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Supplemental Data

Exome Sequencing Identifies *SLCO2A1* Mutations as a Cause of Primary Hypertrophic Osteoarthropathy

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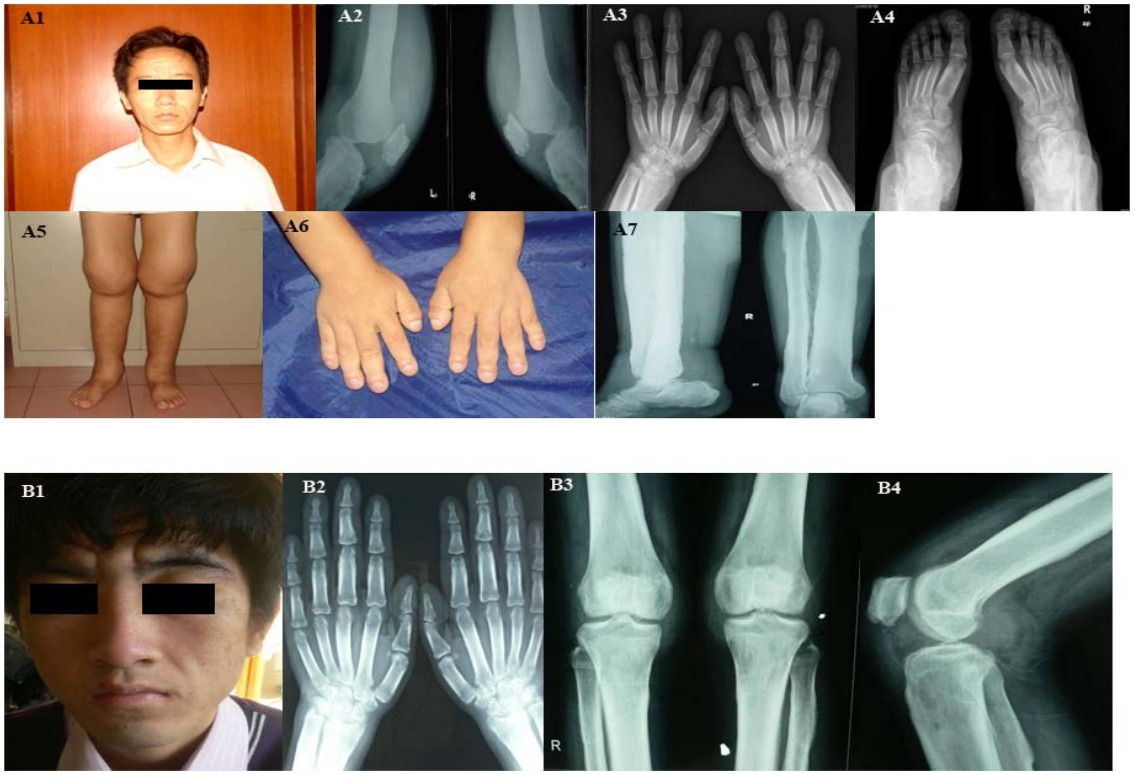

Figure S1. Clinical images of affected individuals (P2 and P3) from pedigrees family 2 (A) and family 3 (B)

The images show the thickening and furrowing of the facial skin (**A1** and **B1**) and clubbing of the fingernails and toenails (**A2** and **A5**). Hand radiographs show the loss of normal tabulation of the metacarpals and phalanges, cortical thickening of the metacarpals and proximal and middle phalanges as well as marked soft-tissue swelling (**A3** and **B2**). Feet radiographs show cortical thickening and acro-osteolysis (**A4**). The knee images show marked swelling, and the radiographs show periosteal hyperostosis of the knee region with patellar sclerosis and sclerosis of both the distal femur and tibiofibula (**A5-7** and **B3** and **B4**). All images are published with permission from the patients.

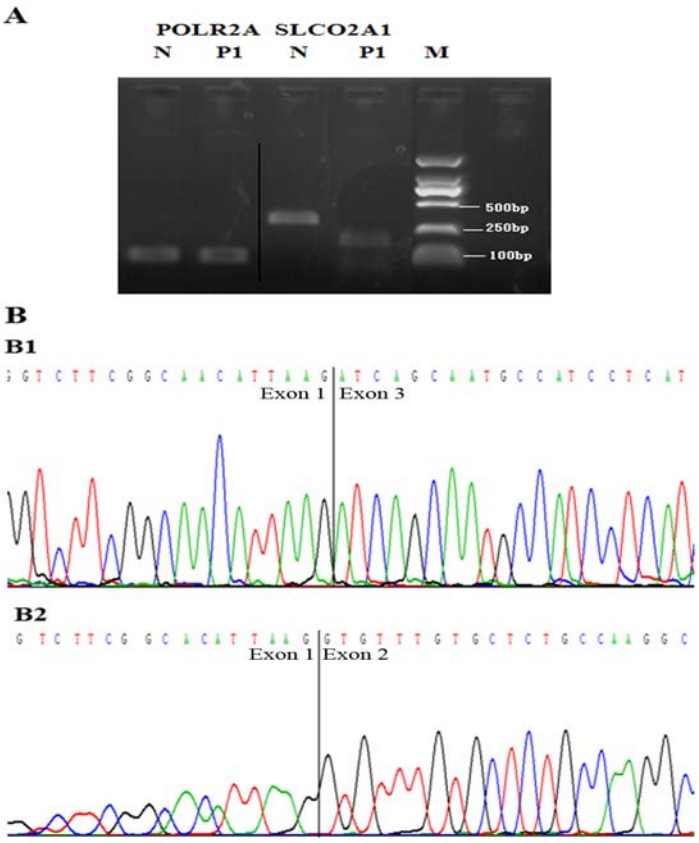

Figure S2. mRNA expression and cDNA analysis by RT-PCR and sequencing in family1-P1 with *SLCO2A1* c.97-1G>A mutation

Total RNA was extracted from the conchal cartilage of family1-P1 and articular cartilage of the knee of control individual, respectively, and then subjected to reverse transcription (RT) with the PrimeScript 1st stand cDNA synthesis kit (TakkaRa). PCR amplification was performed to produce cDNA fragments spanning the c.97-1G>A mutation with primers 5 ' -TCCCAGGGCAGCGACACCTCTACT-3 ' and 5 ' -CGGAGAGGAAGTGTGGGAGGGTGA-3 ' , and a 119bp fragment of human *POLR2A* by primers 5 ' -CCCCCAAAGGCTCAACCTACTC-3 ' and 5 ' -GTGCCCTCAGTTCTCCTCGTCA-3 ' .

(A) Electrophoresis of RT-PCR products. The expected 340bp fragment was only seen in the control individual whereas an extra short 202bp fragment was found in the affected individual. M: DNA marker; N: control individual; P1: family1-P1. **(B)** Analysis of cDNA sequencing. cDNA sequencing demonstrated the skipping of exon 2 in family1-P1 (**B1**), and normal sequence in control individual (**B2**).

Table S1. An overview of the whole exome sequencing data production

Exome Capture	**Family1-P1**
Initial bases in target	37,640,396
Initial bases near target	57,236,802
Initial bases in or near target	94,877,198
Total effective reads	20,553,554
Total effective yield (Mb)	1,784.61
Average read length (bp)	86.83
Effective sequence in target (Mb)	1,262.10
Effective sequence near target (Mb)	188.81
Effective sequence in or near target (Mb)	1,450.91
Fraction of effective bases in target	70.70%
Fraction of effective bases in or near target	81.30%
Average sequencing depth over target	33.53
Average sequencing depth near target	3.3
Mismatch rate in the target region	0.37%
Mismatch rate in all of the effective sequence	0.39%
Bases covered in target	36,854,069
Coverage of the target region	97.90%
Bases covered near target	27,825,307
Coverage of flanking regions	48.60%
Fraction of target covered at least 20×	57.30%
Fraction of target covered at least 10×	78.90%
Fraction of target covered at least 4×	92.30%
Fraction of flanking regions covered at least 20×	3.70%
Fraction of flanking regions covered at least 10×	9.80%
Fraction of flanking regions covered at least 4×	22.50%

Table S2. A summary of the SNPs from an exome capture sample

Exome Capture	**Family1-P1**
Number of genomic positions for calling SNPs	106,163,831
Number of high-confidence genotypes	63,403,381
Number of high-confidence genotypes in the target region	36,119,062
Number of known SNP sites in the target region	155,125
Coverage of population SNPs in the target region	141760 (91.38%)
Total number of SNPs	31,738
Synonymous coding	7,871
Missense	6,677
Nonsense	51
Read through	4
Splice site	320
Introns	15,179
5' UTRs	539
3' UTRs	909
Intergenic	188

Table S3. Direct identification of the causal gene for Family1-P1 by exome sequencing

Filter	Family1-P1 (whole / homozygous)
Total number of SNPs	31,738
NS/SS in the coding region	7038 / 3136
NS/SS not in dbSNP129	718 / 46
NS/SS not in Hg18	614 / 43
NS/SS not in 1000 genome	472 / 28
NS/SS not in YanHuang	468 / 28

Table S4. Identified 28 genes containing homozygous mutations in Family1-P1 by exome sequencing

Gene name	MIM number	Mutation
AMBRA1	611359	N952S
OR4C46	614273	H120R
OR6Q1	-	A190T
PYGM	608455	R642L
ATG2A	-	R1212H
NPAS4	608554	P207S
DPP3	606818	L183S
NADSYN1	608285	E322K
KRTAP5-7	-	C36S
SERPINH1	600943	A63V
GNPTAB	607840	R1191H
STAB2	608561	L96H
ALDH1L2	613584	L577V
IFT81	605489	M83I
KRTAP9-3	-	Q20K
KRT37	604541	Q235X
ABCA7	605414	R1885H
NCLN	609156	K157Q
LILRB3	604820	H61D
TFCP2L1	609785	Y249C
CCDC74B	-	N104D
PTPN18	606587	T251A
SLCO2A1	601460	c.9797-1G>A, Splice mutation
MAGEC1	300223	P232S
MAGEA9B	300764	R295G
MAGEA9	300342	R295G

ITIH5L	-	L846F
SHROOM2	300103	A898V