Dr. Patocs and colleagues describe a family from Hungary with VHL. 6 patients have VHL manifestations. The index case has the VHL Ser80Ile mutation. This mutation has been detected in 6 relatives of whom 1 had no tumors: the mother of the index case. In addition the Pro25Leu polymorphism was found in 2 persons: the mother of the index case (II.1) and one family member who does not have the mutation and the disease (III.6).

The spectrum of manifestations was RCC in 1, Pheo in 4, Brain Hbl in 4, Eye Hbl in 4 cases. I carrier had renal cysts and one relative had pancreas cancer.

The authors conclude that Pro25Leu may represent a protective variant for VHL. They classify this family as VHL type 2.

What we learn from this case and why the authors possibly find this family interesting are:

1. The genetic alterations of the index case and the mother are not identical, and Pro25Leu may be a pitfall and falsely classified as a mutation.
2. The mother of the index case shows no VHL manifestation.

Concerns and questions

The Pro25Leu is a well known polymorphism (see: NCBI:dbSNP127). The prevalence data 1:36000 and 1:85000 must be checked and are incorrect.

The classification of VHL has meanwhile been softened and reads now not exclusively, but predominantly without pheo (type 1) predominantly without RCC (2A) and (predominantly) only with pheos (2C): See WHO Classification of Tumours; Pathology and Genetics, Tumours of Endocrine Organs 2004.

Renal cysts occur in VHL, but should be only carefully be assigned to VHL.

Pancreas carcinoma is not a manifestation of VHL: Mostly one understand here pancreas adenocarcinoma, but in VHL there occurs islet cell pancreatic tumor; the authors must check.

Table 1 must be checked for case II5 and III1: Not RCC but Pheo? Case II4 must be removed from the table unless islet cell tumor has been confirmed.
Suggestion: The symbols of figure 1 are somewhat confusing: What they use for Not tested is usually the sign for dead person, what they use for Ser80Ile is mostly the sign for disease manifestation.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.