

Prof. Li Zhang: what can serve the nation can only serve the world

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Introduction

The ancient Greek aphorism “*know thyself*” engraved on the forecourt of the Temple of Apollo epitomizes the human desire for the exploration into the unknown. In fact, never has mankind dragged their feet in understanding themselves, as in the achievements scientists have made all these years in the studies of disease and pathology.

Ere the 2017 WCLC journey, AME Editors were sent across China to conduct in-depth interviews with an army of distinguished experts in the field of lung cancer. Together we learned how these soldiers fought for the nation that has the largest number of patients, and how they dedicated their lives to inventing the most-advanced weapons and probing into the enemy camp. From the past, they reflect and learn from mistakes; at present, they work hard and make changes; for the future, they make plans and improvements.

May this issue take you to the innermost world of these Chinese scholars, where you can delve into their wealth of knowledge and be inspired.

Expert's introduction

Li Zhang, MD (Sun Yat-sen University Cancer Center Guangzhou, China).

Dr. Li Zhang is Professor of Medical Oncology, Deputy Director of Lung Cancer Research Centre of Sun Yat-sen University (SYSU), Chief of the Department of Clinical Research, Department of Medical Oncology and Phase I Unit of Sun Yat-sen University Cancer Centre (SYSUCC). He is the member of ASCO, ESMO, IASLC, MASCC, CSCO and Board of Directors of MASCC, Board Member of communication committee of IASLC. He is also a standing committee member of the CSCO.

Professor Zhang's research interests include the development of molecular, prognostic and therapeutic approaches to improve the care for patients with lung cancer and head and neck cancer (including nasopharyngeal carcinoma). He is actively involved in numerous trials as a principal investigator and or member of the steering committee.



Figure 1 Li Zhang, Sun Yat-sen University Cancer Center (SYSUCC).

Professor Zhang has published more than 130 clinical papers in peer-review journals. He has also presented many abstracts and lectures at major international congresses. At present, he is a senior consultant to the Centre of Drug Evaluation (CDE), Chinese Food and Drug Administration (CFDA) and had formerly drafted the CFDA Guidance for Industry: Clinical Trial for the Approval of Cancer Drugs and Biologics (second version, 2006).

Foreword

Serving as a physician for more than three decades, specializing in the field of cancer and digging into oncology research, he dedicated his best 30 years to medicine and his patients.

Respect was what he showed for Prof. Yan Sun. Gratitude was what he expressed for Prof. Zhongzhen Guan and Prof. Meiling Liao. Passion blended with humor, tenderness and ecstasy was what he demonstrated for academia.

Born with the courage to choose from the uncertainties, and the perseverance to explore the unknowns, he led Chinese cancer clinical research to set foot on the international arena. He is a top strategist with grand vision and profound foresight.

He is Prof. Li Zhang (*Figure 1*) from Sun Yat-sen University Cancer Center (SYSUCC), Guangzhou, China.



Figure 2 In 2011, Prof. Zhang Li presented their clinical research findings on lung cancer, INFORM, at the annual conference of the American Society of Clinical Oncology (ASCO).

Living out his dream as a physician, Prof. Li Zhang has been serving at SYSUCC and engaging in chemotherapy treatment, teaching and clinical research in anti-cancer drugs. He is known for rich experience and outstanding practice in the management of lung cancer and nasopharyngeal cancer using chemotherapy, targeted therapy, immunotherapy, multidisciplinary treatment, palliative treatment in advanced cancer and so forth.

He is one of the national pioneers and leaders in the academic field of cancer clinical trials, where he has made plenty of remarkable achievements. He led the preparation of a dozen of national and international multicenter clinical research, and was involved in more than 30 research of the kind. He has contributed more than 140 articles in an array of SCI journals, including “*The Lancet*”, “*The Lancet Oncology*”, “*Journal of Clinical Oncology*”, “*Journal of the National Cancer Institute*”, “*Blood*” and “*Annals of Oncology*”. He has also published more than 90 articles in several significant Chinese journals and served as the editor-in-chief or editor of 9 cancer-related books.

A visionary and wise warrior

Graduating from the School of Clinical Medicine, Sun Yat-sen University of Medical Sciences, Prof. Zhang was allocated to SYSUCC in 1986 that set his foot in chemotherapy, education and clinical research in anti-cancer drugs. In the wink of an eye, it has been more than 30 years since the very first day he knocked on the door of the center.

Speaking of his initial thoughts, Prof. Zhang admitted that he chose the path of internal oncology because it was a rather new discipline unlike other “old” ones such as cardiovascular

medicine, respiratory medicine and digestive medicine that had had nearly hundred years of history. As a discipline newly risen in the early 19th century, it is like a barren island in the middle of the vast ocean awaiting mankind who knows no fear to uncover its secrets. “*I had always wanted to become a physician. I was inspired by Prof. Zhongzhen Guan when he introduced in class that internal oncology was the youngest discipline in internal medicine—the youngest discipline, which can probably be the most promising one as well.*”

When everyone else was “forced” to knuckle down to internal oncology, Prof. Zhang took the initiative to single out this discipline without any hesitation or fear, “*I readily applied for it. Prof. Guan often used my example to show other students that there was someone who actually voluntarily applied for internal oncology.*”

Today, Prof. Zhang has made tremendous contributions in the field of internal oncology, which has become one of the most popular disciplines of clinical research with plenty of eye-catching research and discoveries every year. Many medical students scramble to get into this field every year.

A pioneer who attracts worldwide attention

Work together to engage the world

In June 2011, on behalf of the Chinese Thoracic Oncology Group (CTONG) and the nation, Prof. Zhang presented their clinical research findings on lung cancer, INFORM, at the annual meeting of the American Society of Clinical Oncology (ASCO) for the very first time (Figure 2). “*This was a large-scale, randomized, placebo-controlled phase III clinical study that made use of EGFR TKIs to perform maintenance therapy, a study that gave advanced NSCLC patients greatest benefits out of all maintenance therapies.*” Not only had the study successfully gained worldwide attention, as the first Chinese that gave speech at ASCO, Prof. Zhang was also made an instant hit across the Chinese territory.

What laid behind the success, however, were days and nights of relentless effort. It, in fact, was not without pain or challenges. “*Never is it easy to obtain fund for clinical research in China,*” admitted Prof. Zhang. To gain manufacturer’s support, his team flew twice to London. When they were at the final stage of data analysis, statisticians’ work was hindered by an earthquake in Japan, where they were only allowed to work 4 hours per day due to power failure. They had to pit their wits and courage and seize every single second to have their report submitted on time. Under Prof. Zhang’s leadership, the team was able to get



Figure 3 Prof. Zhang gave oral presentation at ASCO 2016 Annual Conference.



Figure 4 The research on recurrent or metastatic nasopharyngeal cancer led by Prof. Zhang was awarded as one of top 10 New Medical Technologies of 2016 in China.

rid of all obstacles and had the INFORM study chosen for presentation at ASCO.

Chinese scholars are gradually engaging the world, and this would not be possible without the existence of close-knit teamwork. As the Vice Present of CTONG, Prof. Zhang pointed out that under the co-leadership of various national lung cancer experts like Prof. Yilong Wu, Prof. Shun Lu and Prof. Caicun Zhou, CTONG designed a number of multicenter clinical trials in the area of thoracic cancer, published a number of significant papers in various high-level international journals, and had their research findings presented at several key world conferences like ASCO, ESMO and WCLC. These quickly made CTONG one of the most active academic units in the lung cancer research field both nationally and globally. As long as we unite and cooperate, more outstanding scholars and masterpieces representing China and our clinical research

level can soon be in the spotlight.

“What can serve the nation can only serve the world”

Prof. Zhang stressed the utmost importance in carrying out clinical research based on national conditions. What can serve the nation can only serve the world. Southeast Asia and Southern China are regions with high incidence of nasopharyngeal cancer. Due to the lack of high quality clinical research, there had been no standardized approach to the management of recurrent or metastatic nasopharyngeal cancer. In light of this, Prof. Zhang took the initiative to carry out a multicenter, randomized, controlled phase III clinical research on recurrent or metastatic nasopharyngeal cancer by uniting 22 centers across the country. Eventually, their findings were presented orally at the ASCO 2016 Annual Conference (Figure 3), and were published in *“The Lancet”* on August 23, 2016 in the form of fast track. Prof. Zhang led the Chinese team to work up the first standard of advanced nasopharyngeal cancer chemotherapy, and became the first Chinese who published in *“The Lancet”* in the field of clinical oncology. The achievement was awarded as one of the Top 10 Chinese New Medical Technologies of 2016 (Figure 4). He used action to prove to the world that China’s cancer clinical research can actually come to the world’s forefront.

Prof. Zhang emphasized that this clinical study of phase III nasopharyngeal cancer published in the main page of *“The Lancet”* demonstrated that Chinese scholars had made full use of their own advantages of resources and their quality work had gained recognition from the globe. The 2011 INFORM study also made adequate use of the population with EGFR-positive mutations which was most common in China. *“What can serve the nation can only serve the world. This is what I always bear in mind. From examining the unique and common cases in our nation, to discussing what are worth being studied, each one of us makes a little contribution; together we bring our nation’s academic research to another level.”*

Prof. Zhang is a real role model revealing our national spirit of the pursuit of continuous improvement.

World-level clinical trials of cancer drugs

“It was not until I went to the Institut Gustave Roussy Cancer Center in Paris in 1996 that I had the concept of Good Clinical Practice (GCP)”. After returning to the country, Prof. Zhang

started drilling into GCP for 20 years. Now, as the director of Good Clinical Practice Center, Sun Yat-sen University Cancer Center, he has had considerable experience in conducting multicenter clinical studies and hosting a wide range of national and international clinical research. He is also a member of the Independent Data Monitoring Committee (IDMC) and the Steering Committee (SC). “Great things may be done by mass effort”—this is a notion that he firmly believes throughout the years.

Looking back at the three decades of cancer clinical research, Prof. Zhang said he witnessed the three stages of clinical trials of cancer drugs in China. The first stage was the introductory phase in 1980s when experience-guided medicine was the mainstream in the study of oncology. Clinical trials at that time were single-center and retrospective instead of prospective based. The second stage, from the 1990s to the early 2000s, was when evidence-based medicine and the concept of GCP were getting prevalent. Upper first-class hospitals scrambled to carry out clinical trials, and the medical teams were getting more mature. It was not until the third stage, starting from 2010, that the quality of our clinical trials was comparable with the world standard.

Prof. Zhang proudly said, *“it will soon be our combat time. The foundation of the ‘National Clinical Research Center’ is sophisticated enough. We aim at doing the best clinical research and ultimately benefiting patients. I think this is what a clinician sees as the most essential thing. Sooner or later, more and more Chinese scholars will enter the world arena to showcase their research findings.”*

The inheritance and innovation of palliative treatment in cancer

Prof. Zhang has been adhering to the belief that “innovation can only be made out of inheritance, as innovation is built on the basis of predecessors”.

Speaking of palliative treatment in cancer, senior experts in internal oncology including Prof. Yan Sun, Prof. Zhongzhen Guan and Prof. Tongdu Li introduced the nation to the “three-step ladder” for cancer pain relief suggested by World Health Organization (WHO). It was true in 30 years ago that the “three-step ladder” approach was effective in relieving cancer pain, but prior to 2009, a campaign named “Painless New Year” suggesting cancer pain relief had caught Prof. Zhang’s attention, “We let cancer patients enjoy a painless month of the new year, but what then? How do we prevent them from getting any more

pain afterwards, or for the rest of their life? How do we standardize the clinical practice to manage their pain? How do we get rid of the obstacles that influence the treatment?”

Therefore, in 2009, Prof. Zhang together with his Guangdong palliative team took the lead to propose the concept of “painless ward for cancer patients”, an idea of “Good Pain Management (GPM)”, and established the first batch of standardized demo wards in Guangdong Province. This innovative idea was warmly received by the majority of patients, and was at the same time regarded as “a humane project” by the media like Sohu and Baidu. It was further supported by the National Health and Family Planning Commission of the People’s Republic of China. Under the leadership of Chinese Society of Clinical Oncology (CSCO) and the support of Mundi Pharma, the project of GPM demo wards was launched and carried on vigorously, and was rated as one of the top ten Chinese oncology advances in 2012.

Only by learning from a hundred of other’s fortes can one make innovation. “It’s only after we comprehended the ‘three-step ladder’ approach well that we could build our own standardized painless treatment that stresses individualization and normalization.” Data has shown the escalation in the number of morphine consumption per cancer patient in China. The value has reached the level of moderately developed countries. This adequately proves that people are now more open to the concept of death, and the development of palliative treatment in cancer is getting better and stronger.

A great physician of benevolence and humanity

Putting oneself in patient’s shoes

Prof. Zhang often made this joke, *“Don’t make yourself an ‘idol’ of your patients, one that patients dare not get close to.”* During the cancer treatment, the objective indications we usually pay attention to include: whether the tumor becomes smaller and whether the tumor markers are reduced. Yet, often do we overlook their symptoms such as pain, nausea and vomiting, sleep, diet and nutrition, fatigue, anxiety and depression. As tumor grows in patient’s body, we should never forget what we are dealing with is the patient as a whole instead of the tumor alone. Is the patient satisfied with the treatment? How do we improve our services? We have to keep asking these questions and put ourselves in the patient’s shoes. This is an approach of palliative treatment.

“He is a kind man. There was a time when he learned that a whole family to be cancer patients, he immediately helped them

out with the application for medical fund. Another time, when he realized a family member of his colleague got sick, he led the whole team to visit her,” shared Dr. Ting Zhou, Sun Yat-Sen University Cancer Hospital.

Warming patients with empathy

“We have to strike a balance between anti-cancer therapy and palliative treatment. Not only do physicians cure diseases, but save patients’ lives. Effective and active communication between physicians and patients is thus very crucial.” As an oncologist, Prof. Zhang believes, other than chemotherapy, “communication therapy” is the same important. Many doctors often take “inform” as “communicate”. This is very wrong. We have to realize what we tell our patients are often “bad news”. A good doctor should be able to empathize patients by thinking from their perspectives. To take an example, when explaining the treatment methods to patients or their family, we recommend a few approaches and let them choose. This way of expression sounds rather robotic and short of human touch. However, expressing in another way would make patients feel better, “Imagine if the patient were your family member, which treatment approach would you choose? We are dealing with advanced cancer, and we cannot completely eliminate the tumor. What we can do is to prolong the survival time of the patients. In other words, we cannot charge forward, but to protect the patients and show mercy for their families.”

Motivating colleagues with new year letters

Other than patient’s emotions and needs, the psychological conditions of the oncologists have been another concern of Prof. Zhang. He indicated that they are currently working on a national survey regarding the occupational burnout of more than 3,000 Chinese oncologists. This thought was originated from a sharing session with a Canadian doctor he worked with a few years ago, who revealed her feelings, “The whole team is low-spirited. Everyone is burnt out.” Prof. Zhang explained with knitted brows, “*The US is facing the same problem. The age of 40 is a watershed. The occupational burnout of doctors below 40 is obviously more serious than those above 40. For example, when the wages younger doctors make are not proportional to their workload, they gradually lose passion for their occupation. We should have this problem sorted out.*” Dr. Yunpeng Yang, the mentee of Prof. Zhang, mentioned, “*Prof. Zhang shows much solicitude for the control of inertia and humanity of students. What most inspired us was the letter*

he wrote us in the beginning of each year. On the first working day of every new year, Prof. Zhang would write us a letter of a few thousand words. Whenever I got his letter, I would be full of energy, and promise myself not to be lazy in the coming year.”

Creating a strong academic ambience

“*I admire how Prof. Zhang strives for learning and improvement. He is always ahead of the times. He requests us to submit reading reports every Wednesday and share our understanding of the latest scientific research, to which he even gives comments and guidance,*” Dr. Ting Zhou shared gratefully.

“*We learned the idea of a weekly academic report from the Fox Chase Cancer Center in the US,*” Prof. Zhang explained, “*The entire hospital is so full of strong learning atmosphere. The hospital’s leaders of several generations are particularly concerned about our academic ambience. Here in our hospital we see experts from different regions coming over to do academic reports. All professors, including those making ward rounds, are mulling academic research and clinical trials.*” In 1988, Prof. Zhang left for the Fox Chase Cancer Center. Over the year, he was more aware of the significance of a good academic ambience, “*There we had group discussion every week on academic reports, which I think was the key element that opened the door to good academic ambience.*” Prof. Zhang, therefore, applied the knowledge acquired in the States back in the hospital, where he began to practise a non-conference report that each team had to share their latest knowledge with their peers on a weekly basis. “*We have been practising this for 20 years. Advice from others may help us overcome our shortcomings. Here we have clashes of thoughts that help spark off new ideas,*” said Prof. Zhang ecstatically.

Dr. Yunpeng Yang showed the same feeling, “*Prof. Zhang takes 3–4 hours every week to marshal our thoughts about clinical research work.*”

Prof. Zhang is such a great physician and teacher who is full of humanity. From him we see the concept of inheritance and innovation; we see the endurance and perseverance of a selfless great man.

Learn from predecessors; pass on to descendants

AME Publishing Company: Over the years, who have had great impacts on you?

Prof. Zhang: Since the first day I entered the field, I have been under the tutelage of Prof. Zhongzhen Guan. He

influenced me a lot by teaching me by words and deeds. He made me understand the importance of “the pursuit of perfection”. When I was young, I had to do simultaneous interpretation in many major academic conferences, but there were many bits of bitterness, as the interpretation required both expertise and the ability to be resourceful. One time when I was doing simultaneous interpretation at a conference, I translated “diabetes” wrongly, which then was immediately corrected by Prof. Guan. This is what we call “the pursuit of perfection”. Never can we be sloppy towards any single detail. Now I also demand the same from my students, to whom I always say, “*If I teach you 70% of the knowledge, you gain at most 70%. $7 \times 7 = 49$, which is a half off. If I teach you 90%, and you gain 90%. $9 \times 9 = 81$. Perfection has to be accumulated bit by bit.*”

And of course, in the professional aspects, I have been influenced by many of my fellows. In the area of lung cancer, Prof. Meiling Liao had profound impact on me. Despite being in different unit, she gave me much guidance and advice for both my career and my life. She has always been a good teacher in my eyes. What impressed me most was that she always stressed the importance of “taking care of your fellow’s feelings” during academic exchanges. I am lucky enough to have such a great teacher who can give me such kind of advice.

AME Publishing Company: *What sort of qualities that you learned from these mentors would you pass on to your students or descendants?*

Prof. Zhang: First of all, the pursuit of perfection is of no doubt an essential quality that I would teach my students. Secondly, one has to be modest and open-minded enough to tolerate dissenting views, which I think is equally important.

Learn from anyone virtuous and talented; put what you learn into action

AME Publishing Company: *You have been to the Institut Gustave Roussy Cancer Center in France, the Fox Chase Cancer Center and the MD Anderson Cancer Center in the United States. What do you regard as the major differences between the West and the East in terms of clinical practice and management? What can we learn from them?*

Prof. Zhang: Objectively speaking, I think the reason they can provide such high-quality medical services because the number of patients is relatively small. Each doctor sees around 15 patients every day, which is not possible in

China, where clinicians have to see 15 patients in an hour. So I often make this joke—if we can lower the number of patients, we can completely provide high-quality medical services and patient care. It is, thus, very important to have a triage system in our new medical reform.

Besides, the West has better experience in the use of outpatient resources. During my study at the MD Anderson Cancer Center, I saw many of the treatments carried out at the clinics. It’s worth learning. After returning from the States, in my own team, I started executing the program that sped up the cycle of hospitalization, the kind that patients can immediately be discharged after undergoing chemotherapy. The average length of hospitalization is shortened from originally 60 days to now 2–3 days. Many people thought patients receiving chemotherapy should be hospitalized to avoid infection. However, our experience has told us that the acceleration of turnover rate has nothing much to do with infection. The renewal of concept is, thus, very essential. What’s more, we should optimize the entire procedures of hospitalization. Regardless of Fudan University Shanghai Cancer Center, Chinese Academy of Medical Sciences Cancer Hospital, or Beijing Cancer Hospital, reduction of the average length of hospitalization is the current trend. These hospitals are even using our practice as the standard, as we have the shortest average number of hospitalization in Oncology nationwide.

AME Publishing Company: *What is the biggest optimization of this procedure?*

Prof. Zhang: To accelerate the turnover of patients, it requires refinement to every single workflow, and thus requires changes to the entire procedures. Basically, it involves how we make appointments for patients, when they come back for follow-up consultations and when they have to be hospitalized. Even the entire flow nurses receive patients has to be altered drastically.

Epilogue: messages for the younger generation

AME Publishing Company: *What messages do you have for the younger generation?*

Prof. Zhang: The first message I want to convey is that we should cherish life and health. Many people think that health is a matter of course, which is absolutely wrong. Cancer often occurs incidentally and unwittingly. Secondly,

we have to learn to adjust our mentality when dealing with stress. A healthy mind is the best immunity to resist all kinds of tumors. The hottest immune therapy discussed in recent years is to mobilize our own immune system. I always encourage my patients: whether it is to prevent or treat cancer, our ancestors inherited to us this immune system that can fight against any diseases. So how we adjust our mentality is of paramount importance in treating all kinds of diseases.

AME Publishing Company: Can you share with us a habit that you have always been keeping?

Prof. Zhang: Keep curiosity alive—till now, I am still full of curiosity to a whole lot of things, so I keep on learning. Lifelong learning is really important. No matter how much qualification you obtained—a PhD or higher, you must keep on learning.

Einstein once wrote: “Curiosity is a source of endless

perseverance and patience for scientists”. A heart of pure loyalty dedicates its whole life to light up the world of others. On this path of medicine, Prof. Zhang strives for excellence and chases for perfection.

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Footnote

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