SUDCRRC
SUDC Registry and Research Collaborative

## ACMG GENE LIST FOR SECONDARY/UNRELATED FINDINGS

As of March 2013 (V1.0) (updated 2016 (V2.0), 2021 (V3.0), and 2022 (V3.1)) the American College of Medical Genetics and Genomics (ACMG) specifically recommends minimum evaluation, in the context of exome/genome sequencing, for the following list of 78 specific genes for 38 diseases/disorders in which findings would have actionable medical benefit for the patients and families of patients. These genes include some cancer or tumor syndromes, some connective tissue diseases, cardiomyopathies, and arrhythmias. Some of these conditions have onset in adulthood and an individual may not have recognizable features now. These disorders were selected because there may be changes in medical management for an individual if the individual is known to have a genetic susceptibility to oneor more of these disorders. Details regarding individual genes on this list will be provided to you upon request.

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|---|---|
| Hereditary breast and ovarian cancer | *BRCA1, BRCA2, PALB2* |
| Li-Fraumeni syndrome | *TP53* |
| Familial adenomatous polyposis | *APC* |
| Peutz-Jeghers syndrome | *STK11* |
| Lynch syndrome | *MLH1, MSH2, MSH6, PMS2* |
| *MUTYH*-associated polyposis | *MUTYH* (2 variants) |
| Juvenile polyposis syndrome | *BMPR1A, SMAD4* |
| von Hippel-Lindau syndrome | *VHL* |
| Multiple endocrine neoplasia type 1 | *MEN1* |
| Multiple endocrine neoplasia type 2 | *RET* |
| *PTEN* hamartoma tumor syndrome | *PTEN* |
| Retinoblastoma | *RB1* |
| Hereditary paraganglioma-pheochromocytomasyndrome | *SDHD, SDHAF2, SDHC, SDHB, MAX, TMEM127* |
| Tuberous sclerosis complex | *TSC1, TSC2* |
| *WT1*-related Wilms tumor | *WT1* |
| Neurofibromatosis type 2 | *NF2* |
| Ehlers Danlos syndrome, vascular type | *COL3A1* |
| Familial thoracic aortic aneurysm | *ACTA2, MYH11* |
| Marfan syndrome | *FBN1* |
| Loeys-Dietz syndrome | *TGFBR1, TGFBR2, SMAD3* |

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|---|---|
| Dilated cardiomyopathy | *TNNT2, LMNA, FLNC, TTN* (only loss-of-function variants), *BAG3, DES, RBM20, TNNC1* |
| Hypertrophic cardiomyopathy | *MYH7, MYBPC3, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, MYL2* |
| Catecholaminergic polymorphic ventricular tachycardia | *RYR2, CASQ2* (2 variants), *TRDN* (2 variants) |
| Arrhythmogenic right ventricular cardiomyopathy | *PKP2, DSP, DSC2, TMEM43, DSG2* |
| Long QT syndrome | *KCNQ1, KCNH2* |
| Long QT syndrome; Brugada sydnrome; dilatedcardiomyopathy | *SCN5A* |
| Familial hypercholesterolemia | *LDLR, APOB, PCSK9* |
| Biotinidase deficiency | *BTD* (2 variants) |
| Fabry disease | *GLA* (all hemizygous, heterozygous homozygous) |
| Ornithine transcarbamylase deficiency | *OTC* (all hemizygous, heterozygous, homozygous) |
| Pompe disease | *GAA* (2 variants) |
| Hereditary hemochromatosis | *HFE* (p.Cys282Try homozygotes only) |
| Hereditary hemorrhagic telangiectasia | *ACVRL1, ENG* |
| *RPE65*-related retinopathy | *RPE65* (2 variants) |
| Maturity-onset diabetes of the young | *HNF1A* |
| Wilson disease | *ATP7B* (2 variants) |
| Malignant hyperthermia susceptibility | *RYR1, CACNA1S* |
| Hereditary TTR amyloidosis | *TTR* |

If a genetic change is identified in one of these genes, further testing for that specific gene maybe recommended. The absence of a reportable finding in these genes does not mean that an individual has no disease-causing changes in these genes, so future testing if the individual hassymptoms or features of one of the conditions caused by these genes should be considered.
Coverage of these genes through whole exome sequencing may not be as comprehensive as inpanels specifically designed to investigate them.