Additional file 1

Audiological and molecular-genetic findings in the selected sample of 114 osteogenesis imperfecta patients

Family No.	F/Sp	Individuals		Hearing characteristics			Genotypic characteristics				OI type
		M/F	Age	Hearing (L/R)	Onset	Otological history	*COL*	c-notation p-notation	Struct/Haplo	Location	
1	F	M	31	M/M	25	NE	*1A2*	*c.1009G>A* *p.Gly337Ser*	Struct	Triple helix	IV
		M	43	0/0							
		M	51	0/0		NE					
2	F	F	42	M/M	22	NE	*1A1*	*c.3079delG* *p.Asp1027ThrfsX81*	Haplo	Triple helix	I
		F	43	0/0							
		F	65	M/M	42						
3	F	F	40	S/0	38	SF	*1A1*	*c.2028+1G>A*[a]	Haplo[b]	Triple helix	I
4	F	M	41	S/S	20	OM	*1A2*	*c.2558G>T* *p.Gly853Val*	Struct	Triple helix	I
5	F	F	13	M/C	9		*1A1*	*c.658C>T* *p.Arg220X*	Haplo	Triple helix	I
		M	55	M/M	9	SF					
6	F	F	45	M/M	12		*1A1*	*c.3258delC*[a] *p.Ala1087ProfsX21*	Haplo	Triple helix	I
7	F	F	18	M/M	30	NE	*1A1*	*c.769G>A* *p.Gly257Arg*	Struct	Triple helix	IV
		M	38	M/M	17	NE					
8	F	F	36	S/0	35		*1A1*	*c.3637delG*[a] *p.Gly1213AlafsX26*	Haplo	C-terminal propeptide	I
		F	60	S/S	50						
9	F	F	31	M/M	17		*1A1*	*c.3765delC*[a] *p.Ala1256ProfsX76*	Haplo	C-terminal propeptide	I
		F	32	M/M	30						
		F	67	M/M	18						
10	F	M	40	0/0			*1A1*	*c.1792C>T* *p.Arg598X*	Haplo	Triple helix	I
		M	41	0/0		NE					
		F	42	0/0							
11	F	F	47	0/0			*1A1*	*c.3370-1delG*[a]	Haplo[b]	Triple helix	I
12	F	M	24	M/0	20	NE	*1A1*	*c.1128delT* *p.Gly377AlafsX164*	Haplo	Triple helix	I
		F	53	M/M	39	NE					
13	F	F	16	M/M	14		*1A1*	*c.543+2T>C*[a]	Haplo[b]	N-terminal propetide	I
14	F	F	40	0/0		OM	*1A1*	*c.3495delT* *p.Gly1166ValfsX73*	Haplo	Triple helix	I

Family No.	F/Sp	Individuals		Hearing characteristics			Genotypic characteristics				OI type
		M/F	Age	Hearing (L/R)	Onset	Otological history	*COL*	c-notation p-notation	Struct/Haplo	Location	
15	F	F	22	M/0	21		*1A1*	*c.2128-3T>G*[a]	Haplo[b]	Triple helix	I
		F	49	M/M	35	OM					
16	F	F	40	M/M			*1A2*	*c.2414G>C* *p.Gly805Arg*	Struct	Triple helix	I
		F	54	S/S	49						
17	F	F	21	M/C	16	OM	*1A1*	*c.658C>T* *p.Arg220X*	Haplo	Triple helix	I
18	F	F	26	0/C	18	OM	*1A1*	*c.334-9A>G*[a,c]	Unknown	N-terminal propeptide	I
		F	52	M/0	18						
19	F	F	37	S/S	25		*1A2*	*c.1009G>A* *p.Gly337Ser*	Struct	Triple helix	IV
20	F	M	46	S/S	42		*1A1*	*c.484delC*[a] *p.Gln162SerfsX102*	Haplo	Triple helix	I
		M	49	0/S	15						
		M	75	M/M	22						
21	F	M	30	M/M	22	OM; NE	*1A1*	*c.2016dupC*[a] *p.Ser673LeufsX37*	Haplo	Triple helix	I
22	F	F	46	S/S	12	OM	*1A1*	*c.769G>A* *p.Gly257Arg*	Struct	Triple helix	I
23	F	F	44	0/0			*1A1*	*c.1984-5C>A*	Haplo	Triple helix	I
24	F	M	24	C/C	16		*1A1*	*c.3241delG* *p.Val1081LeufsX27*	Haplo	Triple helix	I
		F	37	C/C	35						
		M	49	M/M	33						
		M	54	0/0							
25	F	F	32	M/M	27	OM	*1A1*	*c.1003-2A>G*	Unknown	Triple helix	I
		M	60	S/M	38	NE					
26	F	M	16	S/S	13		*1A1*	*c.579delT* *p.Gly194ValfsX71*	Haplo	Triple helix	I
		M	45	M/M	35	NE					
		F	50	S/S	10						
		M	50	S/S	28/40						
		F	54	M/M	15/20	OM					
27	F	M	16	M/M	14		*1A1*	*c.2451+94G>T*[c]	Unknown	Triple helix	I
		F	18	0/M	18						
		M	49	0/0		NE					

Family No.	F/Sp	Individuals		Hearing characteristics			Genotypic characteristics				OI type
		M/F	Age	Hearing (L/R)	Onset	Otological history	*COL*	c-notation p-notation	Struct/Haplo	Location	
28	F	F	21	M/M	12	OM	*1A1*	*c.2559+1G>A*[a]	Haplo[b]	Triple helix	I
		F	35	M/M	13						
		F	44	M/M	11	OM					
		M	50	M/M	18	OM					
29	F	M	36	M/M	16	OM; NE	*1A1*	*c.670G>A*[a] *p.Gly224Ser*	Struct	Triple helix	I
		M	46	M/M	30	SF					
		M	46	M/M	15	OM					
		F	54	M/M	25	OM					
		F	73	M/M	37						
30	F	M	19	C/C	19/25		*1A1*	*c.2028+2T>G*	Haplo	Triple helix	I
		M	29	M/M	18/20						
		M	39	M/M	30	NE					
		M	57	S/M	36	NE					
31	F	F	30	0/M	25		*1A1*	*c.3477delT p.Gly1160AlafsX79*	Haplo	Triple helix	I
32	F	M	60	0/S	40		*1A1*	*c.1668delT p.Gly557ValfsX23*	Haplo	Triple helix	I
33	F	F	13	S/S	11	OM	*1A2*	*c.2025+4A>G*	Struct	Triple helix	IV
		M	51	0/0							
34	F	F	26	C/C	12/21		*1A2*	*c.2746G>A*[a] *p.Gly916Arg*	Struct	Triple helix	I
		F	41	M/M	38/29						
		M	89	0/0							
35	F	F	41	M/M	25		*1A1*	*c.2073delT p.Gly692ValfsX74*	Haplo	Triple helix	I
36	F	M	54	M/M	38	OM; SF	*1A1*	*c.3910C>T p.Gln1304X*	Haplo	C-terminal propeptide	I
37	F	F	10	M/M	8		*1A1*	*c.3100-1G>A*[a,c]	Unknown	Triple helix	I
		M	24	0/S	22						
		F	45	S/S	37						
38	F	M	26	M/M	20	NE	*1A1*	*c.1812delT*[a] *p.Gly605AlafsX161*	Haplo	Triple helix	I
		M	35	M/M	30						

Family No.	F/Sp	Individuals		Hearing characteristics			Genotypic characteristics				OI type
		M/F	Age	Hearing (L/R)	Onset	Otological history	*COL*	c-notation p-notation	Struct/Haplo	Location	
39	F	F	12	C/C	5	OM					
		F	14	0/C	14						
		F	30	M/M	15/20		*1A1*	*c.1354-12G>A*	Haplo	Triple helix	I
		F	40	0/0							
		M	67	S/S	45						
40	F	F	19	M/C	16	OM					
		F	39	M/M	5	OM; NE	*1A1*	*c.910insGGGCCCC*[a] *p.Arg304GlyfsX7*	Haplo	Triple helix	I
		F	41	S/S	31						
41	F	F	30	C/C	24		*1A2*	*c.2746G>C p.Gly916Arg*	Struct	Triple helix	IV
42	F	F	28	S/M	15		*1A1*	*c.3540delC*[a] *p.Gly1181AlafsX58*	Haplo	Triple helix	I
43	F	F	49	0/0		OM	*1A2*	*c.838G>A p.Gly280Ser*	Struct	Triple helix	IV
44	F	M	20	M/M	16		*1A1*	*c.1299+1G>A*	Unknown	Triple helix	I
45	F	M	59	M/M	31		*1A1*	*c.3027delT p.Gly1010ValfsX98*	Haplo	Triple helix	IV
46	F	M	50	M/M	35		*1A1*	*c.3046-1G>T*	Haplo	Triple helix	I
47	F	F	24	0/C	23		*1A1*	*c.697-2_697-1del*	Unknown	Triple helix	I
48	F	M	31	M/M	24		*1A1*	*c.757C>T p.Arg253X*	Haplo	Triple helix	I
49	F	F	40	0/0			*1A1*	*c.2028+4A>G*[a]	Haplo[b]	Triple helix	I
50	F	M	23	M/M	18		*1A1*	*c.1299+1G>A*	Unknown	Triple helix	I
51	F	M	11	S/S	11	OM	*1A1*	*c.671delG p.Gly224ValfsX41*	Haplo	Triple helix	I
52	F	M	21	0/S	19		*1A1*	*c.3925C>T p.Gln1309X*	Haplo	C-terminal propeptide	I
53	F	F	23	S/0	18		*1A1*	*c.672_673delTCinsA p.Pro226LeufsX39*	Haplo	Triple helix	IV
54	F	M	11	C/C	9	OM	*1A1*	*c.658C>T p.Arg220X*	Haplo	Triple helix	I
		F	43	M/M	16	OM					
55	Sp	F	28	C/M	24	OM	*1A2*	*c.982G>A p.Gly328Ser*	Struct	Triple helix	III
56	Sp	F	62	0/0			*1A2*	*c.486+1G>C*[a]	Struct[d]	Triple helix	I

Family No.	F/Sp	Individuals		Hearing characteristics			Genotypic characteristics				OI type
		M/F	Age	Hearing (L/R)	Onset	Otological history	*COL*	c-notation p-notation	Struct/Haplo	Location	
57	Sp	M	45	0/0		SF	*1A1*	*c.1065delT*[a] *p.Gly356ValfsX184*	Haplo	Triple helix	I
58	Sp	F	26	C/0	24	OM; SF	*1A2*	*c.1378G>A* *p.Gly460Ser*	Struct	Triple helix	III
59	Sp	M	29	M/M	17	NE	*1A1*	*c.879_880del*[a] *p.Glu294LysfsX16*	Haplo	Triple helix	IV
60	Sp	F	11	M/M	9	OM	*1A2*	*c.3043G>A* *p.Gly1015Arg*	Struct	Triple helix	IV
61	Sp	M	34	M/M	9		*1A1*	*c.3076C>T* *p.Arg1026X*	Haplo	Triple helix	I
62	Sp	F	13	M/M	11		*1A1*	*c.2921G>C* *p.Gly974Ala*	Struct	Triple helix	IV
63	Sp	F	48	S/M	16		*1A1*	*c.2366delC*[a] *p.Pro789LeufsX318*	Haplo	Triple helix	I
64	Sp	M	9	S/S	7		*1A2*	*c.2432G>C* *p.Gly811Ala*	Struct	Triple helix	I

OI=osteogensis imperfecta; F=familial OI; Sp=sporadic OI; M=male; F=female; L=left ear; R=right ear; 0=normal hearing; C=conductive hearing loss; M=mixed hearing loss; S=sensorineural hearing loss; OM=otitis media; NE=noise exposure; SF=skull fracture; *COL*=mutated collagen gene; *1A1=COL1A1*; *1A2=COL1A2*; c-notation: notation of the mutation at cDNA level; p-notation: notation of the mutation at protein level; Struct=structurally abnormal type I collagen; Haplo=haploinsufficiency of type I collagen; C-terminal propeptide=mutation located in the carboxy-terminal propeptide of the α-chain; N-terminal propeptide=mutation located in the amino-terminal propeptide of the α-chain.

Nomenclature of mutations and numbering of the *COL1A1* and *COL1A2* genes is based on the wild-type sequences submitted under [GenBank:NG_007400.1] and [GenBank:NG_007405.1], respectively.

[a]Sequence variant that has not been reported before as it was not yet included in the osteogenesis imperfecta variant database (Dalgleish, R: D**atabase of osteogenesis imperfecta and type III collagen mutations.** [http://www.le.ac.uk/genetics/collagen]).

[b]Haploinsufficiency of type I collagen has previously been confirmed by reduced biochemical migration of type I collagen and a positive *COL1A1* null allele test on the proband's cDNA obtained from skin fibroblasts.

[c]Causality of the mutation was verified using the splice site prediction software **Fruitfly** [http://www.fruitfly.org/seq_tools/splice.html] and **Netgene2 server** [http://www.cbs.dtu.dk/services/NetGene]. Sequencing of 95 controls revealed negative outcomes for this sequence variant.

[d]Deviant biochemical elektrophoretic pattern for type I collagen confirmed the synthesis of structurally abnormal type I collagen.