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Comment

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Patients affected with von Hippel-Lindau are at risk for the development of tumors in a number of locations, including the kidneys (clear cell RCC), adrenals (pheochromocytomas), CNS (hemangioblastomas), eyes (retinal angiomas), pancreas (pancreatic neuroendocrine tumors), ears (endolymphatic sac tumors) and epididymis (cystadenomas). Although the gene for this autosomal dominant inherited renal cancer disorder was identified in 1993, we still do not know why patients develop tumors in some organs and not others. To date, over 377 unique *VHL* gene mutations from North America, Europe and Japan have been described in the Leiden Open Variation Database maintained by Zhejiang University Center for Genetic and Genomic Medicine (1). However, until recently comparatively few Chinese cases of VHL have been reported. In the current issue of Urology, XXX and coworkers evaluated 19 VHL families recruited from various regions of China for *VHL* mutation, phenotypic manifestations and family history. These investigators identified a broad spectrum of mutation subtypes (missense, nonsense, indels, deletions) including 9 novel and 10 previously reported *VHL* mutations. VHL subtypes 1, 2A and 2B were all represented in their cohort. Together with their previous work in which 16 VHL families from China were evaluated (2), this represents the largest composite study of Chinese VHL families reported to date. Unique to these 19 VHL families and the authors' previously reported Chinese VHL cohort is the fact that no family history of VHL was reported by over half (18/35) of the probands presented in these two reports. Additionally the frequency of novel *VHL* mutations in this Chinese VHL cohort (47.4%) was much greater than that reported in Western countries (~20%)(3), and more families with novel mutations reported absence of family history (66.7%) than those with previously reported mutations (30%).

This study underscores the need to consider VHL disease in the differential diagnosis of patients with characteristic manifestations of VHL even in the absence of family history, and may suggest a higher prevalence of *de novo* mutations in the *VHL* gene in the Chinese population. While access to care, practice patterns and disease phenotype recognition can vary from region to region, the phenotypic and genetic disease spectrum in China seems to have number of unique features. Whether this reflects an increase in VHL new mutation

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and/or mosaicism in the Chinese population will require further studies of large Chinese VHL cohorts.

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