Metabolic cutis laxa

Cutis laxa is a rare skin disorder characterized by wrinkled, redundant, inelastic and sagging skin due to defective synthesis of elastic fibers and other proteins of the extracellular matrix. Wrinkled, inelastic skin occurs in many cases as an acquired condition. Syndromic forms of cutis laxa, however, are caused by diverse genetic defects, mostly coding for structural extracellular matrix proteins. Surprisingly, a number of metabolic disorders have been also found to be associated with inherited cutis laxa. Menkes disease was the first metabolic disease reported with old-looking, wrinkled skin.

Cutis laxa has recently been found in patients with abnormal glycosylation. The discovery of the COG7 defect in patients with wrinkled, inelastic skin was the first genetic link with the Congenital Disorders of Glycosylation (CDG). Since then, several inborn errors of metabolism have been described with cutis laxa (wrinkled skin) of variable severity. These include P5CS, ATP6V0A2-CDG, MAN1B1-CDG, TALDO and PYCR1 defects. New syndromes link copper metabolism to other cutis laxa phenotypes, like MEDNIK syndrome. In spite of the evolving number of cutis laxa-related diseases, a large part of the cases remain genetically unsolved. Our group aims at discovering new cutis laxa syndromes by the use of next generation sequencing. In metabolic cutis laxa syndromes the clinical and laboratory features might partially overlap, however there are some distinct, discriminative features. We use the power of combining metabolic markers and phenotyping in our several novel gene discoveries.