Table e-3. List of homozygous non-synonymous variants shared by the probands

Chr .	Region	Type	Ref.	Alt	Gene Name	Coding region change	Amino acid change	MAF (ExAC)	OMIM Phenotype #	RVIS Score	Polyphen HumVar Score
1	24426195	SNV	C	G	MYOM3	ENST00000330966:c.634G>C	ENSP00000332670:p.Gly211Arg	$8,28x10^{-6}$	-	1,16 (92,65%)	1.000
1	**110168394**	**Del**	**G**	**-**	**AMPD2**	**ENST00000528667:c.495delG**	**ENSP00000436541:p.Arg165fs**	**-**	**615809**	**-1,46 (3,79%)**	**na**
3	194126709	SNV	G	A	ATP13A3	ENST00000256031:c.3620C>T	ENSP00000256031:p.Thr1207Ile -	-	-	-0,97 (8,95%)	0.169
9	130690399	SNV	C	T	PIP5KL1	ENST00000388747:c.379G>A	ENSP00000373399:p.Gly127Ser	$7,55x10^{-5}$	-	0,19 (67,03%)	0.031
22	26937461	SNV	G	A	TPST2	ENST00000403880:c.136C>T	ENSP00000385192:p.Arg46Trp	$1,74x10^{-5}$	-	-0,84 (11,18%)	0.000

MYOM3: Myofibrillar structural protein myomesin-3 links the intermediate filament cytoskeleton to the M-disk of the myofibrils in striated muscle. MYOM3 mutations have been not yet associated to human phenotypes. Two fragments of the MYOM3 protein are abnormally present in sera of Duchenne muscular dystrophy (DMD) patients, limb-girdle muscular dystrophy type 2D (LGMD2D) and their respective animal models. The gene is selectively expressed in the skeletal and cardiac muscle and in the kidney.
The gene is highly tolerant to DNA variations (RVIS score 1.16). The AA substitution is potentially functional (Polyphen score 1.000)

ATP13A3: Member of the P-type ATPase family of proteins that transport different cations across membranes. The biological function of ATP13A3 gene is largely unknown. ATP13A3 mutations have been not yet associated to human phenotypes. The gene is ubiquitariously expressed. The gene is moderately intolerant to DNA variations (RVIS score -0.97). The AA substitution involves and is expected to be non-functional (Polyphen score 0.169).

PIP5KL1. Phosphoinositide kinase-like protein that lacks intrinsic lipid kinase activity but associates with type I PIPKs and may play a role in localization of PIPK activity (Chang et al., 2004). Phosphoinositide (PI) signaling networks have been implicated in the regulation of numerous cellular processes, including cell survival, cell proliferation, motility, cytoskeletal regulation and intracellular vesicle trafficking. This suggested that PIP5KL1 appear to be a potential tumor suppressor in gastric tumor formation (Shi et al., 2010). The gene is preferentially expressed in parathyroid gland.
PIP5KL1 mutations have been not yet associated to human phenotypes
The gene is tolerant to DNA variations (RVIS score 0.19) and the AA substitution is expected to be non-functional (Polyphen score 0.031)

TPST2: The protein encoded by this gene catalyzes the O-sulfation of tyrosine residues within acidic regions of proteins. The encoded protein is a type II integral membrane protein found in the Golgi body. TPST2 mutations have been not yet associated to human phenotypes. The gene is ubiquitariously expressed.
The gene is moderately intolerant to DNA variations (RVIS score -0.84) and the AA substitution is is expected to be non-functional (Polyphen score 0.000).

REFERENCES

Chang JD et al. Identification and characterization of a phosphoinositide phosphate kinase homolog. J Biol Chem. 2004 Mar 19;279(12):11672-11679
Shi L et al. Overexpression of PIP5KL1 suppresses cell proliferation and migration in human gastric cancer cells. Mol Biol Rep. 2010 J;37:2189-2198.