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Supplemental Data

De Novo GMNN Mutations Cause Autosomal-Dominant Primordial Dwarfism Associated with Meier-Gorlin Syndrome

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Table S1. WES Sequencing Data of Subjects 1 and 2

Subject	Illumina Platform	Unique Aligned (Mb)[a]	Total Pass Filter (Mb)[b]	Avg % Align (PF) Read 1[c]	Avg % Align (PF) Read 2[d]	Avg % Error Rate Read 1[e]	Avg % Error Rate Read 2[f]	Unique-ness %[g]	Dupli-cate %[h]	Total Reads Aligned %[i]	Avg Coverage[j]	Reads Hit Target/ Buffer[k]	Bases 20+ Coverage[l]
1	HiSeq2000	17,066	18,622	98%	97%	0.5%	1.0%	94%	9%	98%	226	75%	97%
2	HiSeq2000	9,369	10,366	94%	94%	0.9%	1.4%	96%	7%	94%	116	80%	92%

[a]Unique Aligned (Mbp): the total number of base-pairs in reads that align best to a single location in the reference genome

[b]Total Pass Filter (Mbp): the total number of base-pairs in reads that pass the Illumina quality filters

[c]Avg % Align (PF) Read 1: the average percentage of pass filter base-pairs in Read 1 that align best to a single location in the reference genome

[d]Avg % Align (PF) Read 2: the average percentage of pass filter base-pairs in Read 2 that align best to a single location in the reference genome

[e]Avg % Error rate Read 1: the calculated error rate of bases on Read 1, as determined by aligning to reference genome

[f]Avg % Error rate Read 2: the calculated error rate of bases on Read 2, as determined by aligning to reference genome

[g]percentage of unique reads

[h]duplicate %: fraction of reads that are identified as duplicate reads – reads whose alignment location is identical to other reads from the same library

[i]Total Reads Aligned: the number of reads that align to the reference genome

[j]Average Coverage: the total number of uniquely aligned bases to the reference genome divided by the size of the reference genome

[k]Reads hit target/buffer: the number of reads whose alignments overlap either a region targeted by the capture reagent, or the 100bp buffer (or both)

[l]Bases 20+ Coverage: the fraction of bases targeted by the capture reagent that are covered by 20 or 40 times or more uniquely aligned reads.

Table S2. Primer information

Gene	Target	Forward/ Reverse	Chr.	Start Position	End Position	Primer sequence (5' to 3')	Purpose
GMNN	Exon 01	F	6	24775062	24775082	cggtcctcaagtactcgctac	genomic sequencing of patient 3
GMNN	Exon 01	R	6	24775481	24775498	accgttcaacaaccccttc	genomic sequencing of patient 3
GMNN	Exon 02	F	6	24777312	24777331	attgacagggctgagtttgg	genomic sequencing of patient 2 and 3
GMNN	Exon 02	R	6	24777559	24777578	cttttagccccatgctttct	genomic sequencing of patient 2 and 3
GMNN	Exon 03	F	6	24780770	24780789	tgttccttttccacccctaa	genomic sequencing of patient 3
GMNN	Exon 03	R	6	24781138	24781157	tgcacccgacgaacttctta	genomic sequencing of patient 3
GMNN	Exon 04	F	6	24781584	24781608	gatccagagatgtgaaaaagttaga	genomic sequencing of patient 3
GMNN	Exon 04	R	6	24782022	24782041	actgggcctccttttcctaa	genomic sequencing of patient 3
GMNN	Exon 05	F	6	24784224	24784244	tgggggtactaagattggaaa	genomic sequencing of patient 3
GMNN	Exon 05	R	6	24784469	24784489	aaagctagcccatattgctct	genomic sequencing of patient 3
GMNN	Exon 06	F	6	24784577	24784596	gctgcatgtcctccatgtta	genomic sequencing of patient 3
GMNN	Exon 06	R	6	24784835	24784860	caaagtgatcacactacactacctca	genomic sequencing of patient 3
GMNN	Exon 07	F	6	24785781	24785805	tgctatacgggtcagctatatcagt	genomic sequencing of patient 3
GMNN	Exon 07	R	6	24786058	24786078	tggaggtaaacttcggcagta	genomic sequencing of patient 3
GMNN	Exon 02	F	6	24777385	24777415	tgtaagtattttaaacctagactccaccttc	genomic sequencing of patient 1
GMNN	Exon 02	R	6	24777557	24777579	acttttagccccatgctttctac	genomic sequencing of patient 1
GMNN	cDNA	F	6	24777461	24777486	tcaccatctacataatgaatcccagt	cDNA sequencing of patient 1
GMNN	cDNA	R	6	24781754	24781773	cccagggctggaagttgtag	cDNA sequencing of patient 1
GMNN	cDNA	F	6	24777446	24777467	ctggtcttctgtgcttcaccat	cDNA sequencing of single clones for patient 1
GMNN	cDNA	R	6	24786056	24786078	tggaggtaaacttcggcagtaaa	cDNA sequencing of single clones for patient 1
GMNN	cDNA	F	6	24777480	24777501	tcccagtatgaagcagaaacaa	cDNA sequencing of patient 2
GMNN	cDNA	R	6	24785869	24785888	tccagaggttcaccattcag	cDNA sequencing of patient 2

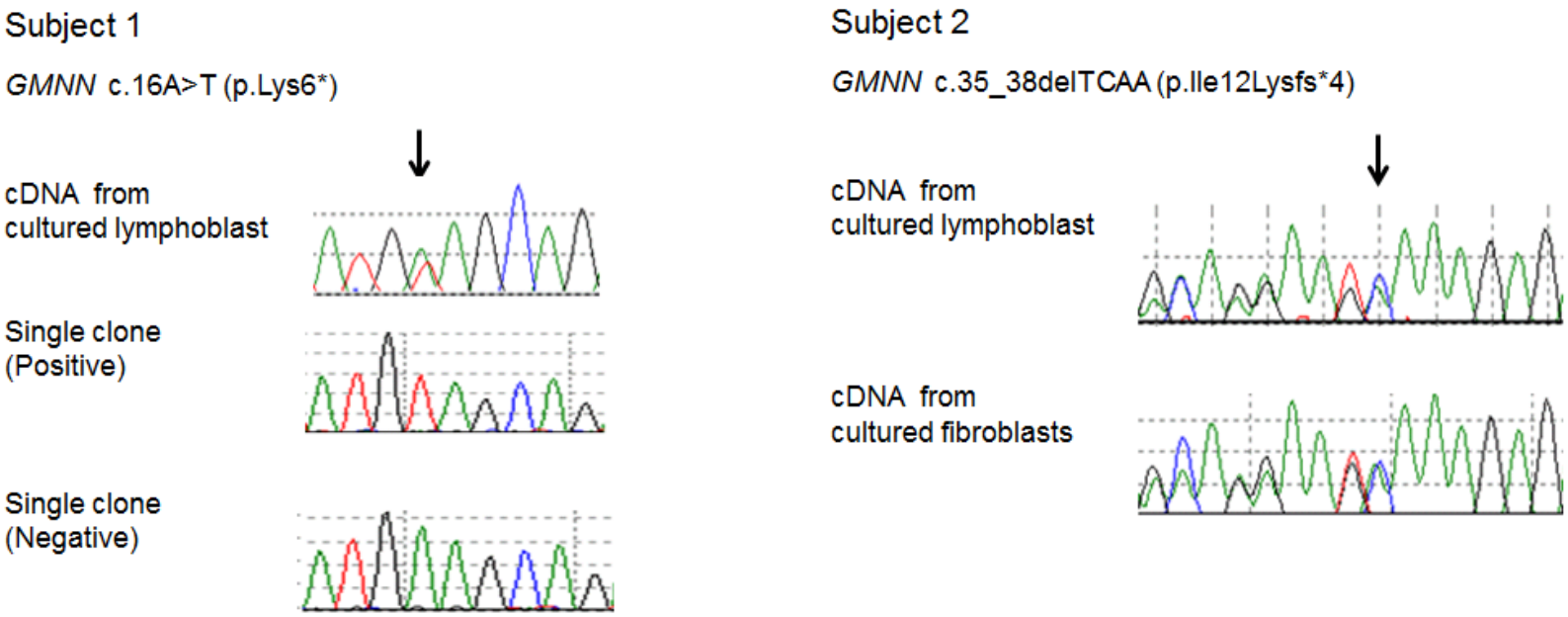

Figure S1. mRNA studies of subjects 1 and 2.

Sequence traces of RT-PCR products from cell lines of subjects 1 and 2 show the presence of both mutant and wild type sequence at about 1:1 ratio. TOPO TA-cloning of the RT-PCR product from subject 1 and Sanger sequencing of individual clones (8 total) indicates that the mutant allele is present in 50% (4 out of 8) of GMNN transcripts. The data suggest that the mutant alleles are not subject to NMD.

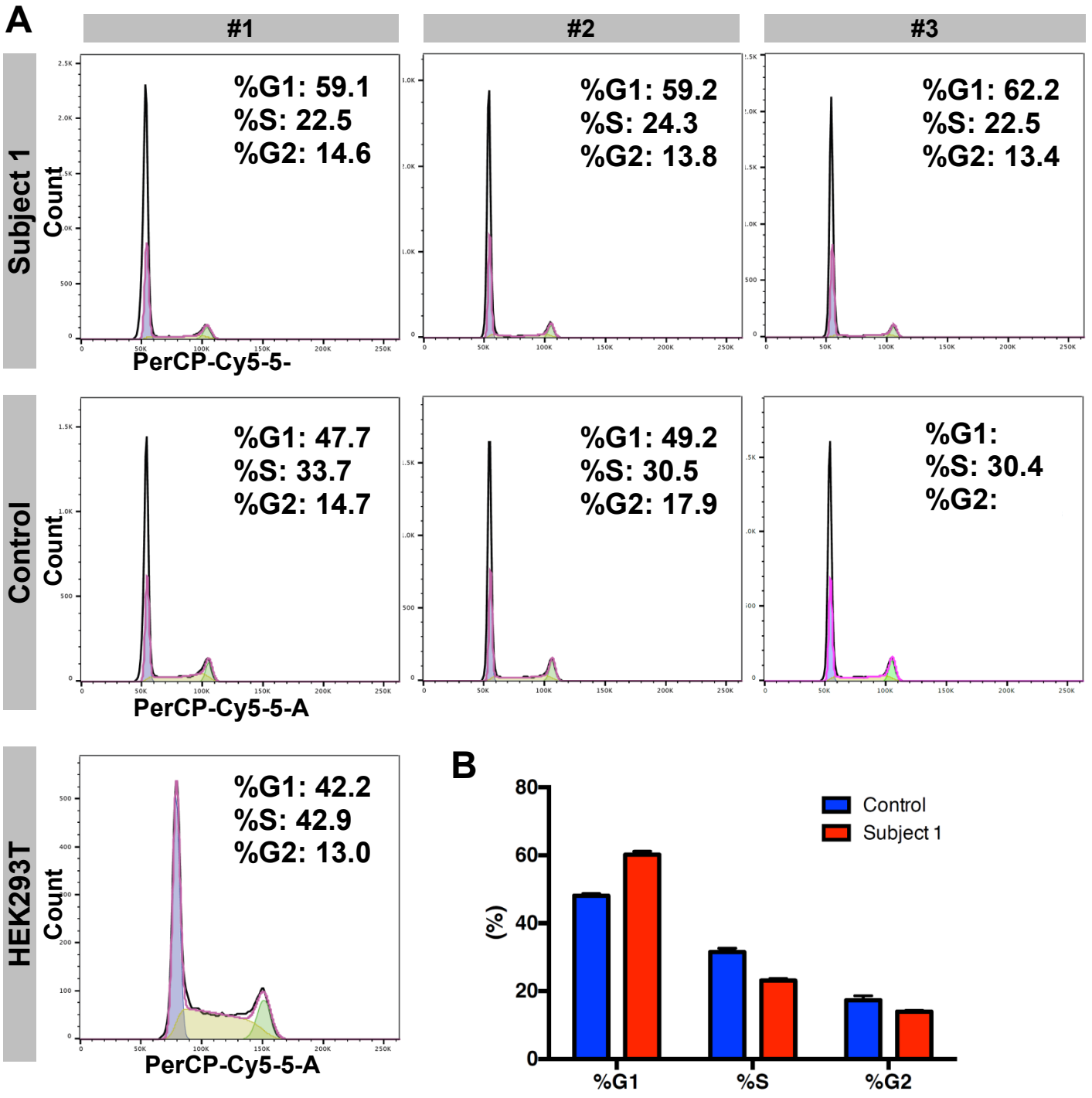
A
#1
#2
#3
Subject 1
%G1: 59.1
%S: 22.5
%G2: 14.6
%G1: 59.2
%S: 24.3
%G2: 13.8
%G1: 62.2
%S: 22.5
%G2: 13.4
Count
PerCP-Cy5-5-
Control
%G1: 47.7
%S: 33.7
%G2: 14.7
%G1: 49.2
%S: 30.5
%G2: 17.9
%G1:
%S: 30.4
%G2:
Count
PerCP-Cy5-5-A
HEK293T
%G1: 42.2
%S: 42.9
%G2: 13.0
Count
PerCP-Cy5-5-A
B
Control
Subject 1
(%)
80
60
40
20
0
%G1
%S
%G2

Figure S3. Flow cytometric analysis of cell cycle phases.

(A) Flow cytometric analyses of lymphoblast of subject 1 and the father (as a control) stained by propidium iodide (PI) (control). X axis presents the cell content as determined by intensity of Propidium Iodide (PI) staining corresponding to 2n (G1 phase), 4n (G2 phase), and areas in between (S phase). Y axis presents cell number. Non-synchronized HEK293T cell was used as a control for cell cycle PI staining. The data were obtained from three independent experiments (labeled as #1, #2, #3 in the figure).The statistical analyses were performed using Student's *t*-test.

(B) Histogram of cell distributions in G1 (60.2%±1.8% vs. 48.1%±0.9%), S (23.1%±1.0% vs. 31.5%±1.9%), and G2 (13.9%± 0.6% vs. 17.3%± 2.4%) phases in lymphoblast of subject 1 and the father (as a control) respectively. Values for the bars represent means for the three independent experiments ± 1 standard deviation (1 SD).