Reviewer's report

Title: Prevalence of Von Hippel-Lindau gene mutations in sporadic Renal Cell Carcinoma: results from the Netherlands Cohort Study

Version: 2 Date: 9 March 2005

Reviewer: Eamonn Maher

Reviewer's report:

General
Kjeld et al report the results of a population based survey of somatic VHGL mutations in sporadic renal cell carcinoma (RCC). A study such as this is not novel (it is more than 10 years since somatic VHL mutations were demonstrated in RCC) and the methodology (SSCP) is not optimum. However information on mutation spectrum will be helpful for other researchers and therefore, in principle, such data should be published.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Details of all VHL mutations should be listed individually with the corresponding clinical and pathological characteristics of the specific tumour to allow future meta-analysis studies.

Some mutations were detected 5' of codon 54 - these are unusual and would be predicted to affect pVHL30 but not pVHL19 translation products - this should be discussed.

RCC without VHL mutations may have epigenetic silencing of VHL by promoter methylation - this should be mentioned in the Discussion as it will reduce the likelihood of detecting clinical differences between VHL mutation positive and mutation negative groups.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

'I declare that I have no competing interests'