OSTEOGENESIS IMPERFECTA FOUNDATION
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Facts about Osteogenesis Imperfecta

OI Type Chart

Well over a thousand different mutations involving more than a dozen genes have been associated with OI. Currently, there are several systems for addressing the clinical and genetic variability of OI. Some focus on clinical severity as the overriding measure while others focus on specific gene causes to distinguish types. Others integrate both. Broadly speaking, based on severity of the clinical picture, OI can be grouped into 4 classes – mild, moderate, severe, and extremely severe or lethal. About 85-90% of cases are inherited in an autosomal dominant manner, in which collagen gene mutations affect the quantity or quality of type 1 collagen. These cases are described in Types I-IV on this chart. Genotype/phenotype relationships are incomplete for both dominant and recessive OI and knowing the OI type is not predictive of future function. Knowledge of the mutation provides useful information for genetic counseling. Knowledge of the Type or degree of severity can help establish an initial treatment plan.

This chart is a genetic classification system that includes a description of severity. Additional clinical features are included in the accompanying document, "Distinguishing Clinical Features of OI."

Table: Nosology of Osteogenesis imperfecta

Osteogenesis imperfecta type	Inheritance	Phenotype	Gene Defect
Defects in collagen synthesis, structure or processing			
I	AD	Mild	Null *COL1A1* allele
II	AD	Lethal	*COL1A1* or *COL1A2*
III	AD	Progressive deforming	*COL1A1* or *COL1A2*
IV	AD	Moderate	*COL1A1* or *COL1A2*
XIII	AR	Mild to severe	*BMP1*
Defects in bone mineralization			
V	AR	Variable, distinctive histology	*IFITM5*
VI	AR	Moderate to severe	*SERPINF1*
Defects in collagen modification			
VII	AR	Severe (hypomorphic) Severe to lethal (null)	*CRTAP*
VIII	AR	Severe to lethal	*LEPRE1*
IX	AR	Moderate to lethal	*PPIB*
XIV	AR	Severe	*TMEM38B*
Defects in collagen folding and cross-linking			
X	AR	Severe to lethal	*SERPINH1*
XI/BRKS1	AR	Mild to severe	*FKBP10*
BRKS2	AR	Moderate to severe	*PLOD2*
Defects in osteoblast development with collagen insufficiency			
XII	AR	Severe	*SP7*
XV	AR	Severe	*WNT1*
XVI	AR	Severe	*CREB3L1*

Abbreviations: AD = autosomal dominant; the mutation is inherited in a dominant manner
AR = autosomal recessive; the mutation is inherited in a recessive manner

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References

Forlino, A., Cabral, W.A., Barnes, A.M., and Marini, J.C. (2011) New Perspectives on Osteogenesis Imperfecta. Invited Review. Nature Reviews Endocrinology, 7(9): 540-57.

Marini JC, Blissett AR. 2013. New Genes in Bone Development: What's New in Osteogenesis Imperfecta. Journal of Clinical Endocrinology and Metabolism 98:3095-3103.

Shapiro JR. Clinical and Genetic Classification of Osteogenesis Imperfecta and Epidemiology (253-257). In Shapiro JR, (Ed.). (2014) Osteogenesis Imperfecta: A Translational Approach to Brittle Bone Disease 1st edition. New York, NY: Elsevier Academic Press.

Warman, ML, et al. Nosology and Classification of Genetic Skeletal Disorders: 2010 Revision. American Journal of Medical Genetics, 2011: 155: 943- 968.

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