**Introduction**

- The contiguous gene deletion syndrome, CAH-X, was described in 8.5% of congenital adrenal hyperplasia (CAH) patients with a TNXA/TNXB chimera resulting in deletions of CYP21A2, and TNXB, encoding the extracellular matrix glycoprotein tenascin-X (TNX). There are three TNXA/TNXB chimeras described that differ in the junction site, resulting in TNXB haploinsufficiency, dominant negative effect, or biallelic forms and an Ehlers Danlos syndrome (EDS) phenotype. (Chen et al. Human Mutation. 2016)

- TNXB complete deficiency was first described in a patient diagnosed with CAH and classical EDS, and it was autosomal recessive inherited (Burch et al. Nature Genetics 1997).
- TNXB haploinsufficiency is associated with hypermobility type EDS (characterized by generalized joint hypermobility and recurrent joint dislocations, chronic arthralgias, mild skin manifestations and cardiac disorders) (Zweers et al. Am J Hum Genet. 2003).

**Objective**

The aim of this study was to analyze copy number variations and genetic status of TNXB gene in 58 CAH patients due to CYP21A2 deletion to determine the frequency of TNXB alterations in our population.

**Molecular analysis**

- A total of 58 unrelated CAH patients carriers of CYP21A2 gene deletion (65 alleles) were screened for TNXB defects.
- All the patients were analyzed for the presence of CH1 by MLPA analysis (P050-CAH version C1, MRC Holland) evidenced by a 120 bp deletion in TNXB exon 35, and confirmed by exon 35 sequence analysis.
- In addition, all of them were screened for other TNXB alterations related to CH2 and CH3 by exon 40, 41 and 43 Sanger sequencing.

**Clinical Material and Methods**

**Results**

**Biallelic CAH-X genetics and pedigrees**

- CH1 CH1
  - 12316C>G
  - 12316C>G
- CH1 CH2
  - 12316C>G
  - 12316C>G
- CH2 CH3
  - 12316C>G
  - 12316C>G
- CH1 CH3
  - 12316C>G
  - 12316C>G
- CH2 CH2
  - 12316C>G
  - 12316C>G
- CH3 CH3
  - 12316C>G
  - 12316C>G

**Genetic status of TNXA/B chimeras**

- 65 CYP21A2 Del alleles
- 58 patients

**Conclusions**

A high frequency of TNXB alterations was found in CYP21A2 deletion carrier alleles in our population. MLPA and Sanger sequencing techniques resulted useful to characterize TNXB deletion. Accurate genotype-phenotype correlation remains to be elucidated in this cohort. Nevertheless, based on the high frequency of TNXB alterations in CYP21A2 deletion carrier alleles found in this study, we recommend to evaluate TNXB status in these patients, warranting assessment of connective tissue dysplasia including cardiologic alterations in positive cases.