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MOLECULAR GENETIC STUDY OF A FAMILY WITH NEPHROGENIC DIABETES INSIPIDUS

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Nephrogenic Diabetes Insipidus (NDI) is a rare X-linked renal disorder due to resistance to antidiuretic action of arginine vasopression (AVP) hormone, which is characterized with clinical symptoms of polyuria, polydipsia and dehydration. Previous studies have demonstrated that the NDI is caused by the defects of vasopressin 2 receptor (V2R) in renal tubules. The V2R belongs to the family of G-protein coupled receptors that contain seven distinct transmembrane domains. The gene encoding V2R has been cloned and sequenced, which facilitated the genetic study of NDI at molecular level. Several gene defects of NDI have been identified, including various point mutations, and deletions, suggesting genetic heterogeneity of NDI.

We have identified a family with clinical diagnosis of NDI. By using the polymerase chain reaction (PCR)-based sequencing, we investigated three protein-coding exons and their flanking introns of V2R gene of the patient. A C-to-A transition at nucleotide 1292 was identified. Which predicts a Phe substitution at codon 287 by Leu of V2R. This molecular variant was not reported in literature of V2R mutations, and was also not found in 100 normal alleles from 60 unrelated people. Our study suggests that this 1292 C/A molecular variant might be a novel mutation of V2R causing NDI. Currently we are carrying out functional assay to characterize this molecular variant of V2R gene.