

Supplementary Material

Supplementary Table 1. eMERGEseq consensus gene list		
Category	Phenotype	Gene/genes
Cardiovascular	Ehlers-Danlos syndrome, vascular type	<i>COL3A1, COL5A1</i>
	Marfan syndrome, Loeys-Dietz syndromes, and familial thoracic aortic aneurysms and dissections	<i>FBNI, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH1, MYLK</i>
	Hypertrophic cardiomyopathy	<i>MYBPC3, MYH7, TNNT2, TNNI3, TPM, MYL3, ACTC1, PRKAG2, GLA</i>
	Dilated cardiomyopathy	<i>MYL2, LMNA</i>
	Catecholaminergic polymorphic ventricular tachycardia	<i>RYR2</i>
	Arrhythmogenic right ventricular cardiomyopathy	<i>PKP2, DSP, DSC2, TMEM43, DSG2</i>
	Romano-Ward long-QT syndrome types 1, 2, and 3, Brugada syndrome	<i>KCNQ1, KCNH2, SCN5A, KCNJ2, KCNE1</i>
	Familial hypercholesterolemia	<i>LDLR, APOB, PCSK9</i>
	Diabetes	<i>HNF1A, HNF1B</i>
	Cancer	Hereditary breast and ovarian cancer
Li-Fraumeni syndrome		<i>TP53</i>
Peutz-Jeghers syndrome		<i>STK11</i>
Lynch syndrome		<i>MLH1, MSH2, MSH6, PMS2, POLD1, POLE</i>
Familial adenomatous polyposis		<i>APC</i>
<i>MYH</i> -associated polyposis; adenomas, multiple colorectal, <i>FAP</i> type 2; colorectal adenomatous polyposis, autosomal recessive, with pilomatricomas		<i>MUTYH</i>
Juvenile polyposis		<i>BMPRIA, SMAD4</i>
Von Hippel–Lindau syndrome		<i>VHL</i>
Multiple endocrine neoplasia type 1		<i>MEN1</i>
Multiple endocrine neoplasia type 2		<i>RET</i>
Familial medullary thyroid cancer ^d		<i>RET</i>
<i>PTEN</i> hamartoma tumor syndrome		<i>PTEN</i>
Retinoblastoma		<i>RBI</i>
Hereditary paraganglioma-pheochromocytoma syndrome	<i>SDHD, SDHAF2, SDHC, SDHB</i>	
Other	Tuberous sclerosis complex	<i>TSC1, TSC2</i>

	WT1-related Wilms tumor	<i>WT1</i>
	Neurofibromatosis type 2	<i>NF2</i>
	Wilson disease	<i>ATP7B</i>
	Ornithine transcarbamylase deficiency	<i>OTC</i>
	Neuromuscular disorders	<i>RYR1, CACNA1A, CACNAIS</i>

Supplementary Table 2. Consensus list of actionable single nucleotide variants to be returned.

rs#	Gene	Associated Disease	Disease Category
rs77931234	<i>ACADM</i>	Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency	Inborn error of metabolism
rs387906225	<i>ALDOB</i>	Hereditary fructose intolerance	Inborn error of metabolism
rs386834233	<i>BCKDHB</i>	Maple syrup urine disease	Inborn error of metabolism
rs79761867	<i>BCKDHB</i>	Maple syrup urine disease	Inborn error of metabolism
rs80338898	<i>FAH</i>	Tyrosinemia type I	Inborn error of metabolism
rs1801175	<i>G6PC</i>	Glycogen storage disease type I	Inborn error of metabolism
rs397509431	<i>CPT2</i>	Carnitine palmitoyltransferase II (CPT II) deficiency	Inborn error of metabolism
rs113993962	<i>BLM</i>	Bloom Syndrome	Cancer susceptibility
rs193922376	<i>MSH2</i>	Lynch syndrome [#]	Cancer susceptibility
rs6467	<i>CYP21A2</i>	21-hydroxylase deficiency	Endocrinology
rs6025	<i>F5</i>	factor V Leiden thrombophilia [*]	Thrombophilia
rs1800562	<i>HFE</i>	Hereditary hemochromatosis	Iron storage
rs28940579	<i>MEFV</i>	Familial Mediterranean fever	Inflammatory
rs61752717	<i>MEFV</i>	Familial Mediterranean fever	Inflammatory

Only bi-allelic (homozygous, or if applicable compound heterozygous) variants were returned. Mode of inheritance is autosomal recessive except [#]=autosomal dominant and ^{*}=risk increased.