Dominant and recessive pattern of osteogenesis imperfecta

Science, Biology

Osteogenesis Imperfecta Dominant and Recessive Pattern Background

Osteogenesis Imperfecta (OI) is heterogenous genetic disorder in the type I collagen and is characterized by susceptibility bone fragility and fractures with variable severity and presumed or proven defect in type I collagen biosynthesis.

Type I collagen is the abundant protein composing the extracellular matrix of bone and skin in human body. There are 3 pathogenesis mechanisms of OI: 85-90% of individuals with OI have dominant mutation in type I procollagen genes (COL1A1 and COL1A2) and recessive mutation of OI occur in genes involved in defect of collagen modifying enzymes (CRTAP, LEPRE1 and PPIB) and in genes coding type I procollagen chaperones (SERPINH1 and FKBP10). A new OI candidate recessive pattern had already revealed, SP7/Osterix (OSX), encodes a transcription factor containing three Cys2Hys2 zinc-finger DNA binding domain at its C terminus caused bone formation disorder. Methods To identify the presence of mutations and the pattern of inheritance in collagen type I from individuals with clinical appearance of OI (type I-IV). We performed whole gene sequencing in dominant genes (COL1A1, COL1A2) . For individuals that we can not find mutation in both of those genes and based on biochemical screening of fibroblast sample of patients, we set up whole sequence for overmodification patients to run with CRTAP, LEPRE1 and PPIB genes and for non overmodification to run with SERPINH1 and FKBP10 in a cohort of 107 patients. We proposed to look for a new candidate genes, if we can not find mutations for patients that we already run with known published genes caused OI.

Results In 107 patients with complete analysis, we found 28 mutations, 8 mutations in COL1A1 and 20 mutations in COL1A2. We also found 1 homozygote mutation in FKBP10. Conclusion Key words: OI, overmodification, non overmodification, known published genes of OI, new candidate genes of OI