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New insights into PDGF/PDGFR axis in renal cell carcinomas

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Patients with clear cell renal cell carcinoma (CCRCC) have a highly heterogeneous response to therapy and resistance to therapy appears early during treatment. We aim to study *PDGF pathway* expression profile correlated with tumor vessels type, grade invasion and growth factors expression. Fifty cases of CCRCC were preliminary evaluated by histopathology and selected for immunohistochemistry and molecular analysis. Cases evaluation included histopathology, PDGF assessement by immunohistochemistry and RNAscope, and tumor grouping with emphasis to tumor vessels types previously described by our team. For molecular analysis we used TaqMan array for *PDGF pathway* applied to *PDGF Pathway* 96-well plates containing 92 genes and 4 control genes. Results were evaluated by DATA ASSIST software and gene expression profile was correlated with grade, invasion, tumor vessels types, VEGF. All CCRCC were positive for PDGF BB by immunohistochemistry and RNAscope and 91,6% out of these cases being confirmed by RT PCR. Difference in gene expression profile were observed when we grouped cases according with tumor vessels types. PIK3C3 and SLC9A3 were significantly correlated with reticular and diffuse pattern of tumor vessels types but different 5 genes (STAT1, JAK2, SHC2, SRF and CHUK) were exclusively overexpressed in diffuse pattern compared with reticular pattern of blood vessels. Also, when we grouped cases according with tumor grade, SLC9A3, CHUK and STAT3 were overexpressed in G3 compared with G2. No significant correlation has been found between PDGF gene expression and invasion. PIK3C3 and SLC9A3 were differentially overexpressed according with intensity of VEGF. We may conclude that CCRCC showed a high molecular heterogeneity of *PDGF pathway* gene expression profile with an impact on early maturation of tumor vessels previously observed. Also, this heterogeneous gene expression profile may explain the different response to targeted therapies and in part resistance to therapy differently developed among patients

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