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EDITORIAL COMMENT

Comment to "Immunohistochemical expression of microvascular density and carbonic anhydrase IX in renal carcinoma. Relation to histological type and tumoral progression"

Comentario a «Expresión inmunohistoquímica de la densidad microvascular y de la anhidrasa carbónica IX en carcinoma renal. Relación con el tipo histológico y con la progresión tumoral»

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Over the last few years, and considering that diagnostic criteria based solely on histological architecture are insufficient, an effort is being made to create a molecular characterization of renal cell carcinoma (RCC) to determine new, useful tumour markers both in histological diagnosis and in prognostic prediction and response to the drugs that are currently being developed.

The involvement of the VHL suppressor gene in cases of sporadic RCC[1,2] is known. This gene encodes a protein (pVHL) that is linked to an HIF-1α in conditions of normoxia, enhancing its degradation by means of a prolyl dydroxylase-dependant mechanism. The lack of normal pVHL function (due to genetic or epigenetic changes) generates a similar situation to hypoxia in terms of overexpression of HIF-1α.[3] The increase of HIF-1α entails an increase in the encoding of genes, whose protein product increases the availability of oxygen by activating angiogenic factors. This could explain the hypervascular nature of RCC. Notwithstanding, HIF-1α also regulates other genes, of which carbonic anhydrases (CA) are worth mention, specifically the gene that produces the protein CA-IX. The latter, with the exception of the gastric mucosa, is only expressed in tumour tissue, including RCC, induced by conditions of hypoxia.[4,5]

The overexpression of CA-IX is practically exclusive to clear cell RCC,[6] which is why its determination is useful in the diagnosis of this type of cell subtype. When it appears overexpressed in other subtypes, the possibility of it being a false positive or mixed RCC arises. CA-IX expression can be determined by immunohistochemistry (IHC) or direct methods such as western blot. Recent results of our group have not demonstrated the usefulness of this technique.

The Rubio-Briones J et al. study[7] is another means of becoming familiar with the assocation of CA-IX expression and microvascular density in patients with RCC, with the aim of evaluating the usefulness of CA-IX as a molecular marker that allows personalizing treatments for each patient. Its results confirm those already known to date, and the involvement of CA-IX in the prognosis of RCC in terms of survival or tumour progression or the response to certain immunomodulating or antiangiogenic therapies; this response is solely associated with cases of metastatic RCC.[8,9] Coinciding with the author's opinion, the usefulness of CA-IX appears to be aimed more at the differential diagnosis of the histological subtypes of RCC.

For all these reasons, more studies are required regarding an overall evaluation of this entire signalling path pVHL→HIF-1α→CA-IX, even the analysis of other proteins and

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signalling paths that, like MAPK or ATM, control the activity of HIF-1α.

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