

## Editorial

# Novel discoveries in urology: big data to microbiome - highlights of the society for basic urologic research 2019 annual meeting

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The 2019 Annual Meeting of the Society for Basic Urologic Research (SBUR) convened on November 7-10, 2019, in New Orleans, LA. The meeting started with a keynote session featuring the Leland W.K. Chung lecture given by Dr. Arul M. Chinnaiyan, followed by six plenary sessions on Big Data as Engines for Discovery, Targeting Endocrine and Metabolic Dysfunctions, Immunology and Immunotherapy, Targeting Benign Urologic Disease, Innovative Technologies in Urology, and Microbiome and Inflammation.

Dr. Chinnaiyan presented his recent findings on mutations of Forkhead Box A1 (FOXA1) in prostate cancer progression. FOXA1 mutations were categorized into five classes: class 1 "FAST" mutations disrupt the Wing2 secondary structure, demonstrating strong oncogenesis activity; class 2 "FURIOUS" mutations are cis-terminally-dominant, activate WNT signaling and promote invasiveness and metastasis of prostate cancer; class 3 "LOUD" mutations are novel structural variations comprised of duplications and translocations within the FOXA1 locus to drive overexpression of FOXA1; class 4 "non-coding" alterations are primarily indels in the 3'UTR of prostate cancers; and class 5 "DEAD" hotspot mutations were found in neuroendocrine prostate cancer. FOXA1 mutation is oncogenic, cooperating with AR in AR<sup>+</sup> prostate cancer. FOXA1 anti-sense oligonucleotides inhibit FOXA1 expression and inhibit prostate

cancer growth. It is anticipated that targeting FOXA1 is a potential strategy to impede malignant prostate tumor progression. The American Urological Association (AUA) lecture was given by Dr. Joel B. Nelson. Dr. Nelson presented recent clinical studies showing that prostate cancer screening had not improved population health, yet often led to overtreatment. The treated prostate cancer cases had worse outcomes than untreated ones. Avoiding overtreatment by observing has some risk of increasing rates of progression and metastases. Better diagnostic tools are needed to determine which cases may benefit from surgery, such as multiparametric magnetic resonance imaging (mpMRI). Dr. Oliver Sartor's talk echoed this call for better weapons in clinic management of prostate cancer, including mpMRI and Prostate-Specific Membrane Antigen (PSMA) positron emission tomography (PET) scans. Dr. Sartor also presented the genetics and biomarkers that may influence the way in which patients are staged and treated in clinic practice.

One of the meeting's hotspots was the omics approaches in basic urologic research. Dr. Soryanarayana Varambally introduced UALCAN data mining platform for comprehensive analysis of cancer transcriptome and its applications. This platform integrates multiple large datasets including TCGA, MET500, Pan Cancer, and methylation data, and is free to use online (<http://ualcan.path.uab.edu/cgi-bin/ual>

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can-res.pl). Mining of big data has become a trend in the current research field. Dr. Vinata Lokeshwar reported on intra-tumor basal and luminal heterogeneity of bladder cancer through mining the OncoPrint™ and TCGA datasets. Dr. Shawn Lupold, through mining TCGA dataset, identified miR-21 that did not affect prostate cancer development, but promoted prostate cancer progression. Likewise, Dr. Kai-fu Chen identified 5% of genes with broad H3K4me3 modification and Dr. Qianben Wang revealed that phosphorylated MED1 (pMED1) binding sites were associated with RNA PolII and H3K36me3 across genome. Dr. Rosalyn Adam reported on single-cell transcriptomic profiling of bladder following spinal cord injury, which might provide novel therapeutic targets or rational design of targeted treatment. Dr. Sanja Gupta developed a computational analytics combining histomorphometry and biomarkers for prediction of prostate cancer recurrence.

Several novel therapeutic targets were reported. Dr. Hsing-Jien Kung identified Lysine Demethylase 8 (KDM8) as an ideal therapeutic target for metabolic adaptation and castration-resistance of prostate cancer. Dr. Jiaoti Huang found that glutaminase-1 (GLS1) might be targeted due to prostate cancer's addiction to glutamine. Dr. Hari Koul reported that prostate derived ETS factor (PDEF) might be upregulated to reverse prostate cancer progression. Dr. Yun Qui reported that E2F1/AR3 might be targeted in dealing with resistance to docetaxol/enzalutamide combination therapy. Dr. Xiaoqi Liu demonstrated polo-like kinase 1 as a likely target in the treatment of drug-resistant prostate cancer. Dr. Li Jia identified PARP2 as a new target. Dr. Asim Abdel-Mageed demonstrated that prostate cancer cell-derived exosomes could be targeted to impede prostate cancer progression. Dr. Jin Zeng reported that prostate leucine zipper (PrLZ) could be targeted in prostate cancer therapy. Dr. Zoran Culig demonstrated that AR and IL-6/STAT3 signaling could be targeted in the treatment of prostate cancer.

In confronting benign urologic diseases, Dr. Tamara Bavendam illustrated NIDDK's support and funding opportunities. Dr. William Ricke, Dr. Jonathan Barasch, and Dr. Zhou Wang jointly presented the three O'Brien Centers' leadership, science and training in research on benign

urologic diseases such as BPH and lower urinary tract symptoms (LUTS). Three P20 programs also showed their progresses. Dr. Jerry Lowder presented the challenges of urinary tract infection in post-menopausal women. Dr. Thomas Chi presented an automated clinical registry for translational studies related to kidney stones called Resource for Stones of the Kidney and Ureter (ReSKU), which could be applied to other diseases. Dr. Simon Hayward described the prevalence of pro-inflammatory states that associate with BPH and discussed findings showing reduced incidence of BPH in patients receiving TNF $\alpha$  antagonists for autoimmune conditions. Dr. Timothy Ratliff identified the inflammatory and immune cells subsets in BPH using RNA-seq.

Microbiome and inflammation is another hot-spot of the meeting. Dr. Angelo De Marzo reported that inflammation was prevalent in benign regions of the prostate, which was primarily chronic and to a lesser extent acute and often observed around corpora amylacea. Dr. Michael Liss showed that the gastrointestinal microbiome might influence primary prostate cancer through microbial metabolites. Dr. Wade Bushman presented the challenges in identifying any causal microbes in the prostate. Dr. Jill Macoska reported that fibrosis of the prostatic urethra might contribute to LUTS and fibrosis might be mediated by myofibroblasts via transactivation of the CXCL12/CXCR4 axis and EGFR-mediated signaling. Dr. Joshua Meeks found that the best model of bladder cancer is PTEN and p53 double knockout mice and EZH2 inhibitors did not work in carcinogen-induced bladder cancer in mice that did not have an immune system. Dr. Michelle Downes examined bladder cancer from the perspective of inflammation and inhibition of immune response. She pointed out that pro- and anti-tumor immune responses determined immune environment and immune tolerance outcomes in bladder cancer.

Lastly, 20 trainees (including 9 women and 4 who studied benign urologic diseases) were selected to receive Travel Awards and 8 of them presented Travel Award Presentations at the podium. SBUR promotes the training of next generation of urologic researchers, a mission supported by NIH/NIDDK/NCI.

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### Acknowledgements

A total of 286 people including 57 trainees attended the conference of 42 oral presentations and 173 posters, along with a Trainee Affairs Career Symposium. The full program is available at SBUR website (<https://sbur.memberclicks.net/>). The authors thank the meeting attendees for their wonderful presentations. Special thanks are due to the SBUR 2019 Annual Meeting Program Committee chaired by Dr. Zongbing You and including Drs. Scott M. Dehm, Jindan Yu, Marc B. Cox, Amina Zoubeydi, Christina A.M. Jamieson, Zhou Wang, Hari K. Koul, Rosalyn Adam, Allen Gao, and Ganesh V. Raj. Many thanks are due to Drs. Larisa Nonn and Arun Sreekumar for organizing the Trainee Affairs Career Symposium and to the Session Discussion Leaders including Drs. Zongbing You, Travis J. Jerde, Chang-Deng Hu, Jindan Yu, Gail S. Prins, Benyi Li, Marc B. Cox, Amina Zoubeydi, Rosalyn Adam, Yan Dong, Ganesh V.

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