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Supplemental Data

Variants in *EXOSC9* Disrupt the RNA Exosome and Result in Cerebellar Atrophy with Spinal Motor Neuronopathy

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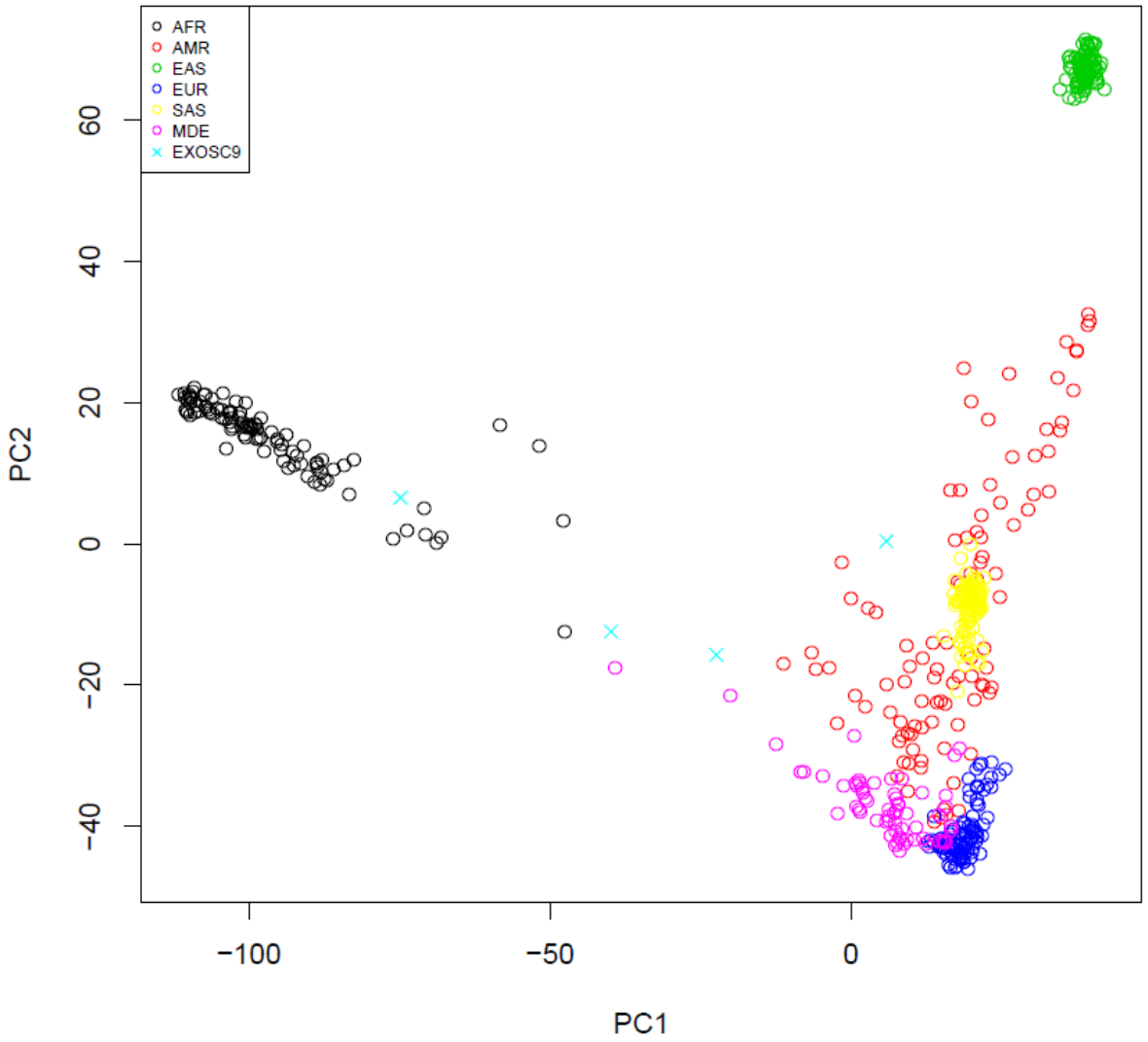
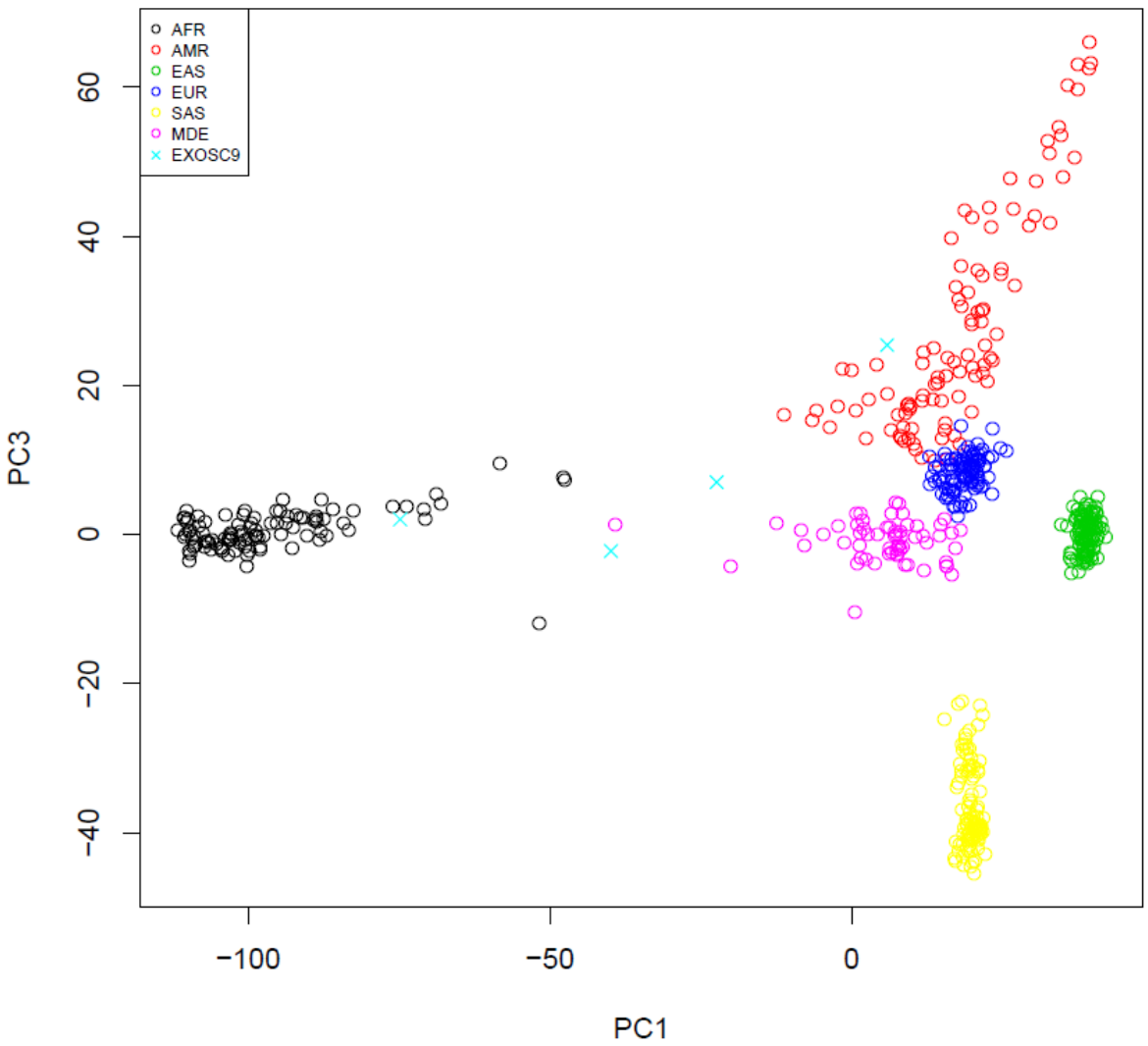
Figure S1:




AFR
AMR
EAS
EUR
SAS
MDE
EXOSC9
PC3
60
40
20
0
−20
−40
−100
−50
0
PC1

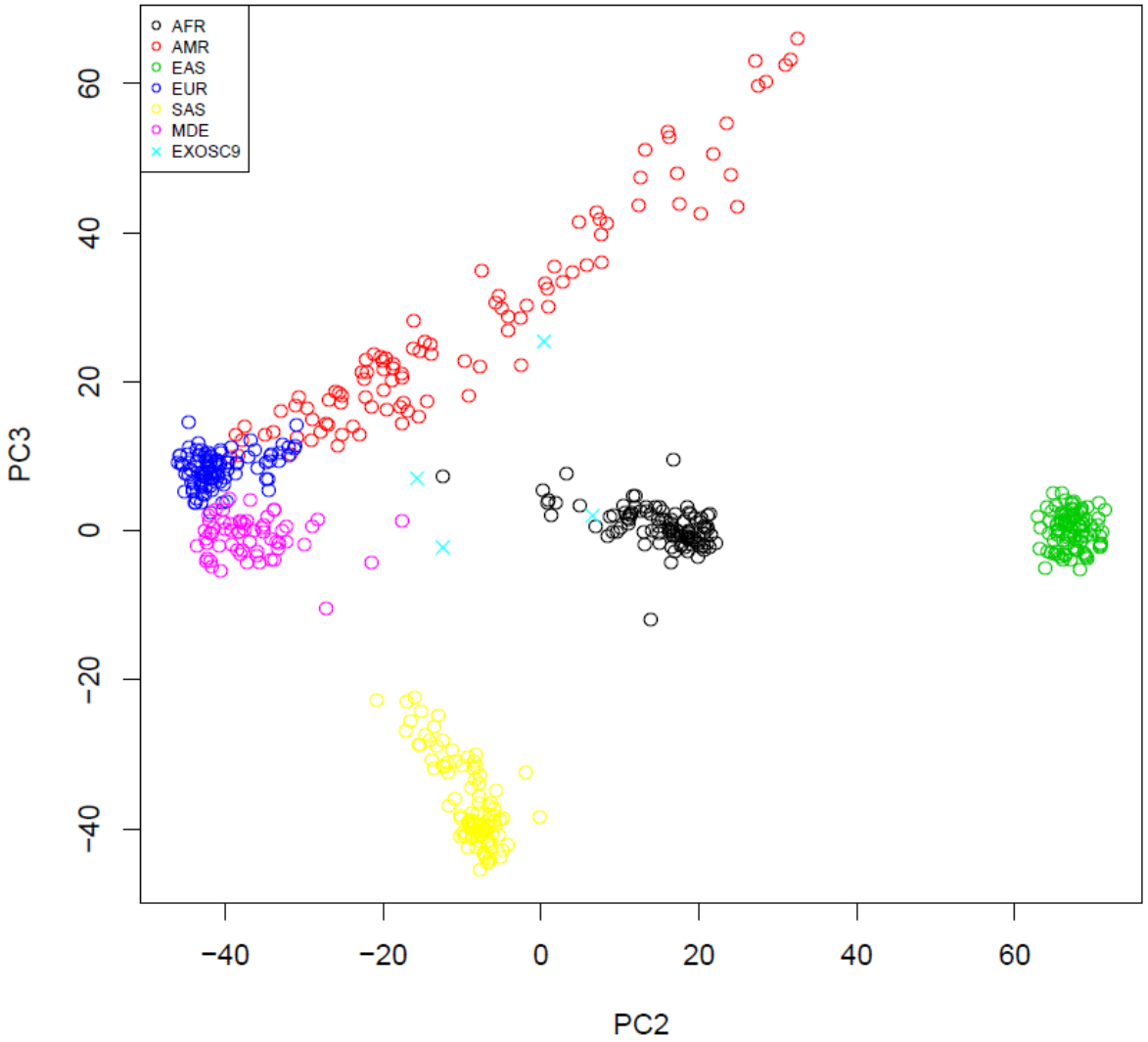

AFR
AMR
EAS
EUR
SAS
MDE
EXOSC9
PC3
PC2
60
40
20
0
−20
−40
−40
−20
0
20
40
60

Figure S1: Principal Component Analysis of exome SNP genotypes compared against random representative samples from the 1000 Genomes Projects Phase 3 super-populations plus a GeneDx-sequenced Middle Eastern (MDE) population. Five total components were calculated (see Table) but only the three most informative components are shown.

Table S1:

Primer name	Forward 3´-5´	Reverse 3´-5´
ZF *exosc9* (I1E2 MO)	CAAACTGCGAGAGGCTTTTCC	TCTCCTGAAACTACACAGAGAG
ZF *exosc9* (E3 gRNA)	TGAGTCAGGTATCCTGTGAGC	TGCAAGAATGTTAACCTGTTTGGTT
pUC/M13	CGCCAGGGTTTTCCCAGTCACGAC	TCACACAGGAAACAGCTATGAC
Morpholino	**Sequence**	
ZF *exosc9* morpholino	GCGCTACAAAACGGTACACAGATAA	

Table S1: Primer sequences used in zebrafish

Table S2:

	Characteristics and Symptoms	HPO ID	Individual 1	Individual 2	Individual 3	Individual 4	Percentage
Mutation in EXOSC9			homo c.41T>C	comp het c.41T>C | c.481C>T	homo c.41T>C	homo c.41T>C	
Effect on translation			p.(Leu14Pro)	p.(Leu14Pro), p.(Arg161*)	p.(Leu14Pro)	p.(Leu14Pro)	
Origin			El Salvador	African-Canadian-Jamaican	Saudi Arabia	African-European-Filippino	
Gender			female	male	female	female	
Age at onset			8 mo	birth	birth	2 weeks	
Age at last assessment			28 mo		4.5 y	19 mo	
Age at death				15 mo			
Head							
	Microcephalus	HP:0000252			+		25
	Low-set ears	HP:0000369		+			25
	Short neck	HP:0000470		+			25
	Blue sclerae	HP:0000592		+			25
	Prominent epicanthic folds	HP:0007930		+			25
	Hypertelorism	HP:0000316		+			25
Respiratory and chest							
	Recurrent infections	HP:0002719	+				25
	Respiratory failure in infancy	HP:0002878	+	+			50
Abdomen							
	Gastrostomy tube feeding in infancy	HP:0011471	+	+			50
	Gastrooesophageal reflux	HP:0002020	+				25
	Feeding difficulties in infancy	HP:0008872			+		25
Skeletal							
	Arthrogryposis multiplex congenital	HP:0002804	+	+			50
	Congenital fractures	HP:0005855		+			25
Neurologic							
	Severe muscular hypotonia	HP:0006829	+	+	+	+	**100**
	Seizures	HP:0001250			+		25
	Type I muscle fiber predominance	HP:0003803	+	+		+	**75**
	Poor head control	HP:0002421	+			+	50
	Failure to thrive	HP:0001508		+			25
	Generalized muscle weakness	HP:0003324	+		+	+	**75**
	Nystagmus	HP: 0000639	+			+	50
	Cerebellar atrophy	HP:0001272	+	+		+	75
	Vermis atrophy	HP:0001284	+				25
	Cerebral atrophy	HP:0002059		+	+		50
	Areflexia	HP:0001284	+				25
	Increased muscle reflexes	HP:0001347			+		25
	EMG: neuropathic changes	HP:0003445	+			+	50
	Muscle / tongue fasciculations	HP:0002380	+				25
	Delayed gross motor development	HP:0002194	+	+	+	+	**100**
	Weak voice	HP:0001621	+		+	+	**75**
Prenatal manifestation							
	Decreased fetal movements	HP:0001558	+	+			30
	Oligohydramnios	HP:0001562		+			25
	Intrauterine growth retardation (< 10^{th} percentile)	HP:0001511		+			25

Table S2: HPO coding of phenotypes due to mutations in *EXOSC9*

Table S3:

Sample	knn.pred	PC1	PC2	PC3	PC4	PC5
Individual 1	AMR	5.86084161991711	0.381779639737347	25.4032514365166	-21.0875664424482	18.6590532074565
Individual 2	AMR	-22.3702289478425	-15.7062479478535	7.02632626688231	13.8203817951703	34.1568567434397
Individual 3	AFR	-39.8713917778595	-12.421418841825	-2.22439179095596	17.719501768131	39.8300579056514
Individual 4	AFR	-74.7967964546837	6.5332515180803	2.02902721367773	3.38496964411094	3.05927032223124

Table S3: Principal Component Analysis of exome SNP genotypes compared against random representative samples from the 1000 Genomes Projects Phase 3 major populations plus a GeneDx-sequenced Middle Eastern (MDE) population. Components are numbered in the order of informativeness and knn.pred is the nearest-neighbor-predicted population.