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Mutations in the *COL1A1 and COL1A2* genes associated with *osteogenesis imperfecta* (*OI*) types I or III

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Although over 85% of *osteogenesis imperfecta* (*OI*) cases are associated with mutations in the procollagen type I genes (*COL1A1* or *COL1A2*), no hot spots for the mutations were associated with particular clinical phenotypes. Eight patients that were studied here, diagnosed with *OI* by clinical standards, are from the Polish population with no ethnic background indicated. Previously unpublished mutations were found in six out of those eight patients. Genotypes for polymorphisms (Sp1 – rs1800012 and *Pvu*II – rs412777), linked to bone formation and metabolism were determined. Mutations were found in exons 2, 22, 50 and in introns 13 and 51 of the *COL1A1* gene. In *COL1A2,* one mutation was identified in exon 22. Deletion type mutations in *COL1A1* that resulted in *OI* type I had no effect on collagen type I secretion, nor on its intracellular accumulation. Also, a single base substitution in I13 (c.904-9 G>T) was associated with the *OI* type I. The *OI* type III was associated with a single base change in I51 of *COL1A1*, possibly causing an exon skipping. Also, a missense mutation in *COL1A2* changing Gly→Cys in the central part of the triple helical domain of the collagen type I molecule caused *OI* type III. It affected secretion of the heterotrimeric form of procollagen type I. However, no intracellular accumulation of procollagen chains could be detected. Mutation in *COL1A2* affected its incorporation into procollagen type I. The results obtained shall help in genetic counseling of *OI* patients and provide a rational support for making informed, life important decisions by them and their families.

Key words: *osteogenesis imperfecta*, *COL1A1*, *COL1A2*, mutation, polymorphism

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Abbreviations: *OI*, *osteogenesis imperfecta*; EMQN, The European Molecular Genetics Quality Network; *COL1A1* or *COL1A2*, procollagen type I genes

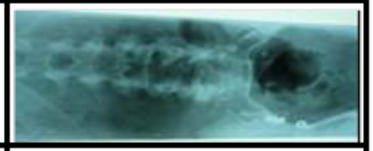
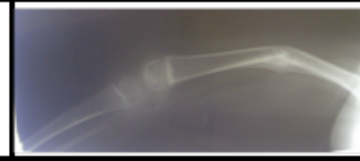
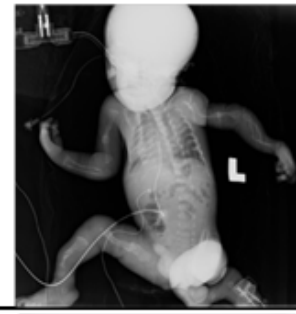
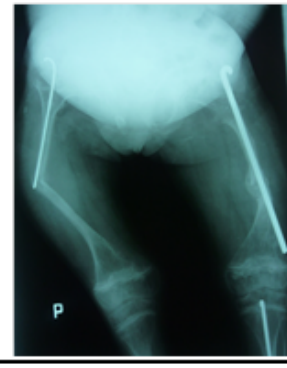
Patient number	Mtated gene	Type of OI	Mutation Polymorphisms genotype	RTG
91-D/F	*COL1A1*	I	**E2**/c.231delG/ p.Thr78Pro/fs*76 SS (G/G) Pp (A/C)	
73-F			**E50**/c.[3881A>T;3882_3891del]/ p.Glu1294Val/fs*32 SS (G/G) pp (C/C)	
137/M		III	**I51**/c.4248+1G>A/exon skipping SS (G/G) PP (A/A)	
19/F	*COL1A2*		**E22**/c.1207G>T/p.Gly403Cys SS (G/G) Pp (A/C)	

Figure S1. Representative X-rays of patients with type I and III *OI*.