NUMBER OF GENES AND ALTERATIONS IDENTIFIED BASED ON BIOINFORMATICS AND INTERPRETATION

	Post-Inheritance Model Filtering			**Post-Medical Review**			**Notable Candidate Genes**		
	HGMD/ OMIM-Morbid*	Clinically novel**	TOTAL	HGMD /OMIM - Morbid	Clinically novel	TOTAL	HGMD/ OMIM-Morbid	Clinically novel	TOTAL
Autosomal Dominant Genes (Alterations)	5 (5)	12 (12)	17 (17)	1 (1)	9 (9)	10 (10)	1 (1)	0 (0)	1 (1)
Autosomal Recessive Genes (Alterations)	8 (23)	11 (26)	19 (49)	0 (0)	11 (18)	11 (18)	0 (0)	0 (0)	0 (0)
X-linked Recessive Genes (Alterations)	3 (3)	7 (7)	10 (10)	0 (0)	7 (7)	7 (7)	0 (0)	0 (0)	0 (0)
X-linked Dominant Genes (Alterations)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Y-linked Genes (Alterations)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL GENES (Alterations)	15 (30)	31 (46)	46 (76)	1 (1)	27 (34)	1 (1)	1 (1)	0 (0)	1 (1)

*HGMD/OMIM-Morbid: Listed in this category are genes that have been described in either the HGMD or OMIM-Morbid databases (the alterations within these genes are located in parentheses)

**A clinically novel gene is a gene which is not currently known to underlie a genetic condition

((((Suppl. table 1)))))

Supplementary table 2

	ACTG2 variant	dbSNP	1000GFreq (%)	EvsEurFreq (%)	EvsAfrFreq (%)	EvsFreq (%)	PhyloP_S	Phylo P_P	SIFT_S	SIFT_P	PP2_S	PP2_P	LRT_S	LRT_P	MT_S	MT_P
Family 1	R257H	None	None	None	None	None	0.999596	C	0.9018	D	0.73	D	1	D	0.98371	D
Family 2	R178H	None	None	None	None	None	0.9997	C	N/A	N/A	N/A	N/A	1	D	0.9837	D
Family 3	R257C	None	None	None	None	None	0.998803	C	0.95275	N/A	0.972	D	1	D	0.99261	D

Keys:

PhyloP Prediction: C(onserved), N(on-conserved)

SIFT Prediction: D(damaging), T(tolerated)

PolyPhen2 Prediction: D - probably damaging, P - possibly damaging, B - benign

LRT Prediction: D(deleterious), N(neutral), U(unknown)

Mutation Taster Prediction: A - disease causing automatic (NMD), D - disease causing, N - polymorphism, P - polymorphism automatic (three genotypes of ref./alt. alleles observed in Ha

ExoVar: D(eleterious), N(eutral)

GERP: -11.6 to 5.82 (most conserved)

All other prediction scores: 0 to 1 (pathogenic)

Supplementary tables:

Table 1: Number of genes and alterations identified based on bioinformatics interpretation of whole exome sequencing data.

Table 2. In silico prediction analysis.