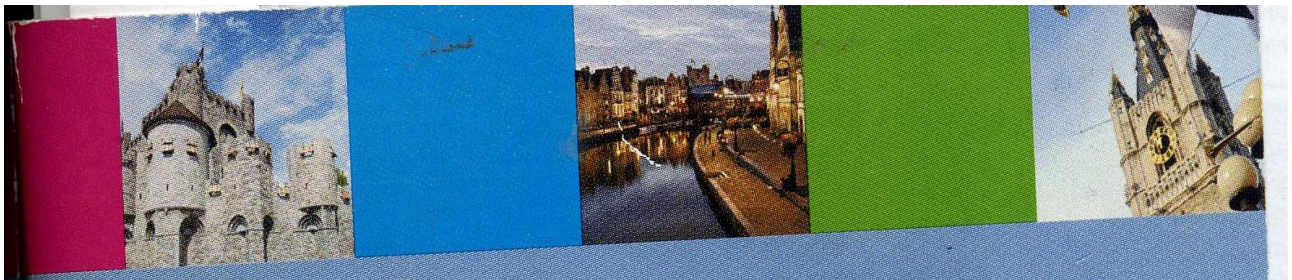
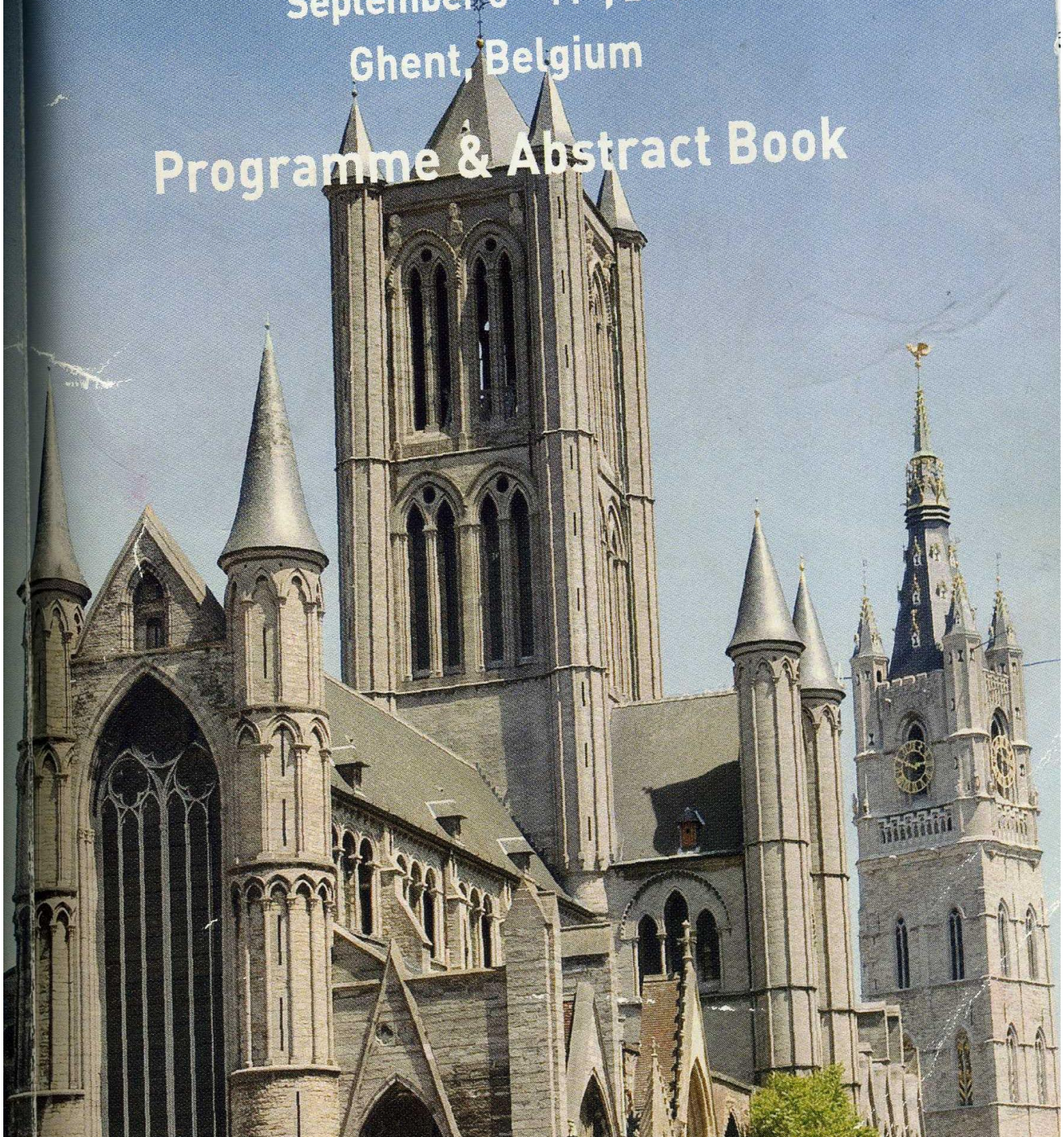


First International Symposium on the Ehlers-Danlos Syndrome

September 8th-11th, 2012

Ghent, Belgium

Programme & Abstract Book



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Classic Ehlers-Danlos syndrome: clinical and molecular characterisation of 37 patients

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Ehlers-Danlos syndrome classic type (cEDS), is a rare autosomal dominant connective tissue disorder characterised by skin hyperextensibility, abnormal wound healing/athrophic scars and joint hypermobility. The prevalence is 1/20.000. In 50% of patients a mutation in genes encoding type V collagen (COLLV), i.e., COL5A1 (46%) and COL5A2 (4%) was reported.

We characterised 37 patients from 27 families: 14 males and 23 females, 13 in the paediatric age and 24 in adulthood, 6 with positive family history. All fulfilled the 4 major diagnostic criteria for the disorder: smooth and hyperextensible skin, atrophic scars, generalised tissue fragility and joint hypermobility except for 2 women without atrophic scars and 1 woman not fulfilling the joint hypermobility criteria. Two patients with the most severe phenotype also showed chronic periarthritis, recurrent enthesopathies, tenosynovitis, asymmetric legs, deep venous thrombosis, rectal and urethral prolapses, hematomas and spontaneous rupture of muscles, and chronic pain syndrome. Wide inter- and intrafamilial phenotypic heterogeneity was observed.

In 24/27 probands COL5A1 or COL5A2 mutations were disclosed by direct gDNA sequencing; 20 were novel COL5A1 mutations (2 recurrent): 6 nonsense, 7 del/ins and 3 splice, all leading to NMD and to COLLV haplo-insufficiency, and 4 missense affecting the structural integrity of COLLV. Two novel COL5A2 splice mutations, leading to in-frame exon skipping, were disclosed in patients with the most severe phenotype. These findings underline the allelic and genetic heterogeneity of cEDS and show that in this patients' series COL5A1/COL5A2 genes are responsible for a larger number of cases (89%) than reported in the literature.