PP124. A new familial mutation in the SRY gene (Arg133Gly)

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Mutations in the testis-determining gene SRY result in XY sex reversal with pure gonadal dysgenesis (PGD). Most of the SRY mutations affect the HMG domain of SRY which plays a central role in DNA binding and bending activity of SRY. The arginine at codon 133 is conserved in the SRY gene of all studied species. It is part of the basic C-terminal region of the HMG box, which was proposed to provide nuclear localization signal. A de novo Arg133Trp mutation was described in two unrelated patients with pure gonadal dysgenesis. Impaired nuclear localization of SRY was proposed as a cause of organogenesis failure for mutations affecting Arg133. Here we describe a novel mutation that affects codon 133 of the SRY gene, resulting in an arginine to glycine substitution in the protein. It was detected in a 17 years old girl with primary amenorrhea, non-mosaic 46,XY karyotype and bilateral gonadoblastoma. The Arg133Gly mutation in the SRY gene was also detected in patient's father, who is a phenotipically normal male. However, the mutation was not found in the SRY gene of 90 other males, thus excluding the possibility of a common polymorphism. Our report of familial Arg133Gly mutation suggests that replacement of Arg 133 of the SRY is not sufficient for impaired organogenesis and emphasizes the importance of modifier genes in the sex determination pathway.

Key words: SRY, XY female, pure gonadal dysgenesis, familial mutation

PP125. Five novel mutations in cystinuria genes SLC3A1 and SLC7A9

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Cystinuria is an autosomal recessive disorder that is characterized by an impaired transport of cystine and dibasic amino acids in the proximal renal tubule and epithelial cells of the gastrointestinal tract. This condition results in an elevated urine concentration of cystine, lysine, ornithine and arginine. The transport of these amino acids is mediated by the rBAT/$b^{0,+}$AT transporter, the subunits of which are encoded by the genes SLC3A1, located on chromosome 2p16.3-21, and SLC7A9, located on chromosome 19q12-13.1. Based on the urinary cystine excretion patterns of obligate heterozygotes, cystinuria is classified into two types: type I and non-type I. Mutations in SLC3A1 gene cause type I cystinuria, while mutations in SLC7A9 gene, are responsible for non-type I cystinuria. Here we present two novel mutations in SLC3A1 gene (C242R and L573X) and three in SLC7A9 gene (G73R V375I, 1233_1236delACTC). The mutations were determined by direct sequencing. C242R and L573X mutations in SLC3A1 gene, and G73R mutation in SLC7A9 gene were found in patients from Serbia, V375I in SLC7A9 gene was found in a patient from Macedonia, while 1233-1236del ACTC mutation in SLC7A9 gene was found in a patient from Turkey.

Key words: Cystinuria, SLC3A1, SLC7A9, mutations, rBAT/$b^{0,+}$AT transporter