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Introduction to High throughput platforms in kidney cancer: genomics, transcriptomics and metabolomics Urologic Oncology: Seminars and Original Investigations

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In this Seminar in Urologic Oncology, we highlight the role of genomics, transcriptomics and metabolomics in kidney cancer. As in many other cancers, the molecular underpinnings of renal cell carcinoma (RCC) have been revolutionized by high throughput, next generation sequencing. Accordingly, expansion in our understanding of the various subtypes of RCC has led to breakthroughs in biologic understanding, prognostic biomarkers and novel therapeutic targets.

Pal et al discuss how the genomic revolution have moves us far beyond the *VHL* gene in clear cell RCC (ccRCC). Specifically, they discuss the prognostic and therapeutic implication of several newly identified tumor suppressor genes such as *PBRM1*, *SETD2* and *BAP1* in ccRCC. They further highlight the frequency and challenges of intratumoral heterogeneity and the enrichment of certain mutations in metastatic tissue compared to primary. The authors then discuss the role of the *MET* oncogene in papillary RCC and point to the fact that there are now *MET* inhibitor directed trials for this rare subtype. Finally, the authors demonstrate the unique mutations enriched in sarcomatoid de-differentiated tumors.

Syed et al delve into the role transcriptomic profiling has played in RCC. The authors explore how the work of the Cancer Genome Atlas (TCGA) has led to prognostic subgroups across the different subtypes. Further other groups have developed gene classifiers associated with risk of recurrence following radical or partial nephrectomy. The authors explain how transcriptomics can also be used for pathway analysis and deconvolution of the tumor microenvironment. Finally, the authors highlight some of the recent studies that have used expression profiles to predict response and resistance to both anti-angiogenic and immune checkpoint blockader therapies.

Conflicts of interest: none

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DiNatale et al highlight the role of metabolic dysfunction across the spectrum of RCCs including mutations in the citric acid cycle (TCA) which define rare aggressive subtypes, along with the well-known tumor suppressor VHL, which leads to dysregulation of oxygen sensing, amongst other factors. Further, the authors highlight mitochondrial gene dysregulation which define chromophobe RCCs, oncocyomas and clear cell papillary RCCs. The authors also how highlighting the metabolic aspects of the tumor microenvironment we both existing and future therapies may help to improve outcomes in metastatic RCC.

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