Conference Report

Our DREAM of defeating cancer: a summary of the 3rd Guangzhou International Symposium on Oncology

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Every 6 seconds, someone dies from cancer somewhere in the world. Every 13 seconds, a cancer patient dies in China. Cancer is currently the biggest threat to life around the world and a critical burden to China. To address this problem, it is especially important for scientists and physicians to remain abreast of cutting edge research and progress in the treatment of this disease.

The 3rd Guangzhou International Symposium on Oncology was held on November 7–9, 2013, in Guangzhou, China (**Figure 1**). The symposium was jointly organized by Sun Yat-sen University Cancer Center (SYSUCC), the US Chinese Anti-Cancer Association (USCACA), the Guangdong Provincial Anti-Cancer Association, and the *Chinese Journal of Cancer* (CJC). The presentations covered several predominant types of cancer and progress in basic, translational, and clinical researches. The symposium revealed that there is still long way to go to reach our dream of defeating cancer, even though there has already been an enormous effort into research. Here, we provide highlights of the presentations.

Figure 1. **Dr. Wei Zhang is giving the opening speech.**

Mechanisms in Oncology

Gene level

The tumorigenic fusion *FGFR3-TACC3* escapes *miR-99a* regulation in glioblastoma multiforme

Brittany C. Parker, from Wei Zhang's lab at M. D. Anderson Cancer Center (MDACC), presented the group's recent discovery that the tumorigenic fusion *FGFR3-TACC3* escapes *miR-99a* regulation in glioblastoma multiforme (GBM). Fusion genes are common aberrations in cancer. Notable examples include *BCR-ABL1* in chronic myeloid leukemia, *ETS* family fusions in prostate cancer, and *Alk* fusions in lung cancer. To answer the question of whether a targetable fusion gene exists in glioma, they performed deep RNA sequencing on glioma tissue of varying grades and searched for reads that spanned exon-exon junctions connecting two distinct genes. The top candidate was *FGFR3-TACC3*, which was only present in GBM samples and not in low-grade glioma samples or normal brain tissues. Real-time polymerase chain reaction (PCR) was performed to validate the presence of the fusion, and the fusion was detected in 4 of 38 GBM patient samples but not in low-grade or normal samples. *FGFR3-TACC3* cells are chemoresistant but

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sensitive to targeted therapy. They also found that *miR-99a* targets *FGFR3* in GBM, which may lead to new targeted therapy.

An omics strategy for understanding the mechanism of colorectal cancer metastasis

Yan-Qing Ding, from Southern Medical University, introduced an omic strategy for understanding the mechanism of colorectal cancer (CRC) metastasis. Because a single-gene research model cannot meet the demand for high-throughput studies, "omics" is an important strategy to elucidate the mechanism of tumor metastasis. At the transcriptome level, single cell-derived progenies were isolated and gene expression profiling revealed that 143 genes were differentially expressed between lowly and highly metastatic single cell-derived progenies. Notably, the five-gene signature *LYN/MAPEK4/SDCBP/MID1/DKK1* was identified as a potential predictor of metastasis and survival in CRC. In proteomics studies, 17 tumor-associated proteins, 12 tumor suppressor proteins, and 13 metastasis-associated proteins were revealed. LASP-1 was found associated with cell growth and migration. *miR-224* is an important prognostic marker and therapeutic target for CRC because it promotes cell proliferation and tumor growth by repressing *PHLPP1* and *PHLPP2*. Also, Ding's group found that the *HMGA1/miR-137/FMNL2* axis and JMJD2B play important roles in CRC metastasis.

microRNA level

Master microRNA regulatory network and new therapeutic tools in ovarian cancer

Wei Zhang, director of the Cancer Genomics Core Laboratory at MDACC and co-director of a Genome Data Analysis Center (GDAC) of The Cancer Genome Atlas (TCGA), described how TCGA is providing new insight into ovarian cancer. In 2000, Hanahan and Weinberg proposed six hallmarks of cancer. In 2011, another two emerged: deregulation of cellular energy and evasion of immune destruction. These features make targeting a single pathway insufficient, as cancers use redundant carcinogenetic mechanisms and shift from one signaling pathway or hallmark to another. The goal of TCGA is to increase scientific understanding of the molecular basis of cancer, providing information that can be harnessed to better diagnose, treat, and prevent cancer. In the next 5 years, the aim is to address 20 major cancer types beginning with GBM and followed by ovarian cancer. TCGA Project Pipeline offers several resources, including Biospecimen Core Resource, Genome Characterization Centers, Genome Sequencing Centers, Proteome Characterization Centers, Data Coordinating Center, and GDACs.

Based on the Institute for Systems Biology (ISB)-MDACC GDAC data, genetic and epigenetic alterations of *BRCA1* and *BRCA2* were associated with ovarian cancer patients' survival and response to platinum-based chemotherapy. The TCGA network defined four subtypes of ovarian cancer based on transcriptome, but the survival of the four types are not significantly different. Integrated genomic analyses revealed an miRNA regulatory network that further defined a robust integrated mesenchymal subtype associated with poor overall survival in serous ovarian cancer. Eight key miRNAs, including *miR-506*, *miR-141*, and *miR-200a*, were predicted to regulate 89% of the targets in this network. Nanoparticle delivery of *miR-506* in orthotopic ovarian cancer mouse models led to E-cadherin induction and reduced tumor growth, whereas delivery of *miR-200* members into the tumor endothelium resulted in marked reductions in metastasis and angiogenesis and induced vascular normalization. These findings indicate that several candidate miRNAs may be useful in treating ovarian cancer.

New perspective on HER2 targeting for breast cancer

Er-Wei Song, an oncologist from Sun Yat-sen Memorial Hospital, Sun Yat-sen University (SYSU), gave a detailed talk on targeted therapy, focusing on progress being made in treating breast cancer. Song's group found that *miR-21* expression is up-regulated in trastuzumab-resistant HER2 breast cancer cells, and ectopic miR-21 expression confers trastuzumab resistance in breast cancer *in vitro* and *in vivo*. When F5-P was used as a mediator, siRNA could be delivered to HER2-positive breast cancer cells via antigen-antibody reaction. Song's group demonstrated that a cocktail of siRNAs targeting *PLK1*, *CCND1*, and *AKT* delivered by F5-P has enhanced antitumor effects in HER2-positive breast cancer cells *in vivo*.

Modification and modulation of signaling by microRNA in cancer cells

Meng-Feng Li, from SYSU Zhongshan School of Medicine, summarized how miRNA can impact signaling in cancer cells. miRNA modulates cellular signaling mainly as an "amplifier," a "fine-tuner," and a "crosstalk mediator" at multiple levels. Li's group found that *miR-30e** overexpression in human glioma cell lines led to hyperactivation of nuclear factor-κB (*NF-κB*) and enhanced expression of *NF-κB*–regulated genes, which promoted glioma cell invasiveness in *in vitro* assays and in an orthotopic xenotransplantation model. These effects of *miR-30e** were clinically relevant, as *miR-30e** was up-regulated in primary human glioma cells and associated with malignant progression and poor survival. In addition, Li's group found that *miR-182* was overexpressed in a different set of gliomas with relatively lower *miR-30e** expression and that *miR-182* directly suppressed cylindromatosis (CYLD), an *NF-κB*–negative regulator. This suppression of CYLD promoted ubiquitin conjugation of NF-κB signaling pathway components and induction of an aggressive phenotype of glioma cells both *in vitro* and *in vivo*. These findings uncover a plausible mechanism for sustained *NF-κB* activation in malignant gliomas and may suggest a new target for clinical intervention.

Metabolic level

Integrated regulation of cancer metabolism and cell cycle progression

Zhimin (James) Lu, from MDACC, introduced findings of his group on how cancer cell metabolism is regulated. Their studies revealed that the pyruvate kinase isoforms PKM1 and PKM2 have differential roles and that PKM2 is instrumental for tumor development. They also revealed the mechanisms underlying epidermal growth factor

(EGF)-induced PKM2 up-regulation in cancer, which was selected as one of the signaling breakthroughs of the year. The essential nuclear functions of PKM2 in tumorigenesis include transcription factor co-activator, histone kinase, G_1/S progression regulation, and the Warburg effect. PKM2 was also demonstrated to regulate chromosome segregation and mitotic progression in tumor cells.

Identification of mitotic regulators as cancer biomarkers and drug targets

Qi-Min Zhan, from State Key Laboratory of Molecular Oncology, Cancer Institute, Chinese Academy of Medical Sciences and Peking Union Medical College, introduced studies of his group identifying mitotic regulators as cancer biomarkers and drug targets. They found that disharmonious traffic in mitotic progression related with tumorigenesis. The human centrosomal ninein-like protein (Nlp) is a new member of the γ-tubulin complex-binding proteins that is essential for proper execution of various mitotic events. Several lines of evidence have linked Nlp to human cancer. Deregulation of Nlp in cell models results in aberrant spindle, chromosomal missegregation, and multinulei; induces chromosomal instability; and renders cells tumorigenic. Overexpression of Nlp induces anchorage-independent growth and immortalizes primary cell transformation. In addition, the expression of Nlp is elevated primarily due to *NLP* gene amplification in human breast cancer and lung carcinoma. Consistently, transgenic mice overexpressing Nlp display spontaneous tumors in the breast, ovary, and testicle, and show rapid onset of radiation-induced lymphoma, indicating that Nlp is involved in tumorigenesis.

Phosphorylation of Dock180 by protein kinases mediates *EGFRvIII*-driven glioblastoma tumorigenesis and characterization of glioma stem cells

Shi-Yuan Cheng, from Northwestern University, reported the role of Dock180 in *EGFRvIII*-driven glioblastoma tumorigenesis and discussed properties of glioma stem cells. *EGFRvIII* (ΔEGFR/de2-7EGFR), a constitutively active *EGFR* mutant that is frequently co-overexpressed with EGFR in GBM, promotes glioma growth and invasion through protein kinase A (PKA)-dependent phosphorylation of Dock180, a bipartite guanine nucleotide exchange factor for Rac1. They demonstrated that EGFRvIII induced serine phosphorylation of Dock180, stimulated Rac1 activation, and promoted glioma cell migration. *In vitro* PKA kinase assays as well as treatment with the PKA inhibitors H-89 and KT5720 and overexpression of a PKA inhibitor (PKI) revealed that *EGFRvIII*-mediated induction of Dock180 serine phosphorylation was PKA-dependent. Significantly, PKA induces phosphorylation of Dock180 at amino acid residue S1250 that resides within its Rac1-activating DOCK homology region 2 (DHR2) domain. Expression of the Dock180S1250L mutant, but not wild-type Dock180, protein in *EGFRvIII*-expressing glioma cells inhibited receptor-stimulated cell proliferation, survival, and migration *in vitro* and glioma tumor growth and invasion *in vivo*. Together, these results provide a novel mechanism by which *EGFRvIII* drives glioma tumorigenesis and invasion through PKA-dependent phosphorylation of Dock180.

Metabolic features and pharmacologic intervention of cancer stem cells

Peng Huang, from SYSUCC and MDACC, showed data suggesting that cancer stem cells exhibit low mitochondrial respiration and high glycolytic activity, likely due to a down-regulation of complex II. Glucose plays a major role in regulation of side population (SP) cells through activation of Akt. Cancer stem cells prefer a hypoxic microenvironment and are highly resistant to conventional chemotherapeutic agents. Inhibition of glycolysis represents a novel strategy to overcome such drug resistance and effectively kills cancer stem cells, especially under hypoxic conditions.

Microenvironment level

New insights into antiangiogenic targeted therapy

Chao-Nan Qian, from SYSUCC, discussed antiangiogenic targeted therapy. Issues in vascular normalization include reduced vascular turnover, less chaotic branching, less vascular density, and a hierarchical pattern. Increasing evidence has shown that a solid tumor can, during invasion and expansion, "hijack" pre-existing blood vessels and integrate them into the tumor vasculature. This approach to expanding the tumor vasculature is referred to as vessel co-option. Vessel co-option, along with the complementary processes of vessel remodeling and extratumoral angiogenesis, all contribute to tumor angiogenesis. Some biomarkers such as interleukin-8 (IL-8) can predict resistance to antiangiogenic targeted therapy. Additional preclinical animal models should be established to identify novel biomarkers of resistance to antiangiogenic targeted therapy.

Progress in Diagnosis and Treatment

Nasopharyngeal carcinoma

Joseph Wee, a radiation oncologist from National Cancer Centre of Singapore, gave an overview of recent advances in radiotherapy for nasopharyngeal cancer (NPC). During the last decade, several randomized controlled trials and meta-analyses showed the survival advantage of concurrent chemotherapy for loco-regionally advanced NPC patients. The role of adjuvant chemotherapy is still controversial mainly because of compliance. Thus, induction chemotherapy is under investigation for loco-regionally advanced NPC patients. Moreover, chemotherapeutic agents other than cisplatin are under consideration. Another great progress in NPC treatment is intensity-modulated radiotherapy (IMRT), which contributes significantly to better local control and fewer complications, especially for T3 and T4 diseases. Induction chemotherapy is another choice for patients with bulky tumor before radiotherapy. Dose escalation by stereotactic boost may improve survival. Whether lower neck radiotherapy could be omitted in N0−1 patients triggered a clinical study. Both physical and pharmaceutic methods may be effective in the management of xerostomia. Less toxic systemic agents, such as cetuximab, nimotuzumab, nedaplatin, carboplatin, and recombinant adenovirus-p53, may cause less toxicity.

Genitourinary malignancies

Fang-Jian Zhou, a genitourinary oncologist from SYSUCC, talked about advances in diagnosis and treatments of renal cancer, prostate cancer, and other genitourinary malignancies. Concordant with the popularity of imaging techniques, the rate of early diagnosis has increased. Nephron-sparing surgery is the current standard for the treatment of localized renal cell carcinoma because of less chronic renal disease and better survival outcome. Previously, treatment choices for metastatic renal cancer patients include chemotherapy, immune therapy, and surgery. In this decade, targeted therapy contributed to the treatment of late-stage renal cancer, including sorafinib, sunitinib, pazopanib, axitinib, everolimus, temsirolimus, and bevacizumab. Tyrosine kinase inhibitors have been recommended as the first- and second-line treatment for metastatic renal cancer. Combination of prostate-specific antigen screening and ultrasonography-guided biopsy increased the rate of early diagnosis in prostate cancer patients. The use of laparoscopy and robot enabled anatomic removal of the prostate and led to better quality of life for those patients. New drugs, such as abiraterone, orterone, enzalutamine, Ra223 dichloride, and sipuleucel-T, offered hope for prolonged survival in prostate cancer patients with late-stage disease.

Diffuse large B-cell lymphoma

Wen-Qi Jiang, a medical oncologist from SYSUCC, reported the progress of targeted therapy in diffuse large B-cell lymphoma (DLBCL). Various kinds of targeted medicine are under investigation in clinic, including the new anti-CD20 antibody GA101, small molecule−targeted drugs such as BCR pathway inhibitors, mammalian target of rapamycin (mTOR) pathway inhibitors, proteasome inhibitors, and immunomodulators. Because DLBCL is a group of highly heterogeneous diseases, gene expression profiles would be popularized and used directly to guide treatment.

Acute myeloid leukemia

Jun Ma, an expert in malignant homeopathy from Harbin Tumor Institute of Hematology, interpreted the latest international clinical guideline for the treatment of acute myeloid leukemia (AML). For inductive treatment, the combination of anthracycline and arabinoside cytarabine (Ara-C) is the standard regimen for adult AML worldwide, with a 70%−80% complete response rate. The combination of homoharringtonine (HHT) and Ara-C may garner a similar outcome in China. DAC, 5-azacytidine (AZA), and other medicine are under investigation for induction. Personalized treatment is recommended for the maintenance phase after remission. Targeted therapy including CPX-351, DOT1L inhibitor, sorafenib, clofarabine, sapacitabine, and elacytarabine, is also a hot research topic in AML.

Breast carcinoma

Zhi-Min Shao, a surgeon from Fudan University Shanghai Cancer Center, reported the evolution of treatment modalities for early-stage breast cancer. Surgery remains the mainstay for early-stage breast cancer. Since the 1890s, radical surgery has gradually been replaced by conservative surgery for patients with early-stage breast cancer, but a lot of questions still need to be answered. Recurrence rate may be affected by age, menopausal status, lymph node status, and molecular grouping. However, treatment needs to be balanced with the cosmetic effect. Whether sentinel lymph node (SLN) biopsy could replace axillary lymph node dissection (ALND) has also been addressed, and Dr. Shao shared the consensus and controversy of indication for ALND when SLN biopsy reveal lymph node metastasis. Immediate breast reconstruction using autologous tissue is recommended if needed. Core needle biopsy is better than open surgical biopsy, and the majority is guided by ultrasonography. For the overall treatment plan, controversy remains regarding radiotherapy after conservative surgery, selection of chemotherapy regimen according to endocrine responsiveness, drug choice, and duration of endocrine therapy. The trend of individualized medicine was also discussed.

Radiotherapy after breast conservative surgery

Jin-Ming Yu, a radiation oncologist from Shandong Cancer Hospital, discussed adjuvant radiotherapy for early-stage breast cancer patients after conservative surgery. American and European techniques in conservative surgery were compared, negative margin for radiotherapy was defined, and hypofractionated radiotherapy versus conventional fraction was discussed. While whole breast irradiation and tumor-bed boost is the standard choice for early-stage breast cancer patients after conservative surgery, Dr. Yu introduced the indication for omission of whole breast irradiation and tumor-bed boost. Delay between the surgery and radiotherapy and sequence of adjuvant chemotherapy and radiotherapy are also important. Consensus of American Society for Radiation Oncology (ASTRO) and European Society for Radiotherapy & Oncology (ESTRO) on the definition of low-risk patients for accelerated partial breast irradiation was also summarized. Cardiac toxicity was discussed based on a clinical trial.

Proton and heavy ion irradiation

Guo-Liang Jiang, a radiation oncologist from Fudan University Shanghai Cancer Center, introduced the experimental and clinical benefit of particle irradiation. The idea of using particles to treat cancer patients dates back to 1946, and the first patient was treated with protons in 1954 in Lawrence Berkeley Lab. The number of patients who have undergone particle treatment is rising around the world, and as of December 2012, 39 centers provide particle therapy. The advantage of proton therapy mainly centers on pediatric tumors, skull base tumors, and chordoma. The treatment outcomes using carbon ion irradiation is comparable to surgery for medically inoperable lung cancer, liver cancer, and high-risk prostate cancer. While most of the data come from Japan and German, we need more domestic experience in this area. To our great joy, the Shanghai Proton and Heavy Ion Hospital will open in April 2014.

Radiofrequency electromagnetic fields

Boris Pasche, a professor of medicine from the University of Alabama at Birmingham, introduced targeted cancer treatment with radiofrequency electromagnetic fields amplitude-modulated at tumor-specific frequencies. Tumor-specific frequencies have been identified by biofeedback methods based on changes in blood pressure. Intrabuccally administered 27-MHz electromagnetic fields, amplitude-modulated at tumor-specific frequencies, elicited objective responses in several patients with advanced breast cancer and hepatocellular carcinoma (HCC), and several patients experience long-lasting response or disease stabilization without significant adverse events. In concert with this, down-regulation of the *PLP2* and *XCL2* genes and modulation of the IP3/DAG signaling pathway have been observed. The experimental findings suggest the existence of a novel receptor mechanism through which cancer growth can be effectively targeted, thus offering a new therapeutic approach.

Valuable Chinese Experience

Extranodal nasal-type NK/T-cell lymphoma

Ye-Xiong Li, a radiation oncologist from Cancer Hospital, National Cancer Center of China, shared findings on nasal-type natural killer/T-cell lymphoma (NKTCL). According to his report, radiotherapy produced favorable outcomes for early-stage NKTCL compared to chemotherapy, and chemoradiotherapy may be better for high-risk patients. The optimal dose was 50 Gy and a boost of 5−10 Gy was needed for residual disease. High Epstein-Barr virus (EBV)-DNA level before treatment was a negative prognostic factor, and pretreatment or posttreatment EBV-DNA level is a prognostic predictor of survival for early-stage NKTCL after radiotherapy. In addition, NKTCL is heterogeneous depending on location. Waldeyer's ring NKTCL is more common in males, with early-stage disease and cervical lymph node enlargement and relatively better prognosis. The radiation field for NKTCL affecting the nose and Waldeyer's ring should be extended to involved field and extended field.

Hepatocellular carcinoma

Min-Shan Chen, a surgical oncologist from SYSUCC, introduced the multidisciplinary treatment of liver cancer at SYSUCC. Because the effect of surgery suggested the limit for HCC in 1990s, it is important to maximize the benefit of other treatment methods and formulate a comprehensive treatment strategy. Chen's group published data from several clinical trials that have greatly impacted this field. Radiofrequency ablation (RFA) has become an important treatment for primary and recurrent HCC. Good candidates for RFA are patients with HCC at an early stage (solitary tumor $\leqslant$ 5 cm in diameter or $\leqslant$ 3 nodules and $\leqslant$ 3 cm in diameter). Several clinical trials have shown that RFA is effective in treating small HCC. In the future, the standard of care for HCC treatable with RFA should shift toward combination treatment. RFA has already begun to challenge the status of resection as the optimal treatment for HCC $\leqslant$ 2 cm; combined RFA and transarterial chemoembolization (TACE) will certainly broaden this challenge.

Colorectal liver metastasis

Zhi-Zhong Pan, from SYSUCC, reviewed how colorectal liver metastasis is managed and explained a new strategy for resection. The new strategy is to enable R0 resection and retain enough residual liver volume. To achieve this goal, portal vein embolization, two-stage hepatectomy, liver first model, combination of surgery and RFA, *ex vitro* liver resection, and liver transplantation are used selectively for each patient. Dr. Pan also highlighted the positive impact of multidisciplinary team (MDT) when dealing with colorectal liver metastasis resection and recommended MDT for this clinical situation.

Lung cancer

Yi-Long Wu, from the Guangdong Lung Cancer Institute, reviewed their research on three aspects of lung cancer — molecular variables, surgery for early-stage non–small cell lung cancer (NSCLC), and clinical trials for advanced NSCLC — and gave a vision of the near future in China. His group found different epidermal growth factor receptor (*EGFR*) mutation rates in Caucasian and Chinese populations and also tested the frequency of driver genes in subgroups of NSCLC in Chinese. According to their data, discordance rate was 13.9% in the 180 paired samples of multiple pulmonary nodules for *EGFR* and *KRAS* mutation statuses, which will impact our clinical practice. Regarding surgery, they found well-matched patients with NSCLC who underwent standardized video-assisted thoracoscopic surgery (VATS) lobectomy had similar long-term survival outcomes when compared with those who underwent open lobectomy. The Chinese Thoracic Oncology Group (CTONG) conducted several important clinical trials in China, including CTONG-0802, 0803, 0806, and 0902 as well as the ENSURE study, and Dr. Wu shared the published and unpublished data in the symposium. He concluded by discussing whether EGFR tyrosine kinase inhibitors (TKIs) would be used as an option in the adjuvant setting for early-stage lung cancer, how to conquer resistance to TKIs, how to select treatment by mechanism, and how to treat rare diseases with newly found driver genes.

Breast cancer specimen bank

Ke-Xin Chen, from Tianjin Medical University Cancer Institute & Hospital, discussed the establishment and use of a breast cancer specimen bank in their institute. Since its establishment in 2003, the bank has set procedure rules and includes over 37,000 tissue samples and 36,000 blood samples. In addition to samples, the bank also stores biological information on the corresponding patients. Because of this resource, various studies of high quality were possible and future studies along these lines are expected to lead to personalized medicine in the near future.

Haploidentical transplantation

Xiao-Jun Huang, an expert in transplantation from Peking University Institute of Hematology, Peking University People's Hospital & Beijing Key Laboratory of Haploidentical Hematopoietic Stem Cell Transplantation (HSCT), introduced their experience of haploidentical transplantation. According to their published data, they found that Haplo-HSCT has a similar therapeutic effect compared with HLA-matched sibling donor or matched unrelated donor HSCT and similar therapeutic effect compared with unrelated cord blood transplantation. Thus, Huang's group suggests the time for haploidentical transplantation has arrived for all patients. Relapse remains a problem after HSCT. Several clinical trials have been initiated to decrease the relapse rate or delay relapse, including the following: (1) granulocyte colony-stimulating factor (G-CSF) primed peripheral blood progenitor cells instead of steady donor lymphocyte harvests, (2) short-term cyclosporine A (CsA) plus methotrexate (MTX) for prevention of donor lymphocyte infusion (DLI)-associated graft-versus-host disease (GVHD), (3) low-dose glucocorticoid prophylaxis, and (4) low-dose IL-2 for acute GVHD.

Non–small cell lung cancer

Yuan-Kai Shi, an oncologist in lung cancer from Cancer Institute & Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, introduced results of clinical trials his group conducted using EGFR-targeted therapy, anaplasticlymphoma kinase (ALK)-targeted therapy, angiogenesis inhibitor, and lung cancer vaccines. ICOGEN demonstrated non-inferiority of icotinib to gefitinib as second- or third-line therapy for advanced NSCLC patients. The CONVINCE study using icotinib versus first-line chemotherapy plus maintenance treatment in EGFR-positive lung adenocarcinoma patients is in its recruiting phase. Currently underway is the IMPRESS study, a phase III randomized, double blinded, placebo-controlled, parallel, multicenter trial to assess the efficacy and safety of continuing gefitinib (250 mg) in addition to chemotherapy versus chemotherapy alone in patients who have locally advanced or metastatic NSCLC with *EGFR* mutation and have progressed on first-line gefitinib. Shi's group also initiated a randomized, double blinded, multicenter, phase III clinical trial to compare vinorelbine/cisplatin plus recombinant humanized endostatin with vinorelbine/cisplatin plus placebo in initially treated, advanced NSCLC to evaluate efficacy and safety. *EGF* vaccine is being investigated in a phase I trial in China. *EGFR* mutation status is tested according to countries/regions and ALK rearrangement in advanced NSCLC has been detected. Shi's group also found Chinese patients have different molecular biological characteristics, which may have significant impact on the translational medicine for lung cancer. In the aspect of exploring new biomarkers, Shi's group finished a large-scale clinical trial suggesting that hot-shock protein 90α (Hsp90α) may be a potential biomarker for diagnosis and treatment outcome prediction for lung cancer. Shi concluded by sharing an inspiring map showing lung cancer clinical trials in China account for nearly 20% among the whole world. Results that emerge from this type of work is expected to greatly promote the development of the field of lung cancer in China.

Colorectal cancer

Because cancer has become the primary cause of death in the United States and China, it is important to pay as much attention to its prevention and screening as the treatment. Screening for CRC has been effective in decreasing its incidence and mortality in the United States, but the screening technique still needs improvement. Su-Zhan Zhang, an oncologist from Zhejiang University Tumor Institute, explained that a nationwide project on early diagnosis and treatment for CRC was initiated in 2007 and now includes 15 centers. This initiative improved treatment outcomes for CRC patients. Thus, Dr. Zhang encouraged conference attendees to continue to promote this project, help to lower its cost, and strive for policy support.

Anti-Cancer Drug Development

Evolution of antibody as a platform for cancer therapeutics

Helen Chen, from the National Cancer Institute (NCI) in the United States, reviewed how antibodies came to be used as cancer therapeutics. In 1975, hybridoma technology allowed production of murine monoclonal antibodies, and from the 1980s to 1990s, humanization of murine antibodies gradually advanced towards maturity. In 1998, fully human antibodies were available. To date, more than 20 antibodies have been approved for cancer therapy, including naked antibody radioimmunotherpay, antibody-drug conjugate, and bispecific antibodies. Naked antibodies can exert multiple mechanisms of action, including inducing programmed cell death, blocking pathways, stimulating pathway signaling, and triggering antibody-dependent cell cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC). People have tried several methods to enhance the activity of antibodies, such as enhancing ADCC by modulating the Fc portion of monoclonal antibodies, reducing ADCC, selecting the right epitope and affinity for optimal effects, and combining antibodies against different epitopes of the same antigen. Redirecting T cells through novel monoclonal antibody constructs is another novel method, which was used with blinatumomab. Encouraging data in hematologic malignancies showed that using antibody to redirect T cells to target cells is a powerful strategy. Many antibody-drug conjugates have also been tested in clinic and two have been approved. Unstable linker, improper choice of targets and tumor cell intrinsic resistance may account for the failure of antibody-drug conjugates.

New cancer immunotherapies — immune checkpoint inhibitors

Li Yan, from the Merck & Co., Inc., focused on immune checkpoint inhibitors, including CTL4 (targeted by anti-CTL4 monoclonal antibody ipilimumab) and PD1 (targeted by anti-PD1 antibodies). The Food & Drug Administration (FDA) approved clinical use of ipilimumab for

metastatic melanoma in 2011, and now clinical development of MK-3475 is ongoing in melanoma, NSCLC, breast cancer, head and neck cancer, gastric cancer, bladder cancer, myeloma, myelodysplastic syndromes (MDS), and lymphoma. In the future, anti–PD-1 plus anti-CTLA4 combination and other combinations may be tried in cancer therapy.

Third-generation EGFR TKIs

Xiao Xu, from ACEA Biosciences, laid emphasis on third-generation EGFR TKIs, a novel therapeutic concept for overcoming acquired resistance to first-generation TKI and reducing adverse events. Before third-generation EGFR TKIs, there were two major therapeutic strategies developed for targeting EGFR: one is antibody-based, and the other is small-molecule–based. Patients with mutant *EGFR* respond well to EGFR inhibitors but, after a while, develop resistance to the treatment. A total of 50% of the resistant tumors contain the gatekeeper mutation T790M in the ATP-binding pocket of EGFR. Almost 90% of the patients have skin damage after taking first-generation EGFR inhibitors. In June 2013, the third-generation concept was successfully tested in humans with unique features, including more effective and selective, T790M mutation sensitive, and sparing wild-type *EGFR*. Thus, third-generation EGFR TKIs can overcome acquired resistance to first-generation EGFR TKIs and reduce adverse events associated with first-generation inhibitors. Currently, CO-1686 from Clovis Oncology Inc., AZD-9291 from AstraZeneca, and AC-0010 from ACEA Biosciences Inc. are all undergoing phase I studies.

Biomarkers can spark clinical drug development

Sven Tang, Medical Director from inVentiv Health Clinical, talked about the role of biomarkers in medicine and drug discovery. Biomarkers are involved in multiple phases of medical oncology, including prediction, diagnosis, prognosis, monitoring treatment response, and recurrence. Biomarkers are also important in drug discovery as drug targets and/or surrogate endpoints. However, challenges exist with cancer biomarkers, including unsatisfactory specificity and sensitivity, difficult tissue accessibility, and ineffective test for detection. Ideal biomarkers should be involved in the process that causes the cancer and change along with changes in the disease. Levels of biomarker should be measured easily and reliably. The omics sciences allow scientists to study the integration of information as it occurs in the body by looking at multiple genes or proteins, but also produce abundant data. Gaps between research and the clinic exist, and the approval validated biomarkers are not so many. Nevertheless, biomarkers are an integral part of personalized medicine.

Integrative genomics and anticancer drug sensitivity

Yunguang Tong, from Cedars-Sinai, suggested that we have already advanced into a big data era with TCGA, Cancer Cell Line Encyclopedia (CCLE), Genomics of Drug Sensitivity in Cancer (GDSC), Gene Expression Omnibus (GEO), and ArrayExpress. A database to store and search the results derived from microarray and next-generation sequencing studies are essential to guide further studies. An algorithm to prioritize potential biomarkers that predict sensitivity to anti-cancer drugs is also important. Integrative genomic approaches, including genomics, transcriptomics, epigenomics, proteomics, and metabonomics, may play a role.

Encouraging innovation in regulatory thinking and practice

Zhi-Min Yang, from the Center for Drug Evaluation (CDE) and China Food and Drug Administration (CFDA), discussed the status of CDE Oncology Drug Registration as well as the CDE Oncology Drug Review in 2012. Oncologic drugs approximately account for one-third of all innovative drug applications. The number of applications is stable and new breakthrough areas may include a single target or multiple targets, or focus on drug resistance, new pathways, targets, or mechanisms. They may also focus on individualized comprehensive treatment. The innovation of domestic small-molecule targeted drugs is constantly improving, with a trend of “ME-BETTER” versus “ME-TOO” and new mechanism versus modified mechanism. Surprisingly, the “self-innovation model” was established in 2012. A review of timelines of clinical trial applications in major therapeutic areas showed that the average review time for oncology is the shortest, enabling parallel development in China compared to the global study. Dr. Yang said that CDE and CFDA will continue to focus on addressing unmet medical needs and encourage and support domestic self-innovation.

Data Manipulation

Big data, machine learning, and cancer

Olli Yli-Harja, from Tampereen Teknillinen Yliopisto, Tampere University of Technology, Institute of Biosciences and Medical Technology, gave a speech entitled “Big data, machine learning, and cancer,” emphasizing that the 21st century is the century of bioscience. With large and complex data, biology becomes information science. Big data hold promise of revealing secrets of complex diseases, but computers just compute and machine learning is just a tool; these approaches may put forward thousands of false positives but filter out a handful of candidate targets by straightforward thresholding of gene expression. To deal with large and complex data, sophisticated computational tools are the key, and implementation has already started (for example, TCGA). Prediction of tumor phenotype from genomic data is difficult, but Yli-Harja’s group use known associations of genes with pathways. This type of pathway association facilitates prediction of tumor phenotype. Integration of relevant background knowledge may lead to feasible solutions of complex problems in big data.

Integrative analysis of data from the Cancer Genome Atlas

Ilya Shmulevich, from the Institute for Systems Biology, introduced integrative analysis of data from TCGA. He reviewed TCGA data types, the research network, and how the samples and data flow between TCGA centers and groups. The overarching goal of TCGA is to improve our ability to diagnose, treat, and prevent cancer. As representatives from one of the GDACs of TCGA, they are in responsible of developing state-of-the-art tools for integrative data analyses and making the data and analysis results available to the research community. In addition to integrative analysis, their focus has been on making software tools that make it possible for anyone to explore the underlying data as well as associations that can be inferred from the data. They will focus on the most important clinical variables and plan to run the associations at both genetic and pathway levels to gain greater insight into the underlying cancer biology, reduce complexity, and identify most significant associations.

Generation to Generation

USCACA scholarships

During the symposium, four young talented scientists were awarded scholarships by the USCACA, National Foundation for Cancer Research (NFCR), and Asian Fund for Cancer Research (AFCR), which inspired all the dream-chasers to keep on trying (**Figure 2**).

Figure 2. **USCACA-NFCR-AFCR (US Chinese Anti-Cancer Association-National Foundation for Cancer Research-Asian Fund for Cancer Research) scholarships are being awarded to four young researchers.**

Tips for writing an outstanding manuscript from an editor's point of view

Boris Pasche, an associate editor of the *Journal of the American Medical Association*, gave a talk entitled "How to write an outstanding manuscript and get it published: the Editor's point of view" to aid conference attendees in communicating their science effectively in papers. This session was important for all scientists, especially those who are more junior, as a result of the ongoing push to make meaningful contributions to the field.

Perspective

The theme that emerged from this year's conference was a dream. In his opening speech, Dr. Wei Zhang, one of the chairpersons of this symposium, proposed a DREAM of defeating cancer:

D: Declare war on tobacco and pollution;
R: Reduce cancer mortality ratio;
E: Ease the cancer burden in the world, Asia, and China;
A: Assemble international collaborations;
M: Maximize the human and technology resources.

Indeed, fighting cancer remains a difficult challenge, but progress in this field and the obvious determination of those engaged in research and treatment is encouraging. Even more gratifying are the gains in experience and research productivity in China, which contribute to the understanding and treatment of this disease. The international cancer research community and society must collaborate to make a big impact in this field. With such hard work, our DREAM will one day be realized.

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