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ABSTRACT

Understanding VHL Disease: Molecular Characterization of a Spanish Series

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Genetic characterization of VHL patients has leaded a VHL family's classification based on a genotype–phenotype correlation. While type 1 VHL families (lacking pheochromocytoma though presenting other VHL clinical features) are mainly related to protein truncating mutations, type 2 families (with at least one case of pheochromocytoma) are mostly associated with missense mutations (Maher et al., 1996). The latter group is sub-classified into three different groups based on phenotypes. VHL 2A cases are associated with a low risk of ccRCC, although retain predisposition for developing the remaining VHL-tumors. Generally, subjects with VHL 2B are affected by all the clinical manifestations of the disease, and VHL 2C subgroup includes patients with only familial pheochromocytoma.

In these last years, we have witnessed great changes in this field, mainly due to the application of new technologies to diagnostic procedures. The structural analysis of VHL missense mutations has allowed us to understand the phenotypic differences among families carrying mutations affecting the same residue (Ruiz-Llorente S, et al., 2004), and we know now that the risk for CCRC and hemangioblastoma varies among different surface missense mutations (Ong et al., 2007). Regarding type 1 VHL, it has been suggested that complete deletions of the VHL gene that also encompass the BRK1 gene (also known as HSPC300) confers a low risk of CCRC (Maranchie et al., 2004; Cascon et al., 2007). These families could be designated as VHL Type 1B (McNeill A, et al., 2009). A summary of genotype-phenotype correlation found in a large Spanish VHL series molecularly characterized will be presented.