

A Wide Variety of Different Mutations of Collagen Seem to Be Responsible for Most Cases of Osteogenesis Imperfecta

Collagen is responsible for much of the strength of connective tissue. It consists of a triple helix of polypeptides, each with repeating segments of amino acids, with every third amino acid being a glycine molecule. The three polypeptides are tightly wound together, and glycine occupies the axial position. Thus, when mutations occur at a glycine site, the molecule is greatly weakened. Each collagen molecule (more than ten have been described) may be constructed of the same or combinations of different polypeptides.

Most cases of osteogenesis imperfecta (OI) are associated with mutations in type I collagen. Clinical effects depend on the particular position and domain of the collagen molecules in which a mutation or substitution occurs;

the closer the mutation occurs to the carboxyl terminus of the polypeptide of type I collagen, the more severe the clinical defect. Specific mutations have been identified in most cases of the lethal type of OI and for many non-lethal types. Each family has a distinct mutation that is different from mutations found in other families. Identification of a specific alteration or mutation can be used to recognize carriers in a particular family and to assist in prenatal diagnosis.

Sykes B. *Nature* 1987;330: 607-608.

Editor's comment—*OI, a relatively common bone disorder that leads to short stature and multiple fractures in most cases, has several clinical subtypes. Recent research on collagen demonstrates the molecular basis for the disease and allows prenatal diagnosis. Recently, Byers brilliantly reviewed the subject of OI in this publication (vol. 4, no. 2). Readers are encouraged to read Dr. Byers' article.*

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