

## von Hippel–Lindau (VHL) syndrome의 분자 유전학적 연구

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### Molecular Genetic Analysis of Von Hippel–Lindau (VHL) Syndrome

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**Purpose:** Von Hippel–Lindau(VHL) syndrome is a dominantly inherited multisystem family cancer syndrome predisposing to hemangioblastomas; renal cell carcinoma; pheochromocytoma; and endolymphatic sac tumors. Molecular genetic testing of VHL, the only gene known to be associated with VHL syndrome, detects mutations in nearly 100% of affected individuals.

**Subjects and Results:** We identified several mutations in three different families. [1] A 11–year–old girl was presented with hypertension, headache and excessive sweating. Abdominal CT revealed bilateral adrenal tumor. This pheochromocytoma was removed by adrenalectomy. She had de novo 161Arg(CGA)>Gln(CAA) heterozygous mutation in exon3. [2] A 10–year–old boy presented with generalized seizures followed by loss of consciousness and with a diagnosis of hypertensive encephalopathy. Abdominal CT revealed bilateral adrenal mass I–123–MIBG scan was consistent with the diagnosis of pheochromocytoma and the tumor was removed. Two years after the symptom onset of index case, his brother had the similar clinical manifestation of systemic hypertension at his age of 10. Also adrenal pheochromocytoma was diagnosed and removed by surgery. His father had same tumor. All three family members had a 199Glu(GAG)>Stop(TAG) heterozygous nonsense mutation in exon3. [3] A 55–year–old man was referred for genetic diagnosis of von Hippel–Lindau disease. At the age of 45 he was found to have a cerebellar hemangioblastoma, which was then resected. Three years later, renal cell carcinoma was treated with open radical nephrectomy of left kidney. The diagnosis of von Hippel–Lindau disease was suspected at this time. Ophthalmologic exam revealed retinal hemangioma on his left eye. He has a heterozygous c.188\_215del28 in exon1. Genetic analysis was performed for his asymptomatic sons. Same mutation was detected in both sons. They are under close follow up for possible tumors.

**Conclusion:** Early detection and removal of tumors to minimize secondary deficits is crucial. Therefore surveillance for individuals with VHL syndrome, those with a VHL mutation and at–risk relatives of unknown genetic status are recommended.

**Key Words:** von Hippel–Lindau 증후군, 돌연변이  
von Hippel–Lindau syndrome, mutation