Appendix: Composition of the cardiomyopathy gene panel (CM_v4)

Gene	Transcript reference (Ensembl)	Alternative transcripts/exons (Ensembl)
ABCC9	ENST00000261200	ENST00000261201: exon 38
ACTC1	ENST00000290378	
ACTN2	ENST00000542672	ENST00000366578: exon 8
ALPK3	ENST00000258888	
ANKRD1	ENST00000371697	
BAG3	ENST00000369085	
CALR3	ENST00000269881	
CAV3	ENST00000343849	
CRYAB	ENST00000526180	ENST00000524660: exon 1; ENST00000533971: exon 2
CSRP3	ENST00000265968	
CTNNA3	ENST00000433211	
DES	ENST00000373960	
DSC2	ENST00000280904	ENST00000251081: exon 16
DSG2	ENST00000261590	
DSP	ENST00000379802	
EMD (STA)	ENST00000369842	
FHL1	ENST00000394155	ENST00000370683: exon 1, exon 6
FHL2	ENST00000409177	
FLNC	ENST00000325888	
GLA	ENST00000218516	
JPH2	ENST00000372980	
JUP	ENST00000393931	
LAMA4	ENST00000230538	
LAMP2	ENST00000371335	ENST00000434600: exon 9; ENST00000200639: exon 9
LDB3	ENST00000429277	ENST00000372066: exon 4; ENST00000372056: exon 8; ENST00000361373: exon 7
LMNA	ENST00000368300	ENST00000368297: exon 2, exon 11
MIB1	ENST00000261537	
MYBPC3[a]	ENST00000545968	
MYH6	ENST00000405093	
MYH7	ENST00000355349	
MYL2	ENST00000228841	
MYL3	ENST00000292327	
MYOZ2	ENST00000307128	
MYPN	ENST00000358913	
NEBL	ENST00000377122	ENST00000417816: Exon 1, Exon 2, Exon 3, Exon 4
NEXN	ENST00000334785	
PKP2	ENST00000070846	
PLN	ENST00000357525	
PPA2	ENST00000341695	
PRDM16	ENST00000270722	
PRKAG2	ENST00000287878	
RAF1	ENST00000442415	
RBM20	ENST00000369519	
RYR2	ENST00000366574	
SCN5A	ENST00000333535	ENST00000413689: exon 6
SDHA	ENST00000264932	
SGCD	ENST00000337851	ENST00000517913: exon 10
SYNE1	ENST00000367255	
TAZ	ENST00000601016	
TCAP	ENST00000309889	
TGFB3	ENST00000238682	
TMEM43	ENST00000306077	
TNNC1	ENST00000232975	
TNNI3	ENST00000344887	
TNNT2[b]	ENST00000236918	
TPM1	ENST00000403994	ENST00000334895: exon 1, exon 8; ENST00000559397: exon 2; ENST00000358278: exon 6; ENST00000288398: exon 9; ENST00000559556; exon 9
TTN[c]	ENST00000589042	ENST00000360870: exon 46
TTR	ENST00000237014	
VCL	ENST00000211998	

[a]To be able to detect some known deep intronic pathogenic variants extra probes were added for parts of *MYBPC3* intron 9, intron 13, intron 19, intron 20 and intron 32

[b]All annotations are based on the Hg19/GRCh37 genome build, with exception of *TNNT2,* for which the GRCh38 build is used

[c]The most complete *TTN* transcript is ENST00000589042 that contains a total of 363 exons. From this transcript, we have opted to exclude the exons that are not present in the cardiac isoforms: N2BA, N2B, Novex-1, Novex-2 and Novex-3. This means that the following exons are not included in the gene panel: exon 147, exon 149, exons 158 to 201 with the exception of exon 174, exons 212 to 216 (https:/cardiode.org/titin website).

For the listed genes, a coverage of 20x for >99% of the coding sequence is postulated. Large deletions/duplications are not detected with the current version of the assay.

Classification of detected sequence variants is, when appropriate, discussed at a multidisciplinary meeting with clinicians with specific expertise in the gene or disease in question, and is performed according to the 5-class system: non-pathogenic (class 1, polymorphism), probably non-pathogenic (class 2), clinical significance unclear (class 3), likely pathogenic (class 4) and pathogenic (class 5, mutation).