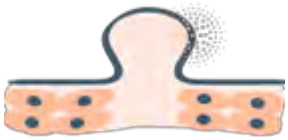
ACMG Actionable Diseases

Precision Panel



Overview

The American College of Medical Genetics and Genomics (ACMG) Actionable Diseases Gene Panel shows a comprehensive selection of genes by ACMG. Mutations in these genes lead to disorders that have been scientifically proven to be actionable, meaning that early intervention improves prognosis, life expectancy, quality of life and overall well-being. Early identification before the onset of manifestations allows the prevention of symptoms thus initiating prompt multidisciplinary treatment. The main goal is to report the known or expected pathogenic variants in these genes while performing exome and genome sequencing, even if those are unrelated to the primary medical reason for testing.

The Igenomix ACMG Actionable Disorders Precision Panel can be used to identify those genes and perform a screening, whether the patient shows symptoms or not, to locate mutations and start an early treatment.

Indications

The Igenomix ACMG Actionable Disorders Precision Panel is indicated as a screening and diagnostic test in those cases where there are:

- Family history of cancer or cardiomyopathy
- Multiple relatives on the same side of the family with any form of cancer or cardiomyopathy.
- Asymptomatic patients who wish to check the chance of developing any of the reported diseases.

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.
- Early initiation of multidisciplinary treatment including lifestyle modifications, early surveillance from malignancy, regular follow up with a specialist, and medical or surgical care if needed.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Family planning for adequate reproductive decisions, using available assisted reproduction technology.

Genes & Diseases

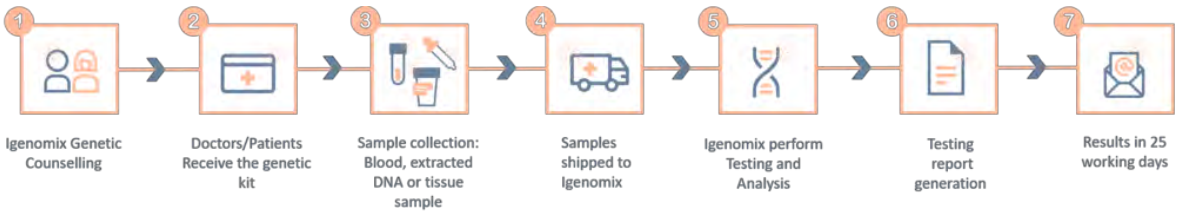
GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
ACTA2	Aortic Aneurysm, Moyamoya Disease, Multisystemic Smooth Muscle Dysfunction Syndrome	AD	100	88 of 88
ACTC1	Atrial Septal Defect, Cardiomyopathy	AD	99.93	72 of 74
APC	Desmoid Disease, Familial Adenomatous Polyposis, Hepatocellular Carcinoma, Cenani-Lenz Syndrome, Gardner Syndrome, Turcot Syndrome, Colorectal Cancer, Gastric Cancer	AD	98.92	1846 of 1882
APOB	Hypercholesterolemia, Hypobetalipoproteinemia	AD,AR	99.62	369 of 375
ATP7B	Wilson Disease	AR	99.97	989 of 1000
BMPR1A	Polyposis Syndrome, Familial Colorectal Cancer, Hereditary Mixed Polyposis Syndrome	AD	100	124 of 127
BRCA1	Breast And Ovarian Cancer, Fanconi Anemia, Familial Pancreatic Carcinoma, Peritoneal Carcinoma	AD,AR,MU	98.97	2783 of 2894
BRCA2	Breast And Ovarian Cancer, Fanconi Anemia, Glioma, Medulloblastoma, Pancreatic Cancer, Prostate Cancer, Wilms Tumor, Nephroblastoma	AD,AR,MU	98.51	3343 of 3451
CACNA1S	Hypokalemic Periodic Paralysis, Malignant Hyperthermia, Thyrotoxic Periodic Paralysis	AD	100	64 of 64
COL3A1	Ehlers-Danlos Syndrome, Polymicrogyria, Acrogeria, Cerebral Saccular Aneurysm	AD,AR	100	676 of 676
DSC2	Arrhythmogenic Right Ventricular Dysplasia	AD,AR	100	123 of 124
DSG2	Arrhythmogenic Right Ventricular Dysplasia, Cardiomyopathy	AD	99.38	167 of 169
DSP	Arrhythmogenic Right Ventricular Dysplasia, Cardiomyopathy, Epidermolysis Bullosa, Skin Fragility-Woolly Hair Syndrome, Carvajal Syndrome, Idiopathic Pulmonary Fibrosis, Palmoplantar Keratoderma	AD,AR	99.91	366 of 369
FBN1	Acromicric Dysplasia, Ectopia Lentis, Geleophysic Dysplasia, Marfan Syndrome, Mass Syndrome, Stiff Skin Syndrome, Weill-Marchesani Syndrome, Familial Thoracic Aortic Aneurysm, Aortic Dissection, Glaucoma, Microspherophakia, Shprintzen-Goldberg Syndrome	AD	100	2836 of 2845
GLA	Fabry Disease	X,XR,G	98	-
KCNH2	Long Qt Syndrome, Short Qt Syndrome, Romano-Ward Syndrome	AD	98.69	908 of 930
KCNQ1	Atrial Fibrillation, Beckwith-Wiedemann Syndrome, Jervell And Lange-Nielsen Syndrome, Long Qt Syndrome, Short Qt Syndrome, Romano-Ward Syndrome	AD,AR	93.23	600 of 624
LDLR	Hypercholesterolemia	AD	99.89	1921 of 1996
LMNA	Cardiomyopathy, Charcot-Marie-Tooth Disease, Emery-Dreifuss Muscular Dystrophy, Heart-Hand Syndrome, Hutchinson-Gilford Progeria Syndrome, Lipodystrophy, Malouf Syndrome, Mandibuloacral Dysplasia, Werner Syndrome, Laminopathy, Hypergonadotropic Hypogonadism	AD,AR	100	619 of 620

MEN1	Endocrine Neoplasia, Hyperparathyroidism, Insulinoma, Pituitary Gigantism, Prolactinoma	AD	99.9	871 of 876
MLH1	Colorectal Cancer, Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome, Lynch Syndrome	AD,AR	99.94	1079 of 1118
MSH2	Lynch Syndrome, Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome	AD,AR	99.99	1032 of 1057
MSH6	Colorectal Cancer, Hereditary Nonpolyposis, Endometrial Carcinoma, Mismatch Repair Cancer Syndrome, Lynch Syndrome , Muir-Torre Syndrome	AD,AR	99.28	613 of 641
MUTYH	Adenomatous Polyposis, Gastric Cancer	AR	100	183 of 183
MYBPC3	Cardiomyopathy, Left Ventricular Noncompaction	AD,AR	99.95	1072 of 1079
MYH11	Aortic Aneurysm, Thoracic Aortic Aneurysm, Aortic Dissection, Megacystis, Microcolon, Intestinal Hypoperistalsis Syndrome	AD	100	67 of 67
MYH7	Myopathy, Ebstein Malformation	AD,AR	99.95	1053 of 1054
MYL2	Cardiomyopathy	AD	100	67 of 67
MYL3	Cardiomyopathy	AD,AR	100	42 of 42
NF2	Meningioma, Neurofibromatosis, Schwannomatosis	AD	100	359 of 362
OTC	Hyperammonemia, Ornithine Transcarbamylase Deficiency	X,XR,G	99.97	-
PCSK9	Hypercholesterolemia	AD	100	96 of 98
PKP2	Arrhythmogenic Right Ventricular Dysplasia, Brugada Syndrome	AD	100	306 of 307
PMS2	Colorectal Cancer, Mismatch Repair Cancer Syndrome, Lynch Syndrome	AD,AR	97.17	264 of 285
PRKAG2	Cardiomyopathy, Glycogen Storage Disease Of Heart, Wolff-Parkinson-White Syndrome	AD	99.98	61 of 61
PTEN	Cowden Disease, Macrocephaly, Autism Spectrum Disease, Meningioma, Prostate Cancer, Bannayan-Riley-Ruvalcaba Syndrome, Breast And Ovarian Cancer, Juvenile Polyposis Of Infancy, Lhermitte-Duclos Disease, Proteus Syndrome, Segmental Outgrowth, Lipomatosis, Arteriovenous Malformation, Epidermal Nevus	AD	99.97	609 of 629
RB1	Bladder Cancer, Osteosarcoma, Retinoblastoma, Small Cell Cancer Of The Lung, Monosomy 13q14	AD	99.41	941 of 995
RET	Hirschsprung Disease, Multiple Endocrine Neoplasia, Pheochromocytoma, Thyroid Carcinoma, Haddad Syndrome, Pheochromocytoma-Paraganglioma, Renal Agenesis	AD	100	453 of 454
RYR1	Central Core Disease Of Muscle, Malignant Hyperthermia, Minicore Myopathy, External Ophthalmoplegia	AD,AR	97.63	733 of 746
RYR2	Arrhythmogenic Right Ventricular Dysplasia, Ventricular Tachycardia, Dilated Cardiomyopathy	AD	99.2	466 of 472
SCN5A	Atrial Fibrillation, Brugada Syndrome, Cardiomyopathy, Long Qt Syndrome, Progressive Familial Heart Block, Sick Sinus Syndrome, Sudden Infant Death Syndrome, Ventricular Fibrillation, Romano-Ward Syndrome	AD,AR,MU	99.45	929 of 942
SDHAF2	Paraganglioma, Pheochromocytoma	AD	96.78	8 of 8
SDHB	Carney-Stratakis Syndrome, Gastrointestinal Stromal Tumor, Paraganglioma, Pheochromocytoma, Cowden Syndrome, Succinate-Coq Reductase Deficiency	AD	100	261 of 264
SDHC	Carney-Stratakis Syndrome, Gastrointestinal Stromal Tumor, Paraganglioma, Cowden Syndrome, Pheochromocytoma	AD	99.95	62 of 63
SDHD	Carney-Stratakis Syndrome, Mitochondrial Complex Ii Deficiency, Paraganglioma, Pheochromocytoma, Carcinoid Syndrome, Cowden Syndrome, Succinate-Coq Reductase Deficiency	AD,AR	99.98	164 of 166
SMAD3	Loeys-Dietz Syndrome, Aneurysm-Osteoarthritis Syndrome, Thoracic Aortic Aneurysm, Aortic Dissection	AD	100	128 of 128
SMAD4	Polyposis Syndrome, Myhre Syndrome, Pancreatic Cancer, Thoracic Aortic Aneurysm, Aortic Dissection, Hemorrhagic Telangiectasia	AD	99.56	136 of 136
STK11	Pancreatic Cancer, Peutz-Jeghers Syndrome, Testicular Tumor	AD	81.99	456 of 470
TGFBR1	Loeys-Dietz Syndrome, Self-Healing Squamous Epithelioma, Thoracic Aortic Aneurysm, Aortic Dissection	AD	94	96 of 100
TGFBR2	Colorectal Cancer, Esophageal Cancer, Loeys-Dietz Syndrome, Thoracic Aortic Aneurysm, Aortic Dissection, Lynch Syndrome	AD	99.9	165 of 166
TMEM43	Arrhythmogenic Right Ventricular Dysplasia, Emery-Dreifuss Muscular Dystrophy	AD	99.98	26 of 26

TNNI3	Cardiomyopathy	AD,AR	100	139 of 139
TNNT2	Cardiomyopathy	AD	100	169 of 169
TP53	Adrenocortical Carcinoma, Osteosarcoma, Li-Fraumeni Syndrome, Basal Cell Carcinoma, Bone Marrow Failure Syndrome, Glioma Susceptibility, Papilloma Of Choroid Plexus, Thrombocythemia	AD,MU,P	98.92	557 of 563
TPM1	Cardiomyopathy	AD	100	108 of 108
TSC1	Focal Cortical Dysplasia Of Taylor, Lymphangioleiomyomatosis, Tuberous Sclerosis	AD	99.86	390 of 406
TSC2	Focal Cortical Dysplasia Of Taylor, Lymphangioleiomyomatosis, Tuberous Sclerosis	AD	100	1157 of 1159
VHL	Erythrocytosis, Pheochromocytoma, Renal Cell Carcinoma, Von Hippel-Lindau Syndrome, Paraganglioma	AD,AR	100	511 of 544
WT1	Aniridia, Denys-Drash Syndrome, Frasier Syndrome, Mesothelioma, Nephrotic Syndrome, Wilms Tumor, Gonadal Dysgenesis, Meacham Syndrome, Nephroblastoma, Wagr Syndrome	AD	98.92	178 of 185

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



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References

1. Kalia, S., Adelman, K., Bale, S. et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. Genet Med 19, 249–255 (2017).
2. Green, R., Berg, J., Grody, W. et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med 15, 565–574 (2013)
3. ACMG Board of Directors. ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. Genet Med 17, 68–69 (2015)