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# A novel PAX2 mutation c.130C>G (L44V) identified by exome sequencing in a family with end-stage renal disease in adulthood

**Taehee Kim**[1], SeungHwan Oh[2], Changwon Keum[3], SunWoo Kang[1], Yunmi Kim[1], Woo Yeong Chung[4], Yeong Hoon Kim[1]
[1]Department of Internal Medicine-Nephrology, Inje University Busan Paik Hospital, Korea, Republic of
[2]Department of Laboratory Medicine, Inje University Busan Paik Hospital, Korea, Republic of
[3]Department of 3Billions Inc., 3Billions Inc., Korea, Republic of
[4]Department of Pediatrics-Nephrology, Inje University Busan Paik Hospital, Korea, Republic of

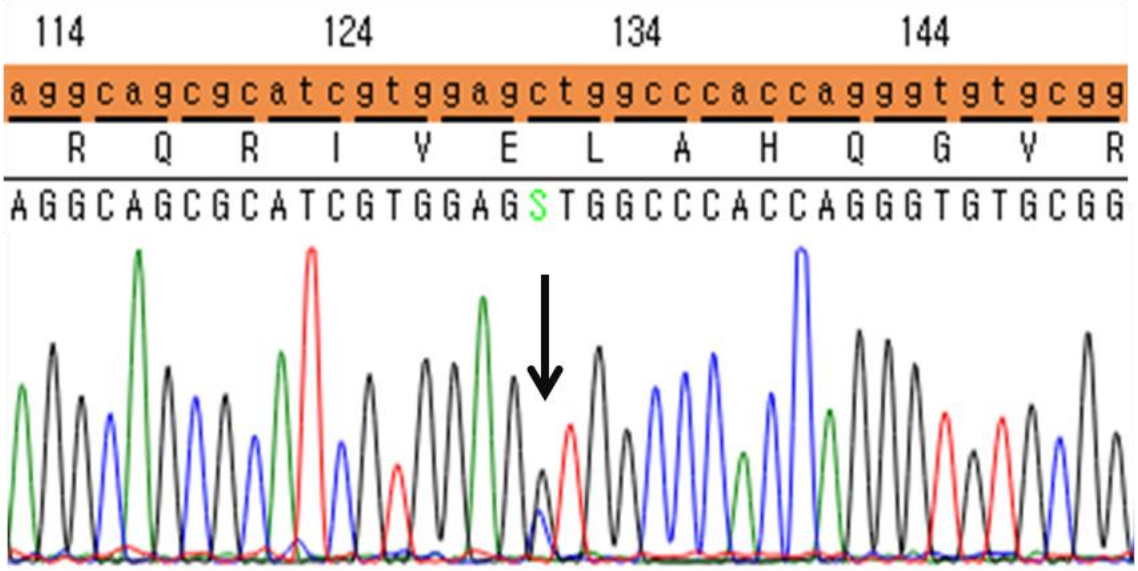
**Objectives:** Paired Box Gene 2 (PAX2) is located on chromosome 10 in humans, and its product plays a key role in kidney development. The first three exons of this gene are highly conserved among species. Recently, 7 familial cohorts of adult-onset focal segmental glomerulosclerosis revealed PAX2 mutations, indicating PAX2 can cause adult-onset renal diseases without ocular manifestation (OMIM #616002) through haploinsufficiency and dominant negative effects.

**Methods:** Genomic DNA was extracted from buccal swabs or peripheral blood samples of the proband and his family members. The variations identified by exome sequencing were also validated by direct sequencing (ABI3500, Applied Biosystems) of the affected regions of PAX2 gene.

**Results:** A 39-year-old male was admitted to our transplant center for kidney transplantation due to end-stage renal disease (ESRD) by an unknown cause. Interestingly, mother and sister among his family members have also suffered from the ESRD in adulthood requiring hemodialysis. The other ocular or brain anomalies were not reported from this pedigree. From this family, *PAX2* gene mutation was identified by exome sequencing and selected to be associated with their phenotypes. This heterozygous *c.130C>G* (p.L44V) missense mutation on the exon 2 was also confirmed by Sanger sequencing (Fig. 1) in the affected members of this family. This mutation is located in the N-terminus of N-terminal paired box domain of PAX2. It was not found in any mutation or polymorphism databases and also predicted as a pathogenic mutation by *in-silico* analysis.

**Conclusions:** We here report a novel *PAX2* mutation identified by exome sequencing in a family with ESRD in adulthood in the absence of other congenital syndromic features. PAX2 mutation should be considered as a causative genetic alteration in the primary ESRD in adulthood with genetic backgrounds to avoid unnecessary immunosuppressive treatment.

Electropherograms obtained from Sanger sequencing of the PAX2 gene, validating the heterozygous c.130C>G (p.L44V) missense changes identified by the whole exome sequencing


114
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a g g c a g c g c a t c g t g g a g c t g g c c c a c c a g g g t g t g c g g
R Q R I V E L A H Q G V R
A G G C A G C G C A T C G T G G A G S T G G C C C A C C A G G G T G T G C G G