

Conference Report

Genomics in personalized cancer medicine and its impact on early drug development in China: report from the 6th Annual Meeting of the US Chinese Anti-Cancer Association (USCACA) at the 50th ASCO Annual Meeting

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Abstract

The 6th Annual Meeting of the United States Chinese Anti-Cancer Association (USCACA) was held in conjunction with the 50th Annual Meeting of American Society of Clinical Oncology (ASCO) on May 30, 2014 in Chicago, Illinois, the United States of America. With a focus on personalized medicine, the conference featured novel approaches to investigate genomic aberrations in cancer cells and innovative clinical trial designs to expedite cancer drug development in biomarker-defined patient populations. A panel discussion further provided in-depth advice on advancing development of personalized cancer medicines in China. The conference also summarized USCACA key initiatives and accomplishments, including two awards designated to recognize young investigators from China for their achievements and to support their training in the United States. As an effort to promote international collaboration, USCACA will team up with Chinese Society of Clinical Oncology (CSCO) to host a joint session on “Breakthrough Cancer Medicines” at the upcoming CSCO Annual Meeting on September 20th, 2014 in Xiamen, China.

Key words Genomics, cancer, personalized medicine

The United State Chinese Anti-Cancer Association (USCACA) successfully held its 6th Annual Meeting on May 30th, 2014 in Chicago, Illinois, the United States of America, in conjunction with the 50th Annual Meeting of American Society of Clinical Oncology (ASCO). The theme for this year’s event was “Genomics in Personalized Cancer Medicine and Its Impact on Early Drug Development in China.” Over 150 participants from academia,

pharmaceutical and biotechnology industries, and cancer research organizations from China and the United States (US) attended the meeting.

On behalf of the organizing committee, Dr. Yun-Guang Tong, Chair of the 2014 Annual Meeting (**Figure 1A**), opened the meeting by introducing the agenda of the Annual Meeting and welcoming the leadership team delegation of Chinese Society of Clinical Oncology (CSCO) led by Dr. Yi-Long Wu, Vice President of Guangdong General Hospital, President of CSCO, and the delegation from Shanghai Institute of Material Medical (SIMM) led by Dr. Jian Ding, former Director of SIMM and Academician of the Chinese Academy of Engineering, and Dr. Mei-Yu Geng, Vice Director of SIMM. Representatives from US oncology community included Dr. George Wilding, former Director of Wisconsin Comprehensive Cancer Center, and Dr. Lou Weiner, Director of Georgetown Lombardi Comprehensive Cancer Center, and senior executives from pharmaceutical and biotechnology companies.

Dr. Shi-Yuan Cheng, President of USCACA (**Figure 1B**), summarized key initiatives and accomplishments of USCACA. These included: (1) Collaborating with associations and organizations dedicated to cancer research, education, treatment and prevention,

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notably Chinese Anti-Cancer Association (CACA), CSCO, Chinese Society for Anti-Cancer Agents (CSACA), American Association for Cancer Research (AACR), ASCO, National Foundation for Cancer Research (NFCR), and Asian Foundation for Cancer Research (AFCR); (2) Supporting *Chinese Journal of Cancer (CJC)*, the official journal of USCACA, to achieve its milestone of being included in the Scientific Citation Index (SCI). USCACA will continue organizing special CJC issues on selected topics in 2014, including the second issue on *Pollution and Cancer*, and issues of *Epstein-Barr Virus and Nasopharyngeal Carcinoma*, *Immunoncology*, and *Cancer Metabolism*; and (3) Implementing and expanding USCACA-NFCR Scholarship Program. With the effort of the Scholarship Selection Committee led first by Dr. Shi-Yuan Cheng and then by Dr. Li-Fang Hou, during the past four years, 16 outstanding junior Chinese investigators have received this award^[1-3]. Dr. Cheng also highlighted the growing influence of USCACA. USCACA was approached for opinion on the rising cancer rates in China, India, and Russia^[4] by the American division of Chinese state broadcaster China Central Television (CCTV-America) (<http://youtu.be/z5CybZlufQs>).

After an introduction of the new initiatives of CSCO and the CSCO-USCACA Collaboration by Dr. Yi-Long Wu (**Figure 1C**), Dr.

Li Yan, Managing Director of USCACA, announced two fellowship programs generously supported by industry collaborators, Jiangsu Hengrui Medicine Corporation (USCACA-Hengrui Fellowship) and ACEA Biosciences (USCACA-ACEA Fellowship), which will strengthen the USCACA commitment to supporting young investigators from China. Dr. Li Xu, Senior Vice President of Oncology R&D of Hengrui (**Figure 2A**), and Dr. Xiao Xu, President and CEO of ACEA (**Figure 2B**) presented donations to Dr. Cheng and Dr. Yan, witnessed by the applauding audience. These donations will add new opportunities for young investigators for observing and training in early stages of clinical cancer drug research in prestigious US cancer centers and National Cancer Institute. USCACA also issued three Outstanding Contribution Awards to honor the exceptional contributions of Drs. Li Xu of Hengrui Medicine, Michael O'Neal, Chief Medical Officer of CoreLab Partners, and Wen-Ru Song, Vice President of Immuno-Oncology Development of AstraZeneca.

Dr. Xiao-Liang (Sunny) Xie, the Mallinckrodt Professor of Chemistry and Chemical Biology, Harvard University and a member of the National Academy of Sciences of USA kicked off the Scientific Program of the Annual Meeting (**Figure 3A**). Dr. Xie described his remarkable discovery of genome sequencing of single cells. A



Figure 1. Opening of the Annual Meeting. A, Chair of 2014 Annual Meeting, Dr. Yun-Guang Tong opens the conference. B, Dr. Shi-Yuan Cheng gives Presidential Address. C, Dr. Yi-Long Wu introduces the development of CSCO and the CSCO-USCACA collaboration.



Figure 2. Drs. Shi-Yuan Cheng and Li Yan accept donations for two industry-sponsored fellowship programs. A, Dr. Li Xu, from Hengrui Oncology, presents a donation to support the USCACA-Hengrui Fellowship. B, Dr. Xiao Xu, from ACEA Biosciences, presents a donation to support the USCACA-ACEA Fellowship.

major challenge in sequencing genome of a single cell is to develop an approach for whole-genome amplification that recovers a high percentage of the genome with minimal amplification bias. This new technology recently developed in Dr. Xie's Lab, named as multiple annealing and looping-based amplification cycles (MALBAC), overcomes the shortcomings of the old methodologies and improves genome coverage from 60% to 93% and efficiency of detecting both alleles of known single-nucleotide variations from 10% to 71%^[5,6]. The development of genome sequencing of single cells therefore opened new avenues of investigation in determining haplotype and genomic variability that can be applied to cancer research and diagnosis of human diseases. Dr. Xie also highlighted his close and productive collaborations with oncologists in China. In collaboration with Dr. Jie Wang, Professor of Thoracic Oncology at Peking University Cancer Hospital, Dr. Xie's new technology was successfully applied to analyze single circulating tumor cells (CTCs) derived from lung cancer patients^[7]. It was observed that every CTC from an individual patient, regardless of the cancer subtypes, exhibited reproducible copy number variation (CNV) patterns, similar to those of the metastatic tumor from the same patient. Different patients with lung cancer adenocarcinoma (ADC) shared similar CNV patterns in their CTCs. Patients of small-cell lung cancer have CNV patterns distinct from those of ADC patients. These findings also suggested that CNVs at certain genomic loci are selected for cancer metastasis. The reproducibility of cancer-specific CNVs offers potential for CTC-based cancer diagnostics and an additional means for improving clinical management of lung cancer patients.

Dr. Zong-Hui Peng, Deputy Director of Pharmacogenomics Research from Beijing Genomics Institute (BGI) Tech, introduced *Multi-Omics Solutions for Cancer Research* (Figure 3B). Dr. Peng highlighted the technical solutions and platforms developed by BGI Tech that would facilitate cancer research by taking advantage of various "-omics" technologies. In collaboration with Dr. Qi-Min Zhan at Chinese Academy of Medical Sciences and Peking Union Medical College, whole-genome sequencing, exome sequencing, and array comparative genomic hybridization analysis were recently used to explore the genomic alterations in esophageal squamous cell cancer (ESCC)^[8], one of the most aggressive cancers and the

6th leading cause of cancer death worldwide^[9]. This collaboration led to identification of eight significantly mutated genes, of which six were well known tumour-associated genes (*TP53*, *RB1*, *CDKN2A*, *PIK3CA*, *NOTCH1*, and *NFE2L2*), and two previously unknown in ESCC (*ADAM29* and *FAM135B*). In addition to the mutations, *MIR548K*, a microRNA encoded in the amplified 11q13.3–13.4 region, was found to be a novel oncogene. Other interesting findings included a frequent alteration in histone regulator genes, *MLL2* (as known as *KMT2D*), *ASH1L*, *MLL3* (*KMT2C*), *SETD1B*, *CREBBP*, and *EP300*. The study also highlighted that somatic aberrations in ESCC were mainly involved in the Wnt, cell cycle, and Notch pathways. These discoveries are expected to facilitate development of targeted therapy in ESCC.

Two subsequent talks were devoted to the topic of *Developing Personalized Medicine for Lung Cancer Patients—Master meets Cluster*. Dr. Vali Papadimitrakopoulou, Professor of Thoracic/Head & Neck Medicine Oncology from MD Anderson Cancer Center (MDACC) (Figure 3C), and Dr. Yi-Long Wu shared their clinical studies of personalized medicines in lung cancer treatment. In the Phase II/III Biomarker-driven Master Protocol in second-line squamous lung cancer trial championed by SWOG and Cluster Trial being conducted at Guangdong General Hospital, lung cancer patients are first profiled for genetic aberrations and subsequently assigned to molecular targeted agents such as PI3K, CDK4/6, cMET, FGFR inhibitors to attack the specific corresponding genetic aberrations harbored in their tumors. By matching patients with appropriate targeted therapies, this approach is designed to expedite cancer drug development and to improve the success rate, ultimately leading to personalized medicine for cancer patients.

Dr. Michael Shi, Global Clinical Program Head, Novartis, and an Executive Member of the USCACA, hosted the panel discussion (Figure 4) on *Genomic Medicine in Oncology R&D and Its Impact on Early Drug Development in China*. Dr. Shi opened the discussion by briefly going over the background and last year's discussion on the topic^[3]. He then raised questions to distinguished panelists from industry and academia included: Dr. Li Xu, USCACA Executive Committee, Senior Vice President of Hengrui Oncology; Dr. Roger Luo, USCACA Executive Committee, Director and Liaison of Asia



Figure 3. Scientific presentations. A, Dr. Xiao-Liang (Sunny) Xie presents researches on genome sequencing for single cells. B, Zong-Hui Peng presents researches on multi-omics analysis of cancer tissues. Vali Papadimitrakopoulou (C) and Yi-Long Wu share their researches on biomarker-based clinical trial design.



Figure 4. Panel discussion on genomic medicine in oncology research and development and its impact on early drug development in China. From left side to right: Dr. Roger Luo, Dr. Li Xu, Dr. Chris Takimoto, Dr. Margaret Dugan, Dr. Michael Shi (Panel Mediator), Dr. Yi-Long Wu, Dr. Vali Papadimitrakopoulou, and Dr. Hua Mu.

Pacific Oncology Clinical Development at Janssen Oncology; Dr. Vali Papadimitrakopoulou, Professor of MDACC; Dr. Margaret Dugan, Senior Vice President of Novartis Oncology; Dr. Chris Takimoto, Vice President, Head of Oncology Translational Medicine & Early Development at Janssen Pharmaceutical Companies; Dr. Hua Mu, Senior Vice President of Global Head of Product Development Business Unit at WuXi AppTec; and Dr. Yi-Long Wu, President of CSCO and Professor of Guangdong General Hospital. The panel discussion showcased the successes and challenges in oncology drug development in China and US as well as highlighted the collaboration of USCACA and China FDA in drafting the Guidelines for Medicinal Products Review and Approval, and the Biomarker Guideline for drug development in China.

At the end, Dr. Cheng closed the Annual Meeting by emphasizing the mission of USCACA and the importance of collaboration with industry and academia leaders in achieving the mission, and acknowledging the outstanding services of the Annual Meeting Organizing Committee and local volunteers from Northwestern University and the University of Illinois at Chicago.

About the USCACA

The U.S. Chinese Anti-Cancer Association (USCACA, 美中抗癌协会) (<http://www.uscaca.org/>) is a non-profit professional organization founded in 2009. With members from academia, industry and government, USCACA facilitates collaboration among cancer research and physicians in the United States and China. Our current focus is on expediting novel cancer drug development by fostering clinical trial networks, sharing best practices and knowledge of clinical trial, and providing education and training opportunities. USCACA collaborates with Chinese Anti-Cancer Association (CACA, 中国抗癌协会), Chinese Society for Clinical Oncology (CSCO), and other professional associations. Our mandate is to improve cancer treatment through research, education, and collaboration.

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The 2014 USCACA Annual Meeting Organizing Committee

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 Li Yan, Peking University and GlaxoSmithKline
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