Mutation of the Proline P81 into a Serine modifies the tumor suppressor function of the von Hippel-Lindau gene in the ccRCC.

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Abstract

The von Hippel Lindau disease is an autosomal dominant syndrome associated with tumor formation in various tissues such as retina, central nervous system, kidney, adrenal glands. VHL gene deletion or mutations support the development of various cancers. Unclassified VHL variants also referred as "of unknown significance" result from gene mutations that have an unknown or unclear effect on protein functions. The P81S mutation has been linked to low penetrance Type 1 disease but its pathogenic function was not clearly determined. **Methods**: We established a stable cell line expressing the $pVHL_{213}$ (c.241C>T, P81S) mutant. Using biochemical and physiological approaches, we herein analyzed pVHL folding, stability and function in the context of this VHL single missense mutation. **Results:** The P81S mutation mostly affects the non-canonical function of the pVHL protein. The cells expressing the $pVHL_{213}$P81S acquire invasive properties in relation with modified architecture network.

Conclusion: We demonstrated the pathogenic role of this mutation in tumor development in *vhl* patients that reinforces the need for medical follow-up of family members carrying the c.241C>T, P81S.