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A Future Where Precision Medicine is the Standard

Medically Actionable Variant Screening

Alamya Health, PBC
411 Lake Branch Road
Clever, MO 65631 USA

Alamya Health, PTE Ltd
No. 8 Burn Road
#04-04 Trivex
Singapore 369977

Medically Actionable Variants

Background

The American College of Medical Genetics and Genomics has curated a set of genes for which detection of a genetic change (aka pathogenic or likely pathogenic variant [previously referred to as mutation]) associated with a disorder can inform health management strategies through surveillance or intervention (see reference section below). If a genetic variant in this list is detected in your test, this could indicate that you have a health disorder though you may not be experiencing any symptoms. Alternatively, it could indicate that you have an increased chance (i.e. predisposition) to develop the health disorder. In these situations, your healthcare provider can organize additional testing and/or management.

The following table lists these 81 genes along with the names of the disorders associated with pathogenic or likely pathogenic variants in these genes. These genetic variants may be referred to as secondary findings in your report since they are often not the primary reason for having genetic testing. The OMIM number for each disorder is also listed in the table. OMIM - Online Mendelian Inheritance in Man - is an online encyclopedia of genetic disorders. It can be accessed at OMIM. This open resource provides additional genetic and clinical information.

The Alamya Health team updates this list in accordance with the published listing from the American College of Medical Genetics and Genomics. Relevant resources and references will be provided for positive test findings.

Limitations

Detection, interpretation, and reporting of genetic variation associated with diseases are subject to several limitations. The interpretation of the testing results relies on current knowledge of the genetic basis of each of these disorders. This knowledge is constantly changing. There is a chance that a positive test result (i.e., your testing identifies a genetic change in one of the genes in this listing) is not associated with an identifiable health concern on follow up investigation. This situation can cause increased anxiety. There is also a chance that a person with one of the disorders in this listing might not be identified by the testing used. This can be related to the ancestry of the individual who is tested as well as limitations of the sequencing technology and interpretation parameters that are used. Additionally, genetic predispositions to disease remain to be discovered and consequently have not yet been curated as a cause of a disorder.

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MEDICALLY ACTIONABLE VARIANT SCREENING

Gene Symbol	Disease	OMIM Number
	CANCER DISORDERS	
APC	Familial adenomatous polyposis	175100
RET	Familial medullary thyroid cancer/multiple endocrine neoplasia 2	155240 / 171400 / 162300
BRCA1, BRCA2, PALB2	Hereditary breast and/or ovarian cancer	604370 / 612555 / 114480
SDHD, SDHAF2, SDHC, SDHB, MAX, TMEM127	Hereditary paraganglioma-pheochromocytoma	168000 / 601650 / 605373 / 115310 / 171300 / 171300
BMPR1A	Juvenile polyposis syndrome	174900
SMAD4	Juvenile polyposis syndrome/hereditary hemorrhagic telangiectasia syndrome	175050
TP53	Li-Fraumeni syndrome	151623
MLH1, MSH2, MSH6, PMS2	Lynch syndrome (hereditary nonpolyposis colorectal cancer)	609310 / 120435 / 614350 / 614337
MEN1	Multiple endocrine neoplasia type 1	131100
MUTYH	MUTYH-associated polyposis	608456
NF2	NF2-related schwannomatosis	101000
STK11	Peutz-Jeghers syndrome	175200
PTEN	PTEN hamartoma tumor syndrome	158350
RB1	Retinoblastoma	180200
TSC1, TSC2	Tuberous sclerosis complex	191100 / 613254
VHL	von Hippel-Lindau syndrome	193300
WT1	WT1-related Wilms tumor	194070
	CARDIOVASCULAR DISORDERS	
FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH11	Aortopathies	154700 / 609192 / 610168 / 613795 / 611788 / 132900
PKP2, DSP, DSC2, TMEM43, DSG2	Arrhythmogenic right ventricular cardiomyopathy (a subcategory of arrhythmogenic cardiomyopathy)	609040 / 607450 / 610476 / 604400 / 610193
RYR2, CASQ2, TRDN	Catecholaminergic polymorphic ventricular tachycardia	604772 / 611938 / 615441
TNNT2, LMNA, FLNC, TTN, BAG3, DES, RBM20, TNNC1	Dilated cardiomyopathy	601494 / 115200 / 617047 / 604145 / 613881 / 604765 / 613172 / 611879
COL3A1	Ehlers-Danlos syndrome, vascular type	130050
LDLR, APOB, PCSK9	Familial hypercholesterolemia	143890 / 144010 / 603776
MYH7, MYBPC3, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, MYL2	Hypertrophic cardiomyopathy	192600 / 115197 / 613690 / 115196 / 608751 / 612098 / 600858 / 608758
KCNQ1, KCNH2	Long QT syndrome types 1 and 2	192500 / 613688
SCN5A	Long QT syndrome 3; Brugada syndrome	603830 / 601144
CALM1, CALM2, CALM3	Long QT syndrome types 14-16	616247 / 616249 / 618782
	INBORN ERRORS OF METABOLISM DISORDERS	
BTD	Biotinidase deficiency	253260
GLA	Fabry disease	301500
OTC	Ornithine transcarbamylase deficiency	311250
GAA	Pompe disease	232300

Gene Symbol	Disease	OMIM Number
	MISCELLANEOUS DISORDERS	
HFE	Hereditary hemochromatosis	235200
ACVRL1, ENG	Hereditary hemorrhagic telangiectasia	600376 / 187300
RYR1, CACNA1S	Malignant hyperthermia	145600 / 601887
HNF1A	Maturity-onset of diabetes of the young	600496
RPE65	RPE65-related retinopathy	204100 / 613794
ATP7B	Wilson disease	277900
TTR	Hereditary TTR amyloidosis	105210

References

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