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The 2nd SAU Annual Conference on Urological Research

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ABSTRACT

The Serican Academy of Urology (SAU), established in the fall of 2022, is an international nonprofit organization dedicated to uniting clinicians and basic scientists to address diseases related to the genitourinary tract. Prostate cancer, particularly castration-resistant prostate cancer (CRPC), remains a significant public health issue. The second annual SAU conference was held from June 13-16, 2024, at Banff Rocky Mountain Resorts, Alberta, Canada. Sponsored by MedChemExpress, ABclonal, and NovinoPath, and chaired by Dr. Xiaoqi Liu, the conference focused on the latest research in urological diseases. Topics included epigenetic regulation, novel treatment targets, bioinformatics, cancer etiology, progression and metastasis, the tumor microenvironment and immunotherapy, and overcoming resistance to existing therapies. Keynote addresses by leading scientists Drs. Jindan Yu and Qianben Wang emphasized the complexity of epigenetic and transcriptional regulation in prostate cancer. The Women's Forum provided a platform to discuss career navigation and leadership development for women scientists in a predominantly male field. The conference concluded with a banquet, including an awards ceremony and committee reports.

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The Serican Academy of Urology (SAU) (http://sericanacademy.org/) is a nonprofit organization composed of urological physicians and basic scientists. Established in the fall of 2022, the Academy aims to provide a platform for regular meetings focused on the presentation and discussion of basic, translational, and clinical sciences related to urology. Prostate cancer, particularly castration-resistant prostate cancer (CRPC), remains a significant public health concern (1). As a result, there is an urgent need to enhance our understanding of its biology, identify new therapeutic targets, develop novel treatment approaches, and improve management strategies for prostate cancer patients.

The First Annual SAU Conference on prostate cancer took place on December 26-29, 2023, in Cancun, Mexico, and was a tremendous success, attracting 60 investigators specializing in urology research from the US, Canada, UK, and China mainland. The Second Annual SAU Conference on Urological Research was held from June 13-16, 2024, at the Banff Rocky Mountain Resorts in Alberta, Canada. This event brought together leading physicians and basic scientists from the US, UK, and China mainland, fostering international collaboration. Sponsored by MedChemExpress, ABclonal, and NovinoPath, the conference was chaired by Dr. Xiaoqi Liu. Presentations covered a range of topics, including epigenetics, bioinformatics, the etiology, progression, and metastasis of prostate cancer, the tumor microenvironment and immunotherapy, novel target identification, and new strategies to overcome resistance to existing therapies.

The conference commenced with a welcome reception in the evening of June 13. Dr. Benyi Li, the Chief of SAU, gave the opening remarks, followed by two keynote speeches. Dr. Jindan Yu, Fray Marshall Chair in Biomedical Urology Research at Emory University, delivered the first presentation, titled "The 4D Nucleome during Neuroendocrine Transformation of Prostate Cancer." She highlighted how prostate cancer development and progression are controlled by aberrant gene expression, orchestrated by lineage-specific transcription factors that shape the epigenetic landscape and cellular identity. After extensive treatment, advanced prostate cancer often develops resistance,

with a significant percentage of these tumors losing their luminal identity and/or gaining neuroendocrine (NE) features. However, the mechanisms behind this transformation remain unclear.

In her talk, Dr. Yu discussed how her team is using single-cell multi-omics, Nanopore long-read sequencing, and Hi-C techniques to investigate these mechanisms. They demonstrated how a set of lineage-specific transcription factors work together to regulate regional DNA demethylation, NE enhancer priming and activation, and 3D chromatin reorganization, leading to transcriptional reprogramming and changes in cell identity. Dr. Yu also discussed how these findings could offer new therapeutic opportunities for currently untreatable NE prostate cancers.

Dr. Qianben Wang, Banks Anderson Sr. Distinguished Professor of Pathology at Duke University, delivered the second keynote speech, titled "Integrated CRISPR/Cas13-Based RNA Editing and Nanotechnology for Targeting Undruggable Transcriptional and Post-Transcriptional Vulnerabilities in Lethal Prostate Cancer." Oncogenic transcription factors such as HOXB13 and N-Myc, which are highly upregulated in advanced prostate cancer, are known drivers of tumor growth and metastasis, representing key transcriptional weaknesses. Additionally, Dr. Wang has identified widespread mRNA 3′ untranslated region (3′UTR) shortening in lethal prostate adenocarcinoma, which may represent a critical post-transcriptional vulnerability. However, traditional small-molecule drug designs have failed to target these transcriptional and post-transcriptional weak points, deeming them "undruggable."

Gene therapy offers a promising alternative by directly targeting these traditionally untreatable areas of vulnerability. Dr. Wang and his lab have engineered several lipid nanoparticles designed for the precise, efficient, and safe delivery of CRISPR/Cas13 or deactivated Cas13 (dCas13) in RNA format to tumor cells in vivo. These Cas13/dCas13-based nano-therapies effectively and safely inhibit prostate cancer growth and/or metastasis, extending survival in mouse models through unique transcriptional and post-transcriptional mechanisms. This groundbreaking research pioneers the targeting of undruggable oncogenic transcription factors using nanoparticle-mediated gene therapy, leveraging CRISPR/Cas13 for RNA targeting. Moreover, it introduces the novel concept of "mRNA 3′UTR-targeted nano-therapy" as a promising approach for treating lethal cancers.

Identification of New Targets for Prostate Cancer

Three sessions were dedicated to this topic. The first session was co-chaired by Drs. Ming Chen and Jason Liu. Dr. Jason Liu, from the University of Texas Health Science Center at San Antonio, emphasized the significance of the Hippo-AP1 interaction in lineage plasticity associated with cancer therapy resistance. Dr. Ming Chen, from Duke University, demonstrated that targeting ACSL4, a fatty acid-CoA ligase, could be a novel approach to treating prostate cancer. Dr. Weiran Feng, from Memorial Sloan Kettering Cancer Center, identified a stem-like population that provides a chromatin context for unmasking ERG oncogenic activity, offering proof of concept for reprogramming cell fate to target novel cancer vulnerabilities (2). Meanwhile, Greg Wang, from Duke University, focused on understanding and targeting both the canonical and noncanonical activities of EZH2 in cancer (3). Dr. Xiaolin Zi, from the University of California, Irvine, argued that phosphoserine phosphatase is specifically overexpressed in prostate cancer in the African American population.

The second session, co-chaired by Drs. Feng Yang and Li Xin continued the focus on target identification. Dr. Feng Yang, from Baylor College of Medicine, demonstrated that MAPK4 is a novel driver of prostate cancer and therapy resistance (4). Dr. Li Xin, from the University of Washington, followed with his recent findings on the tissue microenvironment of prostate zones (5). Dr. Zongwei Wang, from Harvard University, suggested a critical role for WNT signaling in 5-alpha-reductase inhibitor (5ARI) resistance in benign prostatic hyperplasia (BPH) management. Dr. Xiankai Sun, from UT Southwestern Medical Center, described the molecular design of prodrug theranostics (6). The session concluded with a presentation by Dr. Tian Zhang, a physician-scientist at UT Southwestern Medical Center, who shared her work on belzutifan, tracing its journey from the laboratory to clinical application.

The third session, co-chaired by Drs. Lizhen Chen (UT Health at San Antonio) and Ling Cai, also focused on target identification. Dr. Ling Cai, from Duke University, described the role of YY1 in advanced prostate cancer. Dr. Pengbo Zhou, from Cornell University, reported on how G3BP1-driven AR signaling influences prostate cancer pathogenesis. After Dr. Yong-Jie Lu, from Queen Mary University of London, discussed circulating biomarkers for prostate cancer (7), Dr. Lianchun Wang, from the

University of South Florida, demonstrated that PTEN loss upregulates CREB-Heparan Sulfate-FGF signaling to promote prostate tumorigenesis.

Epigenetics in Prostate Cancer

The session on epigenetics, co-chaired by Drs. Will Fong and Di Zhao, featured several important presentations. Dr. Di Zhao, from MD Anderson Cancer Center, opened the session with her recent research on CHD1, a multifaceted epigenetic remodeler in prostate cancer. Dr. Kexin Xu, from the University of Texas Health Science Center at San Antonio, followed with a report on targeting bromodomain-containing proteins to address GR-mediated enzalutamide resistance. Next, Dr. Will Fong, from the University of Kentucky, described the role of TRIM28 in prostate cancer. Dr. Lizhong Wang, from the University of Alabama at Birmingham, presented his findings on the epigenetic regulation of EIF4A1 and its translational targets in prostate cancer (8). The session concluded with Dr. Qi Cao, from Northwestern University, who demonstrated how EZH2 directly methylates PARP1 and regulates its activity.

Bioinformatics and New Technologies

The bioinformatics and new technologies session was co-chaired by Drs. Zheng Xia and Jonathan Zhao. Dr. Zheng Xia, from Oregon Health & Science University, presented a single-cell transcriptome atlas of prostate cancer, providing a valuable resource for the scientific community. Dr. Jonathan Zhao, from Emory University, followed with his recent work on the role of retrotransposons in regulating neuroendocrine prostate cancer (NEPC), as detected by nanopore long-read sequencing (LRS). Next, Dr. Yuanyuan Zhang, from Wake Forest, suggested that urine has the potential for use in precision medicine (9). Dr. David Zhang, from RendrCare, demonstrated the wide application of artificial intelligence (AI) in prostate cancer research and diagnosis (10). The session concluded with Dr. Weixing Zhao, from UT Health at San Antonio, who discussed the roles of the BRCA1-BARD1 E3 ligase in genome maintenance (11).

Cancer Etiology, Progression, and Metastasis

Drs. Xiaohong Li and Ping Yi led a session entitled "Cancer Etiology, Progression, and Metastasis." Dr. Xiaohong Li, from the University of Toledo, described her recent research on the role of PTH1R in prostate cancer metastasis. Dr. Zhou Wang, from the University of Pittsburgh, explained how targeting AR nuclear localization can be effective in castration-resistant prostate cancer (CRPC) (12). Dr. Ping Yi, from the University of Houston, discussed non-classical ubiquitination and its impact on receptor tyrosine kinases during cancer development. Following this, Dr. Jun Luo, from Johns Hopkins University, addressed the question of whether prostate cancer is heritable. Dr. Andrew Wang, from UT Southwestern Medical Center, concluded the session with a report on tri-specific nano-engagers for targeted immunotherapy in kidney cancer.

Tumor Microenvironment and Immunotherapy

The session on tumor microenvironment and immunotherapy was co-chaired by Drs. Zongbing You and Xin Lu. Dr. Zongbing You, from Tulane University, opened the session by suggesting that IL-17 is a valid therapeutic target in prostate cancer. Dr. Xin Lu, from the University of Notre Dame, followed by presenting data on targeting both intrinsic and extrinsic vulnerabilities in common and rare cancers. Dr. Jin-Tang Dong, from the Southern University of Science & Technology in China, demonstrated that KLF5 deletion and acetylation promote prostate cancer progression through microenvironment reprogramming. Dr. Meng Zhang, from UCSF, discussed how alternative promoter usage activates oncogenic programs during prostate cancer progression. The session concluded with Dr. Qiang Shen, from Louisiana State University, who developed natural product oridonin-based therapeutic agents for cancer treatment.

Overcoming Therapy Resistance

The session on overcoming therapy resistance was co-chaired by Drs. Chengfei Liu and Zhiguo Li. Dr. Allen Gao, from UC Davis, began by describing methods to target AKR1C3 in treatment-resistant prostate cancer. Dr. Chengfei Liu, also from UC Davis, demonstrated how to target N-Myc proteostasis in advanced prostate cancer (13). Dr. Zhiguo Li, from the University of Kentucky, presented his findings on targeting ER stress sensors to overcome enzalutamide resistance in prostate cancer. Following this, Dr. Yanquan Zhang, also from the University of Kentucky, introduced a new approach to enhance the efficacy of

BRD4 inhibitors (14). Finally, Dr. Hsin-Sheng Yang, from the University of Kentucky, presented a novel peptide that suppresses tumorigenesis.

Women's Forum

The special Women's Forum session was led by Dr. Jindan Yu from Emory University. Presenters included Drs. Jindan Yu, Runhua Liu, Xiaohong Li, Di Zhao, Lizhen Chen, and Feng Yang. The forum focused on discussing how to support women scientists in building successful careers in a male-dominated field.

The conference concluded with a banquet and an awards ceremony to honor individual achievements. Dr. Xiaoqi Liu received the Dedicated Service Award, while Dr. Jintang Dong was honored with the Lifetime Achievement Award. Dr. Jindan Yu and Dr. Allen Gao were recognized with the Research Excellence Award and the Mentoring Award, respectively. Dr. Di Zhao was awarded the Rising Star Award.

Additionally, the SAU management council members, Drs. Benyi Li, Xiaoqi Liu, Qianben Wang, Zongbing You, and Jindan Yu, gave reports on various activities they had overseen. Dr. Benyi Li delivered the closing remarks.

Conference attendees agreed that more research, both basic and clinical, is needed in urological cancers, particularly in the following areas: epigenetic regulation, targeted therapies, tumor microenvironment, and overcoming resistance to existing therapies.

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