



Recessive Forms of OI

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The Osteogenesis Imperfecta Foundation, Inc. is the only voluntary national health organization dedicated to helping people cope with the problems associated with osteogenesis imperfecta. The Foundation's mission is to improve the quality of life for people affected by OI through research to find treatments and a cure, education, awareness, and mutual support.

Recent discoveries expand our understanding of osteogenesis imperfecta (OI).

Genetics/Inheritance

Two recessive forms of OI were identified in 2006. Unlike the dominant forms of OI, the recessive forms do not involve mutations to the type I collagen genes. Instead, they involve two genes that affect collagen modification – CRTAP (cartilage-associated protein) and LEPRE1, which produces prolyl 3-hydroxylase 1 (P3H1). These two proteins, CRTAP and P3H1, interact with collagen and modify amino acids in the collagen chains.

These discoveries provide important information for people diagnosed with severe OI based on clinical symptoms who do not carry a type I collagen mutation. Defects in CRTAP and P3H1 appear to account for most of the cases of severe/lethal OI which do have biochemically abnormal collagen, but do not have a collagen mutation. Recessive OI has been discovered only in individuals with lethal, severe or moderate OI. There is no evidence to date of a recessive form of mild OI.

When a child has recessive OI, there is a 25 percent chance per pregnancy that the parents will have another child with OI. Siblings of a person with a recessive form of OI have a 50 percent chance of being a carrier of the recessive gene.

The majority of cases of OI (possibly 85-90%) are caused by a dominant mutation in a gene coding for type I collagen (COL1A1 or COL1A2). These forms have recently been referred to as “Classical OI” in the research literature, and are described by the Sillence Classification of Type I through IV OI.

Types of Recessive OI

The information about recessive OI expands and enhances the list of types.

Type VI

- Similar to Type IV classical OI in appearance and symptoms of OI
- Distinguished by a characteristic mineralization defect seen in biopsied bone
- Does not have a type I collagen mutation
- Mode of inheritance is unknown but most likely recessive

Type VII

- The first described cases resemble Type IV classical OI in many aspects of appearance and symptoms
- In other instances the appearance and symptoms are similar to Type II lethal OI, except infants had white sclerae, small head and round face
- Short humeri and femora
- Short stature
- Coxa vara is common (the acutely angled femur head affects the hip socket)
- Results from recessive inheritance of a mutation to CRTAP gene. Partial function of CRTAP leads to moderate bone dysplasia while total absence of CRTAP has been lethal in all 4 identified cases

Type VIII

- Similar to Type II or Type III classical OI in appearance and symptoms except for white sclerae
- Severe growth deficiency
- Extreme skeletal under mineralization (DEXA L1-L4 = -6 to -7)
- Caused by absence/severe deficiency of P3H1 due to a mutation to the LEPRE1 gene

Impact of Discovery of Recessive Forms of OI

- The majority of OI cases (possibly 85-90%) are still caused by a dominant mutation in one of the type I collagen genes
- No specific treatment recommendations can be made for recessive OI at this time.
- It is not clear that people with recessive OI will respond in the same way to the same treatments as people with dominant OI.
- May provide specific information for families when a type I collagen mutation has not been found in the family member who has OI
- Expands the information available to genetic counselors pertinent to the type of OI, prognosis, and odds of recurrence
- Expands information available to genetic counselors regarding severely affected infants
- Allows siblings of a person diagnosed with recessive OI to obtain testing to determine their carrier status
- Allows for prenatal diagnosis in an affected family

Testing for Recessive OI

Testing information for recessive OI is available from Baylor College of Medicine, the National Institutes of Health and the Shriners Hospital for Children in Montreal.

Baylor Medical Genetics Laboratories
Telephone: 1-800-411-4363
Fax: 713-798-6584
E-mail: geneticstest@bcm.edu
Web site: www.bcm.edu/geneticlabs

OI Research Program at NICHD
Telephone: 301-496-0741
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Web site: www.oiprogram.nichd.nih.gov

Genetics Unit, Shriners Hospital for Children – Canada
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References

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