SUPPLEMENTAL MATERIALS

Whole Exome Sequencing Identifies Compound Heterozygous Mutations in TSFM Gene Causing Juvenile Hypertrophic Cardiomyopathy.

Jamie O Yang[1], Hapet Shaybekyan[2,3], Yan Zhao[2,3], Xuedong Kang[2,3], Gregory A. Fishbein[4], Negar Khanlou[4], Juan C. Alejos[2], Nancy Halnon[2], Gary Satou[2], Reshma Biniwale[2], Hane Lee[4,5,*], Glen Van Arsdell[2], Stanley F. Nelson[2,4,5,7], Marlin Touma[1-3, 6-9], on behalf of The UCLA Clinical Genomics Center[1]& The UCLA Congenital Heart Defects-BioCore Faculty[1]

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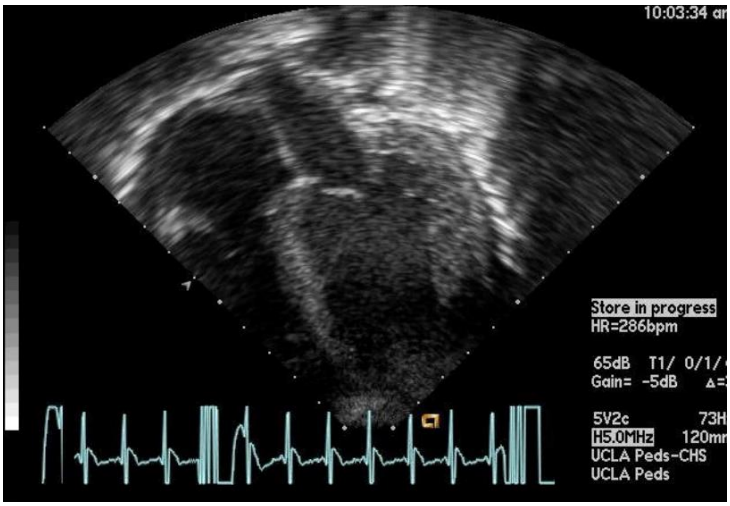
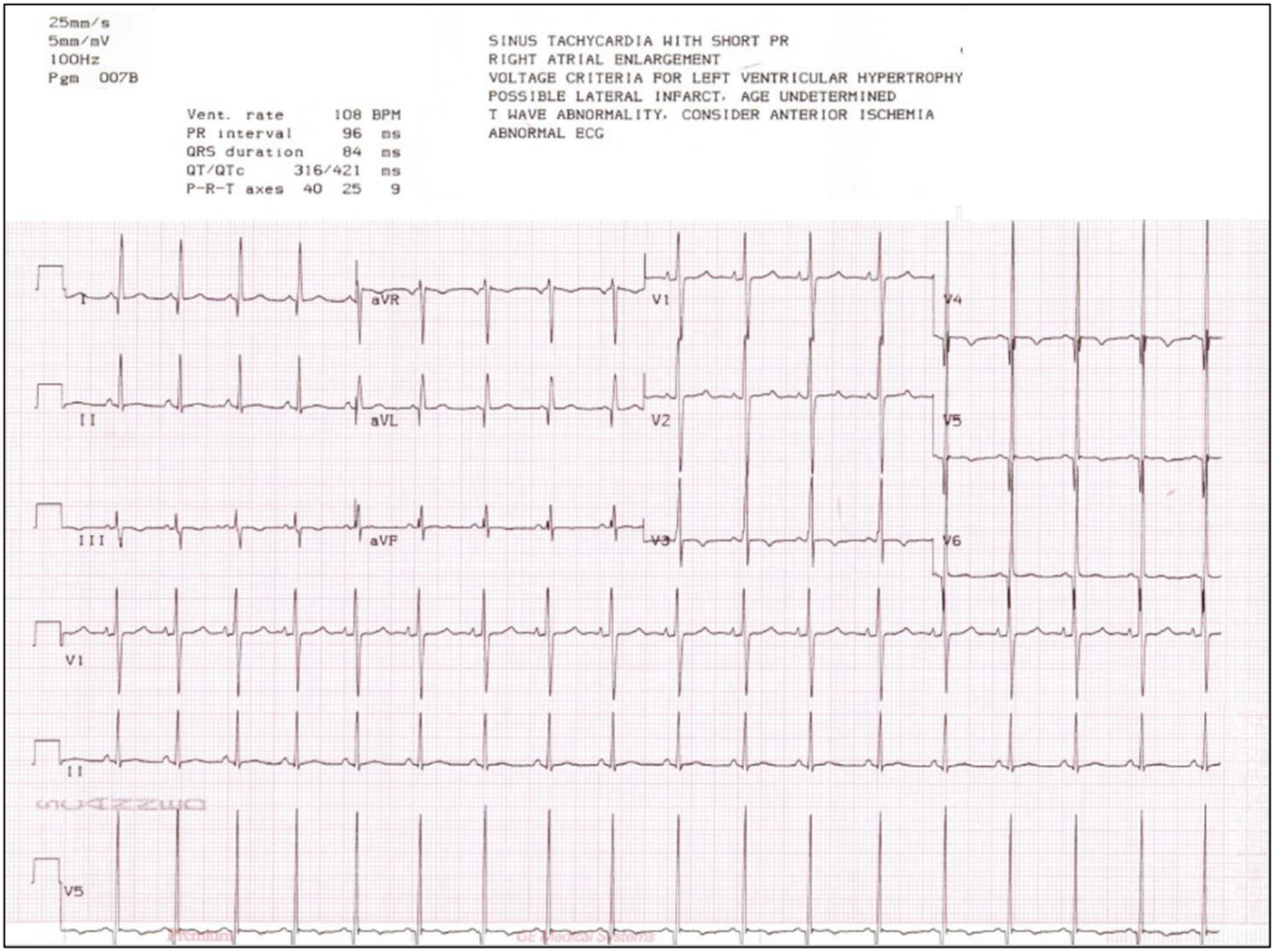
1. David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
2. Department of Pediatrics, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
3. Neonatal/Congenital Heart Laboratory, Cardiovascular Research Laboratory, University of California Los Angeles, Los Angeles, CA.
4. Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
5. Department of Human Genetics, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
6. Children's Discovery and Innovation Institute, Department of Pediatrics, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
7. Institute for Precision Health, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
8. The Molecular Biology Institute, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.
9. Eli and Edythe Broad Stem Cell Research Center, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA.

*Currently at 3billion, Inc, Seoul, South Kore

Supplemental Video 1. Echocardiography (apical view) depicts diminished cardiac function upon admission.



Supplemental Figure 1. Representative electrocardiogram recording of the proband upon admission at 3 years of age. High voltages indicate left ventricular hypertrophy.



Supplemental Table 1. Biochemical Testing Results of the Proband

Test	Result
Newborn Screen	Normal
Serum Lactate	Elevated
Plasma Amino Acid	Normal
Muscle Free/Total Creatinine	Normal
Muscle CPT1 and CPT Activities	Normal
Serum Acyl Carnitine	Normal
Acid Alpha Galactosidase Activity (GAA)	Negative
Urinary Hex4 Concentration	Normal
TORCH Titers	Negative

Supplemental Table 2. *TSFM* Mutations Reported to Date

Mutation(s)	Survival	Presence of Hypertrophic Cardiomyopathy	Clinical manifestations		Serum Lactate	Reference
			Onset	Symptoms		
c.997C>T [Arg333Trp]	7 weeks	No	At birth	Hypotonia, generalized seizures, respiratory failure, encephalomyopathy, rhabdomyolysis	elevated	Smeitink 2006 PMID: 17033963
c.997C>T [Arg333Trp]	7 weeks	Yes	At 36 hours	Hypotonia, irregular breathing, hypertrophic cardiomyopathy	elevated	Smeitink 2006 PMID: 17033963
c.997C>T [Arg333Trp]	Few months (no detail)	Yes	At birth	hypotonia	elevated	Smits 2011 PMID: 21119709
			Exact onset not reported	Mitochondrial encephalomyopathy, hepatomegaly, hypertrophic cardiomyopathy		
c.934C>T [Arg312Trp]1	2 months	No	At birth	trunk hypotonia	elevated	Vedrenne 2012 PMID: 21741925
			6 weeks	liver insufficiency, tubulopathy		
c.934C>T [Arg312Trp]1	2 weeks	Yes	At birth	trunk hypotonia, hypertrophic cardiomyopathy	elevated	Vedrenne 2012 PMID: 21741925
			At 2 days	generalized hypotonia, dystonic movements		
c.997C>T [Arg333Trp]	2 months	Yes	< 1 week	Hypotonia, Hypothermia, Hepatomegaly, hypertrophic cardiomyopathy	Not reported	Calvo 2012 PMID: 22277967
c.997C>T [Arg333Trp]	1 month	Yes	< 1 month	Hypertonia Respiratory arrest Hypertrophic cardiomyopathy	Not reported	Calvo 2012 PMID: 22277967
c.944G>A [Cys315Tyr] / c.856C>T [Gln286X]	> 21 yrs	Yes	10 months	hypertrophic cardiomyopathy	elevated	Ahola 2014 PMID: 25037205
			7 years	cognitive decline		
			9 years	Leigh syndrome		
			Teenage	optic atrophy		
			21 years	neuropathy, dystonia		
c.944G>A [Cys315Tyr] / c.856C>T [Gln286X] (X = nonsense mutation)	> 15 yrs	Yes	16 months	hypertrophic cardiomyopathy	mildly elevated	Ahola 2014 PMID: 25037205
			13 years	neuropathy		
			teenage	optic atrophy		
c.856C>T [Gln286X] / c.106+4A>G [splice error]	> 21 yrs	No	15 years	optic atrophy tremor	normal	Ahola 2014 PMID: 25037205
			16 years	peripheral neuropathy ataxia		
c.944G>A [Cys315Tyr]	>21 yrs	No	18 years	Hyperkinetic movement disorder dystonia	Mildly elevated	Traschutz 2019 PMID 30297209
			20 years	optic atrophy mild cognitive impairment		
c.719G>C [Cys240Ser]	> 23 yrs	Yes	6 years	gross and fine motor clumsiness	normal	Emperador 2016 PMID 27677415
			11 years	hypertrophic cardiomyopathy, dystonia		
			Exact onset not reported	optic atrophy, ataxia		
c.408_409delGT [Leu137Glyfs*24] / c.505C>T [Leu169Phe]	>33 yrs	Dilated cardiomyopathy	Early childhood	gross and fine motor clumsiness mild muscle weakness	Mildly elevated	Perli 2019 PMID 30911037
			27	dilated cardiomyopathy		
c.547G>A [Gly183Ser]	>8 yrs	Yes	3 months	Hypotonia, lactic acidosis	elevated	Scala 2019 PMID 31267352
			11 months	hypertrophic cardiomyopathy		
			5 years	severe speech delay		
			8 years	sensorineural hearing loss		
c.919C>T [Gln307*] / c.161G>A [Arg54Gln] * = nonsense variant	>15 yrs	No	At birth	Hypotonia global developmental delay	elevated	Van Riesen 2021 PMID 33816677
			2.5 years	hyperkinetic movement disorder		
			5 years	optic atrophy		
c.331_340delCAGGAAGGAA [Gln111ThrfsTer5] / c.57G>A [splice error (exon 5 skipping)]	>9 yrs	Yes	3 months	Hepatomegaly, hypoglycemia, hypertriglyceridemia	elevated	Go Hun Seo 2019 PMID 31451716
			4 months	lactic acidosis		
			6 months	hypertrophic cardiomyopathy		
			1 year	infantile spasm, truncal ataxia		
			5 years	optic atrophy		
			9 years	severe mental retardation		
c.934C>T [Arg333Trp] / c.355G>C [Val119Leu]	>14 yrs	Yes	3 years	hypertrophic cardiomyopathy	elevated	Our patient

Supplemental References (Correspond to Supplemental Table 2)

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