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# Identification of a Novel Mutation in an Iranian Family with 17- $\beta$ Hydroxysteroid Dehydrogenase Type 3 Deficiency

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## INTRODUCTION

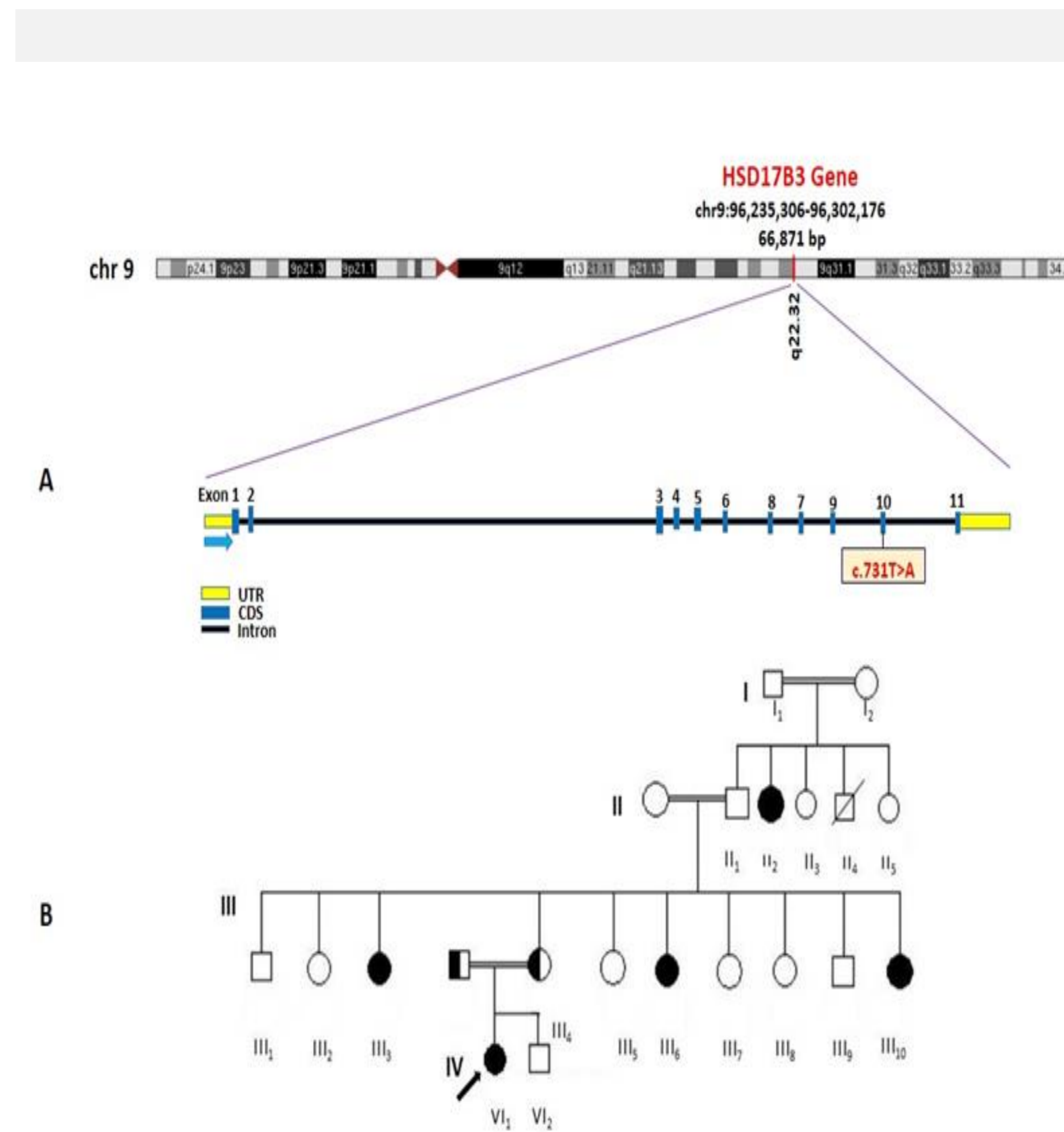
The 17- beta hydroxysteroid dehydrogenase 3 deficiencies (17  $\beta$ HSD-3) affect testosterone biosynthesis and are one of the rare causes of 46, XY DSD. The 17  $\beta$ HSD-3 gene is located on human chromosome 9q22 and includes 11 exons. This gene codes for an enzyme, 17-beta hydroxysteroid dehydrogenase 3, which is the last and key isozymes in the control of male steroid synthesis and exclusively acts on the testes.

## AIM

To present the clinical and genetic features of a male ambiguity due to 17beta-hydroxysteroid dehydrogenase 3 deficiency in a large Iranian family.

## RESULTS

The proposita was an 11-year-old girl and the first child of a consanguineous family. The external genitalia were completely female and had a short vaginal pouch. She had palpable gonads in her inguinal area and underwent bilateral gonadectomy at the age of two. At age 10, she was referred to our clinic for more evaluation. In pelvic sonography, uterine and ovarian were not seen. Her karyotype was 46, XY and her LH and FSH levels were elevated, and three of the patient's aunts and one of the mother's aunts had similar signs.



HSD17B3 gene structure and the mutation. B. Family pedigree of the patient.

|                             | Patient result | Reference range |          |
|-----------------------------|----------------|-----------------|----------|
|                             |                | male            | female   |
| Estradiol, pmol/l           | <33            | 1-288           | 37-258   |
| Testosterone ng/ml          | 0.8            | 2.6-11          | 2.5-10   |
| Androstenedione ng/ml       | 0.4            | 0.6-3.1         | 0.3-3.3  |
| DHEA-S, nmol/ml             | 1.1            | 0.66-6.7        | 0.92-7.6 |
| 17 OH-Progesterone, nmol/ml | 1.3            | 0.2-2.3         | 0.3-4.5  |
| FSH, mIU/ml                 | 140            | 1.4-10.9        | 3.5-9.7  |
| LH mIU/ml                   | 39.6           | 0.1-7.8         | 0.1-7.9  |

Hormonal data on the proposita at age of 10 years

## METHOD

To determine the molecular etiology, whole-exome sequencing (WES) was performed DNAs extracted. The identified mutation was validated using Sanger sequencing. Segregation analysis using Sanger sequencing was performed which confirmed that both parents were heterozygous at the mutation position. We identified a novel homozygous missense variation in HSD17B3 gene. This alteration changes Isoleucine to Lysine in exon 10. This variation – which has not been reported before – is predicted to be a variant of unknown significance (VUS) based on computational analysis.

## CONCLUSIONS

We identified a novel homozygous missense variation (c.731T>A, p. Ile244Lys) in HSD17B3 gene in this patients.

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