

A

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1 agttgtgac cagcctgcc cttgctccc tgctgtctt tgcgccttt gaatgcttg tocttcaag tocttctgg tctgacaaa cagggaocg gtctacottt ggctacogaa
121 gaggaactag taataacgaa tccatgaag aggatgaact cctgcctccc ctgtcagcgg aggatgtgaa ggagatagag agagagtgg aagacattga acctgacgc aaccttccg
241 tgggtctag gcaaaagag ctagacaga aaaccccaa agggacatt agagagagg cactgatgg ctattgggaa aaggagtccc aaaaactctt ggaagaggag aggtctggg
361 aatgtgaaa gtttgagaa gacaaagag aagtgaaga agacttatt tttactgaaa gtaacagtga gtttctgag gaagtgtata cagaggaga ggaaggaggag tccagaggg
481 aagagagaga aagacacagt gacgaagag aaagaacat tgaactgca aaaggatta atggaactgt aaattatgat agtgtcaat ctgacaactc taagccaaag atatttaaa
601 gtcaaataga gaacataat ttgaccaat gacgaatgg gaggaacaca gagtcccaa ctgccattca cctttgtga aatctacag tgattgaga ogotttgag agatttaaa
721 goaatgaccc tgacacaca gaagtaatt tgaacaacat tgaacaacat acaacacaga cootttaoog ottttgtgaa goottoaagg acaaacctgt ggtgaagaog ttoagtctg
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961 toatgagag toctocagac aaacaggtg toaogagot goitttcoat aacogagag cactatgg cagcaagtg gaaatggaga ttgtaagot ggtgaaggag aacogagag
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1321 agactgtgag gagcgtctt ctgtctctg tggcacaac tootctoot oooctooto ootctooto ootctoott toocaaaggo tgaacacac tootctoot oooctooto
1441 cactccaga gaaaagoto tttaocaga acattgaga agtctoaia caaogggga gtgccaagc ggtcttaaa atggacaa aaaaagaaa agggaaaag gtccagaa
1561 agcaaacag tatttaaa attctctag gtaagtgaa gagaagaaa ttgaagacag ttccagact tctacccc agagatcago toatgagaat ctatggaag
1681 caattoggg aagcagata aaacagotaa agoggtgga agttccaga gccctgcat aaaaacatg tocttgaag aggatgcaga actgtcagt ggtattcat gaaatgatt
1801 gtgagatgt tcaaaatc ctcttcaat tcaaatgat cctgacttt aaaaatc toacccat attcaaga gaacttaag aaacatcag catgtttct ctgtaaat
1921 gaaataaat tcttttcta ttgtgtgga ttgtatgg caagaagag ttaattaaa gatgtcttc ctatctgtg atgtgtgtt aactccaggt tgaatgagt tcatgaatg
2041 tctgttatt ttgttaatt caataaagt ggttgaggt ttttccct tttttaag caaacata ttttctgt acttgatac tctgcagt tttgtatc tggataatg
2161 tgtattgag tttttccct ttttttaaa agcaaacat atattttct gtgagtaat acatctgca ggtgtgat taacattact ggcattaaa aaaaatatt acattctac
2281 ccaaaaa

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B

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121 eeeeeqeeeee eedsdeeert ietakgingt vnydsvnsdn skpkifksqi eninltngsn
181 grntespaai hpcgnptvie daldkiksnd pdttevnlnn ienittqtlt rfaeakdnt
241 vvktfslant haddsaamai aemlkvnehi tnvvesnfi tgkgilaimr alghntvlte
301 lrfhnqrhim gsqvemeivk llkenttllr lgyhfelpgp rmsmtsiltr nmdkqrqkl
361 qeqkqegyd ggpnlrtkvw qrgtpssspy vsprhspwss pklpkkvqtv rsrplspvat
421 pppppppppp pppssqrlp ppppppplp ekklitrnia evikqgesaq ralqngqkkk
481 kgkvkqpn silkeiknsl rsvqekkmed ssrpstpqrs ahenlmeair gssikqlkrv
541 evpealr

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**Figure S1. LMOD2 Transcript and Amino Acid Sequences. A.** LMOD2 transcript sequence. Opening (atg) and stop (taa) codons as well as splicing boundaries are underscored. Affected codons in the published reports are bolded in black. **B.** LMOD2 amino acid sequence and structural domains. Colored amino acids are those of the LMOD2 isoform 1~547 corresponding to the boxes on the domain diagram shown in **Figure 5. C.** with corresponding colors. The underscored amino acids are at the splicing boundaries. The bolded amino acids are the first affected amino acid based directly or indirectly on the sequencing results of reported cases.

**Table S1.** Biochemical testing and infection work up for infantile heart failure.

Differential Etiology	Test Parameters	Test Interpretation
Hypothyroidism	TSH Free T4	Negative
Immune hemolytic anemia	Isotiter antibody screen	Negative
Congenital syphilis	RPR	Negative
SARS-CoV-19 infection	PCR/TMA	Negative
Viral hepatitis	HAV, HBV, HCV-PCR	Negative
HIV infection	HIV-1 and HIV-2 Ag/Ab screen 4 <sup>th</sup> generation	Negative
HSV Infection	HSV-1 and HSV-2 DNA (PCR)	Negative
EBV infection	EBV DNA (PCR)	Negative
Rapid Respiratory Panel	Adenovirus, influenza A/B, human metapneumovirus, human rhinovirus/enterovirus, seasonal coronavirus, RSV A/B	Negative
CMV Infection	CMV DNA (PCR)	Negative
Para Influenza Infection	Para influenza Type 1,2,3,4 DNA (PCR)	Positive (Type 4) Negative (Type 1, 2, 3)

PCR, polymerase chain reaction; TMA, transcription-mediated amplification; TSH, thyroid-stimulating hormone; HIV, human immunodeficiency virus; HSV, herpes simplex virus; EBV, Epstein-Barr virus; CMV, cytomegalic virus.

Table S2. Comprehensive Cardiomyopathy Panel*			
ABCC9	DSG2	MAP2K1	RIT1
ACADVL	DSP	MAP2K2	RYR2
ACTC1	ELAC2	MRAS	SCN5A
ACTN2	EMD	MTO1	SDHA
AGL	EYA4	MYBPC3	SGCD
ALMS1	FHL1	MYH7	SHOC2
ALPK3	FKRP	MYL2	SLC22A5
BAG3	FKTN	MYL3	SOS1
BRAF	FLNC	MYL4	SOS2
CACNA1C	GAA	MYLK3	SPRED1
CACNA1D	GATA4	NF1	TAZ
CALM1	GATA5	NKX2-5	TBX20
CALM2	GJA5	NRAS	TCAP
CALM3	GLA	PCCA	TMEM43
CASQ2	HCN4	PCCB	TMEM70
CBL	HRAS	PKP2	TNNC1
CDH2	JUP	PLN	TNNI3
CPT2	KCNE1	PPA2	TNNI3K
CRYAB	KCNH2	PPCS	TNNT2
CSRP3	KCNJ2	PPP1CB	TPM1
DES	KCNQ1	PRKAG2	TRDN
DMD	KRAS	PTPN11	TRPM4
DNAJC19	LAMP2	RAF1	TTN
DOLK	LMNA	RASA1	TTR
DSC2	LZTR1	RBM20	VCL
(*) source: <a href="https://www.invitae.com/en/providers/test-catalog/test-02101">https://www.invitae.com/en/providers/test-catalog/test-02101</a> , accessed 20220626			

Table S3. Comprehensive Glycogen Storage Disease Panel*	
AGL	PFKM
ALDOA	PGAM2
ENO3	PGK1
FBP1	PGM1
G6PC	PHKA1
GAA	PHKA2
GBE1	PHKB
GYG1	PHKG2
GYS1	POLG
GYS2	PYGL
LAMP2	PYGM
LDHA	RBCK1
LPIN1	SLC2A2
PCK1	SLC37A4
PCK2	
(*) source: <a href="https://www.invitae.com/en/providers/test-catalog/test-06156">https://www.invitae.com/en/providers/test-catalog/test-06156</a> , accessed 20220626	