EDITORIAL MISSION
The purpose of Kidney Cancer Journal is to serve as a comprehensive resource of information for physicians regarding advances in the diagnosis and treatment of renal cell carcinoma. Content of the journal focuses on the impact of translational research in oncology and urology and also provides a forum for cancer patient advocacy. Kidney Cancer Journal is circulated to medical oncologists, hematologist-oncologists, and urologists.

Editorial Office
517 Belle Gate Pl, Cary, NC 27519
Email: **office@kidney-cancer-journal.com**

ABOUT THE COVER
Integrated ontological evaluation according to three fundamental axes (tumor cytology, architecture and the microenvironment) identifies distinct trajectories of morphological evolution in clear cell renal cell carcinoma and sheds light on the therapeutic vulnerabilities of different morphologic subtypes.

KCJ TABLE OF CONTENTS

KCJ Editor's Memo

ASCO20 Takeaways And Exploring New Horizons In Precision Oncology


Robert A Figlin, MD

For the first time in its 56-year history, the ASCO Annual Scientific Meeting was held entirely virtually due to the global outbreak of the COVID-19 that swept the world. Despite the odds, the 3-day scientific program was broadcasted to a record-breaking audience of more than 42,700 attendees from 130 countries. Moreover, the content of the conference has been viewed more than 2.5 million times as of June 4, 2020. During the conference sessions, attendees were able to view 5300 abstracts and more than a hundred on-demand and broadcast sessions and over 2300 poster and oral presentations throughout the weekend. "Although the pandemic prevented us from gathering in Chicago, it didn't stop us from fulfilling our mission of sharing knowledge to accelerate progress for millions of people worldwide living with cancer" said Howard A. Burris III, MD, FACP, FASCO, the president of ASCO. This is clearly evident in the way attendees networked with their peers via chat and one-on-one video calls and social media. "#ASCO20", the official meeting hashtag, was used in more than 45,000 tweets from more than 8,800 Twitter users and this meeting generated more than three-quarters of a billion engagements including likes, shares, and comments on social media. This year's scientific sessions highlighted a remarkable progress and the tremendous efforts underway to capitalize the full potential of immunotherapy and targeted therapy, find the best treatment settings and combinations and match them to the right patients. In a way, this ASCO20 meeting was groundbreaking as it overcame the pandemic barrier and brought together a record-breaking number of clinicians from across the globe to fulfill the mission of sharing knowledge to accelerate progress against cancer.

(continued on Page 88)

The meeting will include all of the programming you are accustomed to, only this year it will be in an interactive online format including a robust program of educational and scientific sessions, live SA-CME opportunities, a poster hall with narration from poster presenters, and a virtual Exhibit Hall where you can visit booths to learn and connect with industry colleagues. The meeting opens on October 25 and will be available for 30 days to ensure you have access to all the presentations and materials. This year's Annual Meeting will be uniquely redesigned to ensure that attendees from around the globe continue to access timely scientific and education session. The PRO and ARRO programs will provide curated content addressing issues specific to community practitioners and residents.

Liquid Biopsy Shows High Accuracy in Detecting Early-Stage Renal Cell Carcinoma

A novel plasma DNA assay has shown remarkable accuracy in identifying patients with renal cell carcinoma (RCC) across all stages of disease, making it easier to detect at early-stage, according to the recent report published in Nature Medicine. If validated, this assay could potentially be used initially as a screening test for people who have a family history of kidney cancer or who previously had kidney cancer. This is especially very important as currently, no FDA-approved or recommended screening method is available for the early detection of RCC in the general population.

Of all extracranial tumors, RCC sheds the least amount of cell-free DNA (cfDNA) so cfDNA-based methods alone are insufficient for detecting RCC. Therefore, Cell-free methylated DNA immunoprecipitation and high-throughput sequencing (cfMeDIP-seq), could be potentially efficient in identifying RCC. The investigators in this study used a cfMeDIP-seq approach on plasma and urine cfDNA to detect RCC, which was the first such application of cfMeDIP-seq on urine cfDNA for cancer detection and demonstrated for the first time that this assay can accurately detect RCC by measuring urine cfDNA

Testing was performed on 148 samples, including 99 from cases of stage I to IV RCC, 21 samples of stage IV urothelial bladder cancer, and 28 samples from healthy, cancer-free controls. Across the training test sets, RCC samples had a higher median methylation score than control samples and had a mean area under the receiver operating characteristic (AUROC) curve of 0.990 (95% CI, 0.985-0.995). Among urine cfDNA samples, the mean AUROC for patients with RCC compared with healthy controls was 0.858 (95% CI, 0.831-0.885).

The authors noted that following further validation, this screening method, alone or in combination with imaging, could transform clinical management by enabling early detection of RCC and reducing unnecessary kidney biopsies and nephrectomies.

Reference: Nuzzo PV, Berchuck JE, Korthauer K, et al. Detection of renal cell carcinoma using plasma and urine cell-free DNA methylomes. *Nature Med*. Published online June 22, 2020. doi:10.1038/s41591-020-0933-1

EDITOR'S MEMO *(continued from Page 66)*

It is exciting to see the promising results from KEYNOTE-426, KEYNOTE-146, COSMIC-313 and PDIGREE that highlighted optimal strategies for combining and sequencing treatment modalities of targeted and immunotherapies. The initial results of the open-label phase 2 study of MK-6482 that targets hypoxia inducible factor signaling has opened up an avenue of a new class of therapy for treatment of VHL-associated ccRCC. Some other hot topics especially new approaches exploiting PARP inhibitors, glutaminase inhibitors, newer personalized medicine around immunotherapies, and new tyrosine kinase inhibitor strategies were also presented in ASCO20 plenary sessions.

Despite revolutionary approaches in the RCC treatment, it is apparent that intra-tumoral heterogeneity poses a significant problem for cancer management. Precision oncology approaches harnessing knowledge of heterogeneous tumor is crucial to tailor those therapies to ultimately target and improve prognosis and outcomes for patients. The article in this issue by Payal Kapur and James Brugarolas *et al* present an intriguing molecular genetic and morphologic evolutionary model especially focusing on prototypical model of tumor heterogeneity in renal cell carcinoma. This systematic and comprehensive ontology that captures the breath of ccRCC morphologies has profound implications both for understanding the biology of tumor progression, and for the ability to stratify patients in the clinic. Undoubtedly, this knowledge sets a paradigm for de-convoluting phenotypic complexity and establishes a comprehensive morphologic ontology of ccRCC. The other article by Ritesh Kotecha dicusses the mechanistic insights into the potential mechanisms underlying the counter-intuitive phenomenon known as obesity paradox in clear cell renal cell carcinoma. Emerging trends discussed in this article highlight that differences in the tumour microenvironment could hold the key to apparent survival advantage of obese patients with clear cell RCC versus patients at a normal weight and also emphasize such studies merit careful consideration for designing clinical trials in the future. In the *Letter to the Editor* column, Nirmish Singla and Shyamli Singla illustrate that the deep machine learning may be harnessed to inform clinical prognosis and therapeutic responsiveness using clear cell renal cell carcinoma as a prototype and also envision that such artificial intelligence approach may effectively shape the future of precision oncology.

Robert A. Figlin, MD
Editor-in-Chief