

10th International Conference on Osteogenesis Imperfecta

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Over 150 participants from 22 countries attended this conference in Ghent Belgium. The participants included basic researchers, clinicians and representatives of patient organizations. The keynote lecture reminded the audience that studies of OI were now in their 4th age, having passed through a clinical descriptive age resulting in the classification by David Sillence, a biochemical age that focused on collagen biochemistry and abnormalities in collagen folding, a molecular genetics age in which the genes were cloned and the segments were distributed in the research community, and are now in the database age, with both patient databases and mutations databases containing over a thousand cases for correlation and understanding. The classification was reviewed by Dr Sillence and updated by Dr. Glorieux. The updated results of the Collagen Mutation Consortium continued to support the models of the 2005 publication, suggesting distinct roles in matrix for each alpha chain. Speakers also reviewed the consequences of special collagen mutations, including substitutions in non-glycine residues and in the C-propeptide domains of the COL1A1 and COL1A2 genes.

The meeting also focused on bone resorption and formation in OI, with new insights from the Brl mouse about the important role of osteoclasts in the mechanism of the phenotype. Another murine model, this time for a defect in the C-propeptide of collagen, was shown to have increased cell stress and apoptosis.

An entire session focused on the new recessive forms of OI, caused by deficiency of components of the collagen prolyl 3-hydroxylation complex, CRTAP or P3H1. Speakers presented clinical and molecular features of cases and the occurrence of founder alleles in several populations, including one in the African American population that apparently originates in West Africa.

The clinical session ranged from cardiology, hearing loss, and dental abnormalities to orthopedics, with a strong focus on the role of bisphosphonates in treatment of pediatric OI. A lively discussion concerned whether this family of drugs actually decreased long bone fracture rates or simply affected the spine. The detrimental side effects of high cumulative doses of bisphosphonates were reviewed and treatment limitation at 3 or 4 years was proposed.

The final session of the conference looked to novel therapeutic approaches. Molecular approaches such as RNAi and ribozymes have success in cells in suppressing transcripts from the mutant allele. *In utero* cell therapy was modeled in the Brl mouse, with investigators reporting positive changes in bone mechanics in the context of a low bone cellular uptake.

The meeting outcome includes a plan for a collaborative publication of the updated Collagen Mutation Consortium, after which the consortium list will be posted on the BEMB/NICHHD website.