



The 1st SAU Annual Conference on Urological Research

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ABSTRACT

In the fall of 2022, Dr. Benyi Li from the University of Kansas registered the scientific society with the title of Serican Academy of Urology (SAU), an international non-profit organization. The SAU is dedicated to uniting clinicians and basic scientists to tackle diseases related to the genitourinary tract. Prostate cancer, particularly castration-resistant prostate cancer and neuroendocrine prostate cancer, remains a significant public health issue. The academy held its first annual conference on December 26-29, 2023, in Cancun, Mexico. The conference was chaired by Dr. Xiaoqi Liu from the University of Kentucky, with generous sponsorship from SinoBiological, MedChemExpress, and Admera Health. Aiming to address the most urgent issues related to prostate cancer, the conference focused on topics such as epigenetics, lineage plasticity, therapy resistance, novel target identification, immunotherapy, and emerging technologies in the field. In honor of the late Dr. Changdeng Hu from Purdue University, one of the SAU founder members, Dr. Jiaoti Huang from Duke University presented a keynote address on developing grant applications through collaboration with pathologists. The Career Development Forum provided a platform for discussing career navigation and leadership development for the next generation of prostate cancer researchers. The conference concluded with a banquet, including an awards ceremony and committee reports.

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The Serican Academy of Urology (SAU) (<https://sericanacademy.org/>), a nonprofit organization composed of urological physicians and basic scientists, was 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, remains a significant public health issue (1). Androgen receptor (AR) signaling plays a well-established role in prostate cancer, including castration-resistant prostate cancer. As such, androgen signaling inhibitors such as abiraterone and enzalutamide are becoming first-line treatments for prostate cancer (2, 3). Unfortunately, treatment with androgen signaling inhibitors eventually leads to neuroendocrine prostate cancer, which is AR-independent. Thus, it is highly clinically relevant to dissect the mechanisms of resistance to androgen signaling inhibitors and identify new targets for neuroendocrine prostate cancer (4). Prostate cancer, especially neuroendocrine prostate

cancer, is largely driven by epigenetic dysregulation. As such, epigenetics has emerged as a major research focus in the prostate cancer field, holding promise for revealing valid treatment targets (5). Immunotherapy has dramatically changed the landscape of cancer treatment over the last decade. However, immunotherapy has not yet been effective for prostate cancer, which is considered immune “cold.” Developing strategies to convert prostate cancer into an immune “hot” state will be a major research direction for the field in the upcoming decade.

The First Annual SAU Conference on Prostate Cancer took place on December 26-29, 2023, in Cancun, Mexico. The meeting was attended by over 60 investigators with expertise in urology research. Co-chaired by Drs. Benyi Li and Xiaoqi Liu, the conference was generously sponsored by SinoBiological, MedChemExpress, and Admera Health. The event featured a keynote speech, nine scientific sessions, and one career development session. Topics covered included epigenetics, lineage plasticity, therapy resis-

[#] Committee members: Zhenbang Chen, Qi Cao, Xuesen Dong, Will Fong, Jianfei Qi, Xiaohong Li, Zhiguo Li, Chengfei Liu, Jinghui Liu, Xin Lu, Lizhong Wang, Zhu Wang, Kexin Xu, Chunhong Yan, Feng Yang, Ping Yi, Yuanyuan Zhang, and Xiaolin Zi.

tance, target identification, immunotherapy, and new technologies.

The conference commenced with a welcome reception on the evening of December 26, 2023. Dr. Benyi Li, the Chief of SAU, delivered the opening remarks, followed by a keynote presentation in honor of the late Dr. Chang-Deng Hu from Purdue University. Dr. Jiaoti Huang from Duke University, a lifelong friend and collaborator of Dr. Hu, gave the keynote presentation. Dr. Huang is the Johnston-West Endowed Department Chair of Pathology and a Professor of Pathology, Pharmacology and Cancer Biology, and Cell Biology at Duke University. Dr. Huang shared stories about his interactions with Dr. Hu over the past decade, detailing their highly productive collaborations on neuroendocrine prostate cancer and their success in securing multiple funded grants from the DOD and NIH. He also discussed his extensive experience with NIH study sections and emphasized the importance of collaborating with pathologists when applying for biomarker grants.

Disease relevance is a crucial factor in grant proposals studying human diseases such as prostate cancer. Researchers often aim for their laboratory discoveries to influence patient management and improve clinical outcomes. To achieve this goal, it is essential to demonstrate that mechanistic findings in model systems (such as cell lines, organoids, mouse models, and PDX models) can be validated in disease tissue. Pathologists process human tissue for histologic diagnosis, which guides prognosis and future management. They possess expertise in histologic assessment of tumor tissue, including tumor classification, grading, and staging. Additionally, pathologists usually have access to adjacent benign tissue, which serves as an important control. For scientists with significant laboratory findings using disease models, collaborating with a pathologist is critical to determine whether the molecules or pathways of interest are associated with any characteristics of the tumors. Beyond histologic assessment, pathologists are skilled in performing and interpreting results from tissue-based technologies such as immunohistochemistry, immunofluorescence, and in situ hybridization. In summary, Dr. Huang strongly recommended that researchers collaborate with pathologists during grant applications, study planning, and execution to enhance the translational potential of laboratory findings.

Epigenetics in prostate cancer

Two sessions have been arranged for this topic.

The first session was co-chaired by Drs. Kexin Xu and Will Fong. The session began with a presentation by Dr. Kexin Xu from the University of Virginia, who explained how RNA methylation contributes to de novo cholesterol biosynthesis in prostate cancer. Following this, Dr. Will Fong from the University of Kentucky reported his recent discovery regarding the role of TRIM28 in prostate cancer. Dr. Qianben Wang from Duke University then discussed the regulation of alternative polyadenylation during the progression of prostate cancer to castration resistance. Dr. Jindan Yu from Emory University presented their use of single-cell multimode, nanopore long-read sequencing, and Hi-C approaches to address prostate cancer lineage plasticity. In line with this, Dr. Wenliang Li from the University of Texas Health Science Center at Houston provided new insights into the molecular links between neuroendocrine differentiation and angiogenesis in prostate cancer progression (6, 7). Finally, Dr. Hua Wang from The Lundquist Institute shared his recent findings on BRCA and RNA modification in genome stability and PARP inhibitor sensitivity.

The second session on this topic was co-chaired by Drs. Jianfei Qi and Qi Cao. Dr. Jianfei Qi from the University of Maryland demonstrated the significance of the deubiquitinating enzyme USP11 in prostate cancer (8). Dr. Qi Cao from Northwestern University presented evidence that androgen receptor (AR)-regulated lncRNA PRCAT71 promotes AR signaling through its interaction with KHSRP in prostate cancer. Dr. Yanquan Zhang from the University of Kentucky showed that elevating PLK1 can overcome BETi resistance in prostate cancer by triggering BRD4 phosphorylation-dependent degradation during mitosis (9). Dr. Hansen He from the University of Toronto described the transcriptional and functional landscape of circular RNA in prostate cancer. Finally, Dr. Li Liu from UT Southwestern Medical Center in Dallas discussed the development of imaging technology for urological research.

Prostate cancer lineage plasticity and neuroendocrine prostate cancer

Drs. Jinghui Liu and Xuesen Dong co-chaired the session focusing on prostate cancer lineage plasticity and neuroendocrine prostate cancer. Dr. Jinghui Liu from the University of Kentucky presented his seminal finding on how CK1-associated phosphorylation of ATM drives enzalutamide resistance in castration-resistant prostate cancer (10). Dr. Xuesen Dong

from the University of British Columbia followed with a description of novel Lin28 inhibitors that suppress cancer cell stemness (11). Dr. Dean Tang from Roswell Park Comprehensive Cancer Center then provided a comprehensive review of the cell of origin for prostate cancer and prostate cancer stem cells (12). Dr. Changmeng Cai from UMass Boston demonstrated the role of the FOXA1/AP-1 axis as a driver of prostate cancer lineage plasticity (13). Dr. Ping Mu from Yale University discussed the dual aspects of prostate cancer: lineage plasticity and tumor heterogeneity (14). The session concluded with a presentation by Dr. Ming Chen from Duke University, who highlighted master transcriptional and epigenetic regulators of PSMA identified through unbiased CRISPRa screens.

Prostate cancer therapy resistance

There are two sessions on this topic. The first session was co-chaired by Drs. Feng Yang and Chengfei Liu. Dr. Feng Yang from Baylor College of Medicine presented solid evidence demonstrating that COP1 regulates AR signaling and prostate cancer therapy resistance (15). Following this, Dr. Chengfei Liu from the University of California, Davis, introduced a novel HSP70 allosteric inhibitor, JG98, which suppresses AR/AR-V7 expression in therapy-resistant cells and promotes STUB1 nuclear translocation to bind AR-V7 (16). Continuing on this topic, Dr. Allen Gao from UC Davis discussed the development of an AKR1C3 inhibitor, targeting androgen synthesis enzymes to restore drug sensitivity and advance from bench to bedside. Dr. Di Zhao from MD Anderson Cancer Center then described a new strategy involving the targeting of tumor suppressor deficiencies in advanced prostate cancer. Dr. Hsin-Sheng Yang from the University of Kentucky presented research on targeting the Plk1/Pdcd4/mTORC2 signaling pathway to overcome enzalutamide resistance in prostate cancer. Finally, Dr. Jane Wang from the University of Pittsburgh discussed strategies for targeting the G2/M checkpoint to induce synthetic lethality in castration-resistant prostate cancer.

The second session on this topic was co-chaired by Drs. Xiaolin Zi and Chunhong Yan. Dr. Xiaolin Zi from the University of California, Irvine, began by describing how targeting the copper exporter ATP7B can improve docetaxel-based chemotherapy in castration-resistant prostate cancer (17). This was followed by a presentation from Dr. Chunhong Yan

of Augusta University, who discussed mitochondrial uncoupling as a strategy for prostate cancer therapy. Dr. Jun Luo from Johns Hopkins University then presented his recent work on prostate cancer genetics, specifically HOXB13 mutations and AR signaling (18). With PARP inhibitors being a focus of numerous clinical trials for prostate cancer, Dr. Jia Li from Harvard Medical School highlighted his recent research on the genetic determinants of PARP inhibitor sensitivity and resistance (19). Dr. Bin-Zhi Qian from the University of Edinburgh demonstrated how macrophages promote anti-androgen resistance in prostate cancer bone disease (20). The session concluded with Dr. Jianmin Xu from Baylor College of Medicine, who showed that the knockout of Ncoa6 accelerates prostate cancer development in mice.

Urological cancer immunology and metabolism

Drs. Xin Lu and Zhiguo Li co-lead a session entitled “Urological Cancer Immunology and Metabolism.” Dr. Xin Lu from the University of Notre Dame introduced the topic of immunosuppression in genitourinary (GU) cancers and proposed solutions to overcome it (21, 22). This was followed by Dr. Zhiguo Li from the University of Kentucky, who demonstrated how targeting Plk1 can enhance antitumor immunity through STING-mediated T-cell activation. Next, Dr. Lisa Zhang from Tulane University presented a novel strategy for modeling age-related cancer to elucidate the role of Th17 inflammation in cancer progression (23). Dr. Qing Deng from Purdue University explained how to train immunity to enhance neutrophil effector functions. Dr. Xiaoping Bao, also from Purdue University, then discussed the critical role of CAR-neutrophils in cancer immunotherapy (24). The session concluded with Dr. Zhou Wang from the University of Pittsburgh, who provided a comprehensive review of inflammation in urological diseases (25).

Novel targets in urological cancers

Drs. Lizhong Wang and Xiaohong Li co-chaired a session focusing on novel targets in urological cancers. Dr. Runhua Liu from the University of Alabama at Birmingham proposed that targeting CD24 offers a strategy to enhance p53-restoring therapies, particularly for prostate cancer patients with mutant p53. Dr. Lizhong Wang, also from the University of Alabama at Birmingham, presented data suggesting an

oncogenic role for TUBB4A, proposing it as a potentially actionable therapeutic target for prostate cancers with TUBB4A overexpression. Dr. Xiaohong Li from the University of Toledo discussed the effects of treatments on prostate cancer dissemination and dormancy. Dr. Qiou Wei from the University of Kentucky demonstrated the oncogenic function of PRX4 in prostate tumorigenesis and cancer progression. Dr. Lizhen Chen from the University of Texas Health Science Center at San Antonio then elegantly described AR phase separation and enhancer function in prostate cancer. Finally, Elizabeth Keene, an MD student from the University of Kansas, presented her work on GAPDH inhibition for neuroendocrine prostate cancer treatment.

Drs. Ping Yi and Zhu Wang co-chaired a separate session, which also focused on novel targets in urological cancers. Dr. Ping Yi from the University of Houston described the role of the E3 ubiquitin ligase TRAF4 in prostate cancer (26). This was followed by a presentation from Dr. Zhu Wang of the University of California, Santa Cruz, who demonstrated the cell-type-specific roles of AR in prostate homeostasis and cancer progression (27). Dr. John Li from Roswell Park Cancer Center discussed DNA repair mechanisms in bladder cancer (28), while Dr. Jason Liu from the University of Texas Health Science Center at San Antonio presented on androgen signaling-induced enhancer dynamics in prostate cancer (29). Dr. Jer-Tsong Hsieh from UT Southwestern Medical Center described the benefits of building a multi-disciplinary translational research team. Dr. Jian Cao from Rutgers University discussed a novel mechanism of oncovirus-induced carcinogenesis (30).

Big data, emerging technologies, and pre-clinical models

The session, co-chaired by Drs. Zhenbang Chen and Yuanyuan Zhang focused on big data, emerging technologies, and pre-clinical models. Dr. Zhenbang Chen from Meharry Medical College discussed the complexity of castration-resistant prostate cancer in vivo. Dr. Yuanyuan Zhang from Wake Forest University demonstrated 3D in vitro models for studying urologic cancers. Dr. Changsheng Zhao from Emory University introduced the use of bioinformatics and new technologies in prostate cancer research. Dr. Xuefeng Liu from Ohio State University described

how patient-derived cells can be utilized in urological cancer research (31, 32).

The Career Development Forum

This special session was led by Drs. Xiaoqi Liu and Benyi Li. Dr. Zhou Wang from the University of Pittsburgh described how he built a very successful career. Dr. Allen Gao from the University of California, Davis, shared his path to becoming SBUR president. Dr. Dean Tang from Roswell Park Cancer Institute discussed his experiences as a department chair. Dr. Ming Chen from Duke University and Dr. Hua Wang from The Lundquist Institute talked about their recent successes with NIH grant applications, while Dr. Feng Yang from Baylor College of Medicine shared his extensive experience as a DoD grant reviewer.

The conference concluded with a banquet and an awards ceremony to honor individuals' achievements. Dr. Benyi Li, who single-handedly built up the SAU, received the well-deserved Dedicated Service Award. Dr. Jer-Tsong Hsieh was honored with the Lifetime Achievement Award, and Dr. Jiaoti Huang received the Mentoring Award. The Research Excellence Award went to Dr. Hansen He, and Dr. Ping Mu was the recipient of the Rising Star Award. Dr. Benyi Li delivered the closing remarks.

The conference attendees agreed that additional research (both basic and clinical) is needed in prostate cancer, in particular, the following specific areas: Epigenetic regulation in prostate cancer progression, Targeted therapies, especially neuroendocrine prostate cancer, Tumor microenvironment, and immunotherapy, and Overcoming resistance of existing therapies.

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