SUPPLEMENTAL MATERIAL

Supplemental Tables

Supplemental Table 1. Genes analyzed for variants for cardiomyopathies and ion channel disorders associated with T-wave inversion

Condition	Priority Genes Tested*	Other Candidate Genes Tested*
HCM	ACTC1, DES, FLNC, GLA, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PLN, PRKAG2, PTPN11, TNNC1, TNNI3, TNNT2, TPM1, TTR	AARS2, ACAD9, ACADVL, ACTA1, ACTN2, AGK, AGL, AGPAT2, ANK2, ANKRD1, ATP5E, ATPAF2, BRAF, BSCL2, CALR3, CAV3, COA5, COA6, COQ2, COX15, COX6B1, CRYAB, CSRP3, DLD, DSP, ELAC2, FAH, FHL1, FHL2, FHOD3, FOXRED1, FXN, GAA, GFM1, GLB1, GNPTAB, GUSB, HRAS, JPH2, KRAS, LDB3, LIAS, LZTR1, MAP2K1, MAP2K2, MLYCD, MRPL3, MRPL44, MRPS22, MTO1, MYH6, MYOM1, MYOZ2, MYPN, NEXN, NF1, NRAS, OBSCN, PDHA1, PHKA1, PMM2, RAF1, SCO2, SHOC2, SLC22A5, SLC25A3, SLC25A4, SOS1, SURF1, TAZ, TCAP, TMEM70, TRIM63, TSFM, TTN, VCL, BAG3, CASQ2, IDH2, KCNJ8, KLF10, LMNA, MURC, MYLK2, OBSL1, PDLIM3
ARVC	DSC2, DSG2, DSP, FLNC, JUP, PKP2, PLN, TMEM43	CTNNA3, DES, LMNA, RYR2, TGFB3, TTN, CASQ2, CTNNB1, LDB3, PERP, PKP4, PPP1R13L, SCN5A
DCM	ACTC1, BAG3, DES,	ABCC9, ACTA1, ACTN2, ALMS1, ANKRD1, ANO5,

	DMD, DSP, FLNC, LMNA, MYBPC3, MYH7, PKP2, PLN, RBM20, TAZ, TNNC1, TNNI3, TNNT2, TPM1, TTN	CAV3, CHRM2, COL741, CRYAB, CSRP3, DNAJC19, DOLK, DSC2, DSG2, EMD, EYA4, FHL2, FHOD3, FKRP, FKTN, FOXD4, GAA, GATA4, GATA6, GATAD1, GLB1, HFE, JUP, LAMA2, LAMA4, LAMP2, LDB3, MURC, MYH6, MYL2, MYL3, MYOT, MYPN, NEBL, NEXN, PRDM16, PSEN1, PSEN2, RAF1, RYR2, SCN5A, SDHA, SGCD, SLC22A5, SPEG, SYNE1, SYNE2, TBX20, TCAP, TMEM43, TMPO, TOR1AIP1, TTR, TXNRD2, VCL, XK, BRAF, DNM1L, GATA5, GLA, IDH2, ILK, KCNJ2, KCNJ8, NKX2-5, OBSCN, OPA3, PDLIM3, PTPN11, SGCA, SGCB, TNNI3K
LVNC	ACTC1, MYBPC3, MYH7, TAZ	ACTN2, DMD, DNAJC19, DTNA, FHL1, HCN4, LDB3, LMNA, MIB1, MYH6, MYL2, NKX2-5, NNT, PLN, PRDM16, RYR2, TNNT2, TPM1, ANKRD1, BAG3, CASQ2, CSRP3, DSP, FLNC, KCNH2, KCNQ1, MLYCD, MYL3, NOTCH1, PTPN11, TNNC1, TNNI3, TTN
LQTS	CACNA1C, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, SCN5A	AKAP9, ANK2, CALM1, CALM2, CALM3, CAV3, KCND2, KCNJ5, RYR2, SCN4B, SNTA1, TRDN, FHL2, HCN4, KCNA5, KCND3, KCNE5, KCNE3, NOS1AP, PTRF, SCN1B

BrS	SCN5A, CACNA1C, CACNA2D1, CACNB2, KCNJ8, SCN1B	SCN10A, ABCC9, ANK2, FGF12, GPD1L, HCN4, KCND2, KCND3, KCNE5, KCNE3, PKP2, RANGRF, SCN2B, SCN3B, SLMAP, TRPM4, ANK3, CACNA1D, KCNH2

ARVC indicates arrhythmogenic right ventricular cardiomyopathy; BrS, Brugada syndrome; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome; LVNC, left ventricular non-compaction.

*For full, official gene names, the reader is referred to the US National Center for Biotechnology Information (NCBI) online searchable database at https://www.ncbi.nlm.nih.gov/gene/

Supplemental Table 2. Summary of criteria used to determine variant pathogenicity

CLASSIFICATION	MAJOR CRITERIA	SUPPORTING CRITERIA
1. PATHOGENIC OR DISEASE CAUSING	1. Widely reported variant with conclusive evidence of a genotype-phenotype association and with consensus about its pathogenicity 2. Demonstrated co-segregation with a phenotype (>10 meioses) 3. Co-segregation in at least 2 families (≤10 meioses), or present in at least 5 probands with the same phenotype, and meeting at least 2 supporting criteria	1. Protein-truncating variant in a gene where loss of function is a proven pathogenic mechanism 2. Functional studies that support pathogenicity 3. *De novo* presentation in the setting of a novel disease in the family (maternity and paternity confirmed) 4. Missense variant that generates the same amino-acid change as a previously reported pathogenic variant 5. Variant with very low frequency/absent in the control population (MAF <0.001%)
2. VERY LIKELY TO BE PATHOGENIC OR DISEASE	1. Protein-truncating variant in a gene where loss of function is a proven pathogenic mechanism that explains the patient's phenotype, and that meets at least 1 supporting criterion	1. Functional studies that support pathogenicity 2. *De novo* presentation in the setting of a novel disease in the family (maternity and paternity confirmed) 3. Affecting a residue in which other pathogenic variants

CAUSING	2. Missense variant/in-frame insertion or deletion in a non-repetitive region of a gene with demonstrated genotype-phenotype association that explains the patient's disease, and that meets at least 2 supporting criteria	were previously identified. (mutational hot spot); or variant located in a relevant functional domain or region of the protein 4. Variant with very low allelic frequency/absent in the control population (MAF <0.001%) 5. Probable co-segregation in at least one family, or various index cases, but that does not meet criteria for being considered pathogenic
3. LIKELY TO BE PATHOGENIC OR DISEASE CAUSING	1. Protein-truncating variant with very low frequency or absent in the control population (MAF <0.001%) that affects a gene where loss of function is not an established pathogenic mechanism or that does not meet criteria to be considered pathogenic 2. Intronic variant outside the consensus region of the gene for which the bioinformatics predictors agree that	1. Variant with very low allelic frequency/absent in the control population (MAF <0.001%) 2. *De novo* presentation in the setting of a novel disease in the family (maternity and paternity unconfirmed) 3. Patient's phenotype or family history suggests that disease could be explained by mutations in the gene (gene with well-established phenotype-genotype

	it would affect the splicing 3. Missense variant/in-frame insertion or deletion in a non-repetitive region of a gene which does not meet criteria to be considered pathogenic/very likely to be pathogenic, but that meets at least 3 supporting criteria	association) 4. Bioinformatics predictors agree that it would be deleterious 5. Located in a mutational hot-spot, functional domain, or relevant region of the codified protein 6. Reported in at least 2 unrelated individuals that presented the same phenotype
4. UNKNOWN CLINICAL SIGNIFICANCE	1. Variants with contradictory information about their pathogenicity 2. Variants that do not meet criteria for being included in another classification category	
5. UNLIKELY TO BE PATHOGENIC OR DISEASE	1. Variant allele frequency in control populations is higher than the expected for disease or has a MAF >0.05% 2. Absence of variant co-segregation with the phenotype in at least 1 family	1. Missense variant in a gene where only variants causing protein truncation have shown association with disease 2. Functional study showing that the variant does not

CAUSING	3. Meeting at least 2 supporting criteria	affect the structure or function of the encoded protein 3. Bioinformatics predictors agree that the variant would not alter the function of the protein (including splicing variants outside the consensus region of the gene) 4. In-frame insertions/deletions in a repetitive gene region without a known function 5. Presence of the variant in homozygosis in control population
NON-PATHOGENIC (NOT DISEASE CAUSING)	1. MAF >5% in any of the control population databases 2. Previously reported in the literature with well-established evidence of consensus about its non-disease-causing classification, and with no contradictory data 3. Absence of co-segregation with the disease in at least 2 reported families	1. Variant allele frequency in control populations is higher than expected for disease or has a MAF >0.05% 2. Absence of co-segregation of the variant with the phenotype in at least 1 family 3. Functional study showing that the variant does not affect the structure or function of the encoded protein 4. Presence of the variant in healthy unaffected subjects

	4. Meeting at least 2 supporting criteria	at an age at which the disease should be fully penetrant (variant must be in homozygosis in recessively inherited diseases, or in hemizygosis in X-linked diseases)

MAF indicates minor allele frequency.

Supplemental Table 3. **Relevant genetic variants found in black and white athletes**

Athlete	Gene	Clinical Disease Associated with Identified Variant	Genotype and Population Frequency of Variant in Individuals in Control Populations	Pathogenicity	Sequence change*	Amino acid change*	Phenotype
White Athletes							
15	MYBPC3	HCM	Heterozygous; mutation (<0.0001, no homozygotes)	Pathogenic	NM_000256.3: c.1624G>C	NP_000247.2:p.Glu542Gln	Positive
74	GLA	Fabry disease	Hemizygous; mutation (not found in controls)	Pathogenic	NM_000169.2: c.902G>A	NP_000160.1:p.Arg301Gln	Positive
77	MYBPC3	HCM	Heterozygous; mutation (<0.0001, no	Pathogenic	NM_000256.3: c.3065G>C	NP_000247.2:p.Arg1022Pro	Positive

			homozygotes)				
49	MYBPC3	HCM	Heterozygous; mutation (<0.0001, no homozygotes)	Likely pathogenic	NM_000256.3: c.2552C>T	NP_000247.2:p.Ala851Val	Positive
55	MYPBC3	HCM	Heterozygous; mutation (<0.0001, no homozygotes)	Likely pathogenic	NM_000256.3: c.2198G>A	NP_000247.2: p.Arg733His	Positive
60	MYH7	HCM	Heterozygous; mutation (<0.0001, no homozygotes)	Likely pathogenic	NM_000257.3: c.3134G>T	NP_000248.2:p.Arg1045Leu	Positive
75	SCN5A	LQTS	Heterozygous; rare variant (<1%)	Likely pathogenic	NM_198056.2: c.3911C>T	NP_932173.1:p.Thr1304Met	Negative
Black Athletes							
39	TTR	Amyloid	Heterozygous; polymorphism (≥1%)	Pathogenic	NM_000371.3: c.424G>A	NP_000362.1:p.Val142Ile	Negative

3	MYH7	HCM	Heterozygous; mutation (not in controls)	Likely pathogenic	NM_000257.3: c.4259G>A	NP_000248.2:p.Arg1420Gln	Positive
92	ACTC1	HCM, DCM, LVNC	Heterozygous; mutation (<0.0001, no homozygotes)	Likely pathogenic	NM_005159.4: c.886T>C	NP_005150.1:p.Tyr296His	Positive

ACTC1 indicates Actin alpha, cardiac muscle 1; DCM dilated cardiomyopathy; GLA, galactosidase alpha; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome; LVNC, left ventricular non-compaction; MYBPC3, myosin binding protein C; MYH7, myosin heavy chain 7; SCN5A, sodium voltage-gated channel alpha subunit 5; and TTR, transthyretin.

*For additional information about genomic variants, see https://www.ncbi.nlm.nih.gov/clinvar