | *PTEN* | |
|  | | Retinoblastoma | | | *RB1* | |
|  | | Hereditary paraganglioma-pheochromocytoma syndrome | | | *SDHD, SDHAF2,*  *SDHC, SDHB* | |
| **Other** | | Tuberous sclerosis complex | | | *TSC1, TSC2* | |
|  | | WT1-related Wilms tumor | | | *WT1* | |
|  | | Neurofibromatosis type 2 | | | *NF2* | |
|  | | Wilson disease | | | *ATP7B* | |
|  | | Ornithine transcarbamylase deficiency | | | *OTC* | |
|  | | Neuromuscular disorders | | | *RYR1, CACNA1A, CACNA1S* | |
| **Supplemental Table 2.** Consensus list of actionable single nucleotide variants | | | | | | |
| **rs#** | | **Gene** | | **Associated Disease** | **Disease Category** | |
| rs77931234 | | *ACADM* | | Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency | Inborn error of metabolism | |
| rs387906225 | | *ALDOB* | | Hereditary fructose intolerance | Inborn error of metabolism | |
| rs386834233 | | *BCKDHB* | | Maple syrup urine disease | Inborn error of metabolism | |
| rs79761867 | | *BCKDHB* | | Maple syrup urine disease | Inborn error of metabolism | |
| rs80338898 | | *FAH* | | Tyrosinemia type I | Inborn error of metabolism | |
| rs1801175 | | *G6PC* | | Glycogen storage disease type I | Inborn error of metabolism | |
| rs397509431 | | *CPT2* | | Carnitine palmitoyltransferase II (CPT II) deficiency | Inborn error of metabolism | |
| rs113993962 | | *BLM* | | Bloom Syndrome | Cancer susceptibility | |
| rs193922376 | | *MSH2* | | Lynch syndrome# | Cancer susceptibility | |
| rs6467 | | *CYP21A2* | | 21-hydroxylase deficiency | Endocrinology | |
| rs6025 | | *F5* | | factor V Leiden thrombophilia\* | Thrombophilia | |
| rs1800562 | | *HFE* | | Hereditary hemochromatosis | Iron storage | |
| rs28940579 | | *MEFV* | | Familial Mediterranean fever | Inflammatory | |
| rs61752717 | | *MEFV* | | Familial Mediterranean fever | Inflammatory | |

Only bi-allelic (homozygous, or if applicable compound heterozygous) variants will be returned.

Mode of inheritance is autosomal recessive except #=autosomal dominant and \*=risk increased.