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# A NOVEL FOUNDER MUTATION OF CYP21A2 IN PATIENTS WITH CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY

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## INTRODUCTION

Mutations in *CYP21A2* are the most common cause of congenital adrenal hyperplasia (CAH). Even though disease linked mutations are rarely classified as founder, in this study, we describe a novel founder mutation, c. 2T>C (p.M1?), inactivating the translation initiation codon. We aimed to investigate genotype-phenotype correlation and population based origin of this novel mutation in CAH patients with 21-hydroxylase deficiency.

## RESULTS

In ten patient, we identified a novel homozygous c.2T>C transition in translation initiation codon of the *CYP21A2* ( Fig. A). *In-silico* evaluation of c.2T>C by using open reading finder supports disruption of protein synthesis by this transition. The c.2T>C transition was not detected in ethnically matched 100 healthy controls and *CYP21A1P*. Haplotype analyses of these seven families with four microsatellite markers covering the *CYP21A2* region showed that all patients with c.2T>C have common haplotype ( Fig.B).

All of patients have homozygous and parents heterozygous manner of this mutation, as expected with otozomal resessive inheritance. Six of the seven familes have fist degree of consanguinity, one family has no apperent consanguinity, but, all the seven familes migrated here from another small village, before 3 generations. Thus all familes possibly were relatives.

## CONCLUSIONS

A novel mutation c.2T>C (p.M1?) is suggested to be a founder effect due to reason that it is not present in pseudogene *CYP21A1P*, and all patients carrying this mutation have the same haplotype. Despite the high prevalence of this mutation in our study group, it was not detected in different regions of Turkey and in other populations. This results point out that c.2T>C mutation is a founder mutation specific to the northeast of Turkey

## METHODS

We had 10 patients of seven families and all of the patients had the same founder mutation of *CYP21A2*. Mutation analysis of *CYP21A2* was performed by Long PCR RFLP and southern blot for detecting large rearrangements. The most frequent eleven mutations scanned by ACRS medhod and RPLP analysis. DNA sequence analysis was performed in patients who do not have any of the scanned eleven most common mutations. Haplotype analysis; to detect whether the novel mutation c.2T>C is inherited from common ancestor or not, four microsatellite markers D6S273, D6S1615, D6S1666, D6S2414 flanking the *CYP21A2* gene were tested in six patients along with their parents.

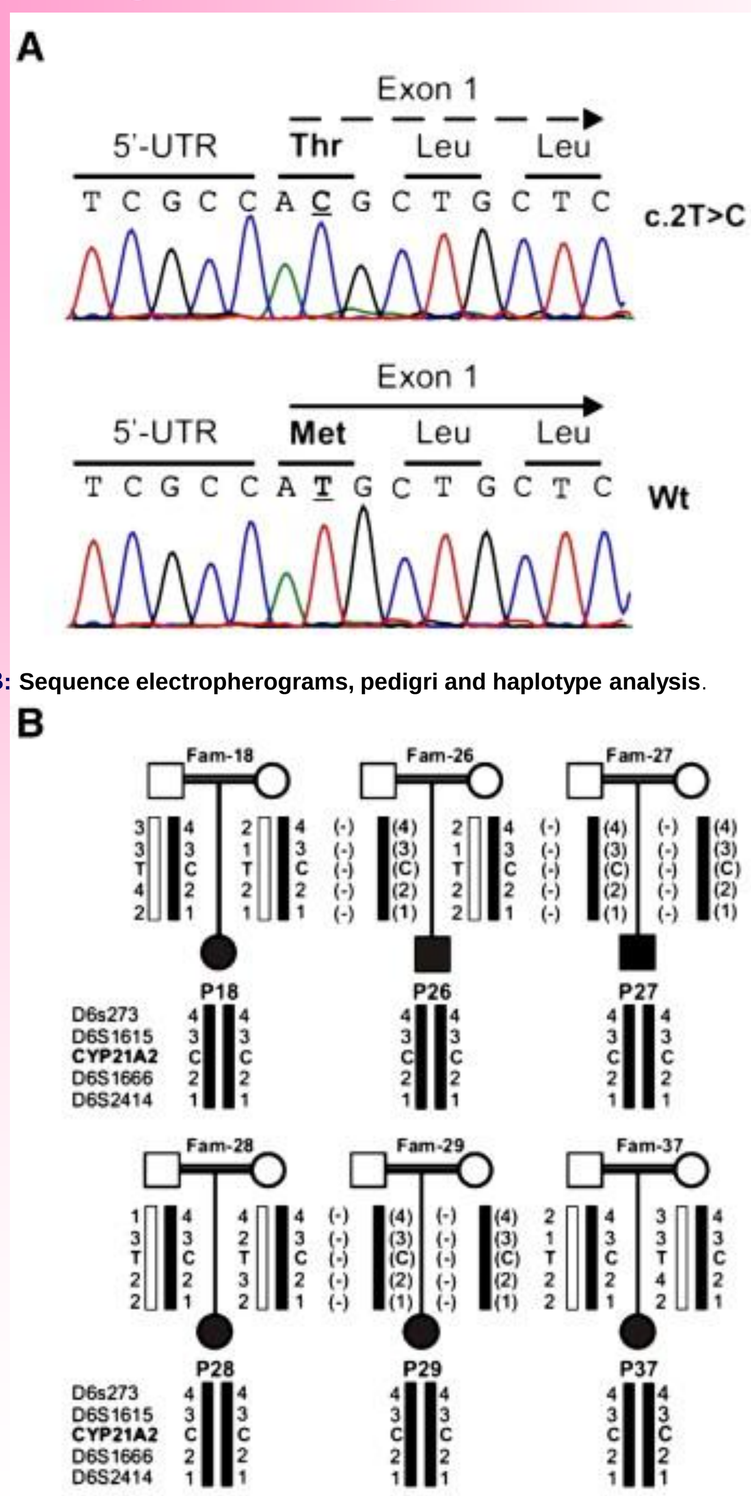


**Figure 1A-B:** Sequence electropherograms, pedigri and haplotype analysis.

Nothing Disclosure