Commentary for the KCJ article "*Molecular and Immune Landscape of Fumarate Hydratase-Mutated Renal Cell Carcinoma*"

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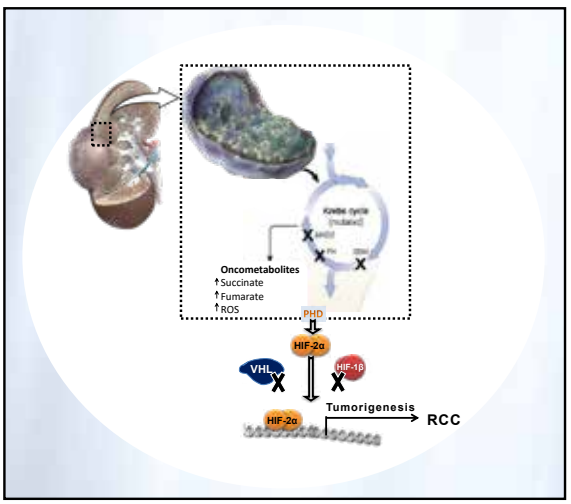
Fumarate hydratase (FH)-deficient renal cell carcinomas (RCC) are a rare yet aggressive type of kidney cancer. Both their rarity and aggressiveness make them particularly challenging to study. The authors of this study (*refer pages 115-124, this Q4 issue*) are to be commended for providing perhaps the largest genomic and transcriptomic characterization of FH-deficient RCC to date. As the investigators acknowledge, there are undoubtedly several limitations to their findings, including the limited clinicopathologic information and outcomes data in their cohort, absence of data concerning therapeutic exposures prior to sample acquisition, and heterogeneity in the tumor sites for the samples analyzed.

Nevertheless, they offer useful molecular insights into a rare disease that may help inform future work. Co-occurrence of NF2 mutations in FH-deficient RCC has been described previously and further corroborated in a considerable subset of the present cohort, suggesting that inhibitors of the Hippo pathway may carry therapeutic potential in some of these patients. Elucidating the immune microenvironment for these tumors may provide a further basis for combined therapeutic strategies.



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