

Prof. Yongqian Shu: I do my best to make patients live longer and better

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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

Professor Shu is the director of Department of Oncology, Jiangsu Province Hospital, and vice president of Institute of Oncology, Nanjing Medical University. He is now the chairman of four academic associations in the field of tumor treatment in Jiangsu province. Besides, he is also an important and active member of many nationwide academic committees, including member of CSCO Executive Committee, standing member of CSCO Esophageal Cancer Professional Committee, member of core expert group of China's Primary Lung Cancer Diagnosis and Treatment, standing member of Precision Medicine Workshop of Chinese Anticancer Association, standing member of Precision Medicine Workshop of China Science and Technology Industry Association. Professor Shu is also expert members in various Oncology Clinical Practice Guidelines. In recent years, Professor Shu has published



Figure 1 Prof. Yongqian Shu.

more than 100 SCI papers as the corresponding author, and the cumulative impact factor is more than 350. Professor Shu presided over the four national natural science funds, and took on more than 10 kinds of funds including key disciplines. He also won the prize of Jiangsu science and technology progress and many others. He is the editor-in-chief of four oncology books.

Prof. Yongqian Shu (*Figure 1*), director of Division of Oncology, Jiangsu Province Hospital, has practiced medicine for 32 years and been dedicated to being an “exquisite” doctor.

Prof. Shu was responsible for establishing Division of Oncology, Jiangsu Province Hospital, at the end of 1999, which was chosen as the key oncology specialty of Jiangsu Health Department in 2003 and key discipline of Jiangsu Province in 2007. In 2012, it was promoted to top ten medical research center in Jiangsu Province. When asked how Division of Oncology, Jiangsu Province Hospital could develop so quickly, Prof. Shu proudly said, “*We have a very strong team working positively and competitively.*” (*Figure 2*). Compared to divisions of Oncology of other hospitals, every doctor in Prof. Shu's team has the enthusiasm to focus on research. Every team member reads the related



Figure 2 Members of Division of Oncology, Jiangsu Province Hospital.

documentation concerning one particular disease. Especially young doctors, every one of them holds a project for young scientists supported by National Natural Science Foundation of China. It's worth mentioning that this young but strong team has published more than 50 articles indexed in Science Citation Index (SCI) every year. Prof. Shu hopes that every subspecialty of the Division of Oncology, Jiangsu Province Hospital, would have a say in the whole nation.

As one of the lab managers of "135 state key laboratories" in Jiangsu Province, Prof. Shu has established a biotherapy laboratory for cell therapy that meets national GLP standards. The laboratory undertook the duties of treatment for malignant tumor and for the first time carried out the multi-center clinical research regarding ACTL cell therapy combined with TKI treatment for EGFR sensitive mutations in no-small cell lung cancers. Prof. Shu hopes that the laboratory can help patients who have TKI drug tolerance but not able to undergo PD-1/PD-L1 treatment find survival hope. Prof. Shu established a molecular testing laboratory which can detect plasma concentration in chemotherapy drug on a daily basis in Division of Oncology, Jiangsu Province Hospital. By using first-generation sequencing and next-generation sequencing to conduct molecular mutation test, Prof. Shu hopes that doctors can rapidly observe the patients' molecular change, clinical treatment, and outcomes when necessary. This is for seeking the best detection combining method for tumor patients so that doctors provide a better guide of clinical medicine.

Oncology is a new branch of science. Many unknown things are waiting to be discovered. Prof. Shu expects that young oncologists can have the enthusiasm for this profession and deepen the knowledge in basic research. Following the newest scientific research achievements,

they should also build creative ideas based on the previous research and work.

One's ability and time are limited. It's impossible to take care of many patients simultaneously. Prof. Shu hopes more doctors devote to this new branch of science, oncology, and create miracles for the majority of tumor patients.

Evaluate patient's condition objectively, provide individualized treatment

Clinically, lung cancer is usually divided into stage I, stage II, and stage III. In order to extend the survival time of patients as long as possible, Prof. Shu subdivided non-small cell lung cancer in stage III into: early stage in stage III, middle stage in stage III, and late stage in stage III, based on factors such as the load of patients in stage III, treatment methods, gene-expression, and individualized outcome. Although the so-called "early stage in stage III" means local treatment could not be used in the main lesion like brain metastasis, adrenal metastasis or lung metastasis, the metastatic lesions can be treated with local treatment, and the quality of patients' life could be changed. For patients in "early stage in stage III", though in stage III, their treatment outcome could still be good after intensive treatment, and may even have similar prognosis just as patients without metastasis do. For patients in "middle stage in stage III", genes of the tumor without being detected appear or the load of tumor gets worse after routine chemotherapy and radiotherapy. A patient could be classified as "late stage in stage III" if he/she is aged, weak, with relatively poor multiple organs and reserve function, worse evaluation, or even not able to undergo chemotherapy and radiotherapy. When treating a patient in "late stage in stage III", doctors could consider temporarily stop anti-tumor therapy. The treatment plan is to alleviate pain and improve their life quality. Clinically, Prof. Shu often encounters the scenario that some patients visit him with no complete medical examination report or report with wrong test results. When facing this kind of situation, Prof. Shu always evaluates the medical report objectively to check whether the detection of the next generation sequencing is complete enough or not. Once, one of his patients with late lung squamous cell carcinoma was just admitted to the hospital and this patient coughed very heavily and his sputum was even mixed with blood and pleural effusion. After detecting pleural effusion gene, Prof. Shu found that EGFR 21 exon L858R mutation still existed and EGFR gene copy number increased. Hence, Professor Shu used afatinib treatment with cetuximab



Figure 3 Listening patiently to the patients.

treatment, and effectively controlled the further growth of the tumor.

Evaluate side effects and effects of clinical medication objectively

The side effects of chemotherapy are mostly damaged to myelosuppression and immunological function of organism, followed by multiple organ dysfunctions, including liver function, renal function, and cardiac function. However, many doctors usually overlook to evaluate the function of heart before chemotherapy. The side effects of molecular targeted drugs are primarily interference in signal transduction, leading to some slow damage to normal cells. In contrast, the side effects of molecular targeted drugs are much lighter than chemotherapy, and have a lighter impact on patient's tolerance and acceptance, too. Clinicians are also more concerned about the toxicity of chemotherapy, but the observation of toxicity of targeted drugs is generally not enough. For example, long-term use of gefitinib will lead to prolonged QT and insufficient blood perfusion to heart, which makes the patient's entire gastrointestinal blood supply inadequate and hinders nutritional absorption, causing patients to suffer from inanition. Clinically, although tumor cells' drug resistance appear after patients use gefitinib for a period of time, heart damage will recur again after stopping taking medicine. And for some patients who have taken gefitinib for 4 or 5 years, doctors should pay attention to the cardiovascular adverse effects.

Know the “measurement” and create the best treatment for patients

MSI-H is a medical indication of PD-1, but not a golden rule. Clinically, the effect of PD1 on some MSI-negative

patients is still very good. For this phenomenon, Prof. Shu's team has been researching it and preliminarily discovered that specificity of miRNA in the venous blood is indirectly in association with the therapeutic value of PD-1. Prof. Shu stressed that clinicians cannot use the absolute standard to treat every patient. Clinicians should set different measurements for every treatment and every patient. Prof. Shu shared a story about a nearly 80-year-old patient with gastric cancer. That patient was classified as stage IIIC after surgery. His pathological slide showed HER2 over-expression. For an elderly person with both cardiovascular disease and cerebral infarction, postoperative adjuvant chemotherapy was not possible. Although anti-HER2 Herceptin treatment for gastric cancer adjuvant therapy was not suggested, Prof. Shu used adjuvant chemotherapy with S1 treatment and Herceptin. It has been 7 years from then and the old man now could still travel around the nation.

Caring home for tumor patients, teaching patients to love themselves more

There are total 121 beds in Division of Oncology, Jiangsu Province Hospital. Numbers of patients for a month are around 1,200 to 1,300. Doctors and nurses are super busy every day, which in some way causes poor communication between medical staff and patients or patients' family. For providing a platform making doctors and patients have a better communication, Prof. Shu led his team to found a “caring home for tumor patients” with strong support from the director of Jiangsu Province Hospital and other departments. By combining the treatment and caring, a platform providing direct interaction with professional doctors for patients was founded. It even provides care and assistance just like from their family members and friends.

Respect lives and constantly bring positive energy to patients

Prof. Shu has been in the front line to treat patients with malignant tumor and miscellaneous diseases and encountered patients with different kinds of problems. He mentioned that doctors should constantly encourage patients when interacting with them, helping tumor patients face the disease with a positive mind. One of his patients with lung cancer in stage III felt depressed after knowing his own condition (liver metastasis and kidney metastasis), and refused to undergo further treatment. Prof. Shu kept using

successful cases to show him that everybody has cancer cells, and chemotherapy is just a way to decrease the numbers of cancer cells in the body. It will do good to let patients know chemotherapy rather than not telling them and then using chemotherapy. Many clinical studies have shown that more care from clinicians to tumor patients, longer the patients' survival time. The care could be a short message, words of encouragement, or talking about daily life.

Take heed of trivial things, listen to what they say and grow together

"Doctors can treat officials carefully, and can also treat farmers patiently. Doctors can treat the rich seriously but also should treat the poor sincerely." Prof. Shu has practiced medicine by following this saying. No matter who the patient is, Prof. Shu always listens to them and evaluates their condition objectively before making a plan for the next treatment (Figure 3). Once a patient talked with Prof. Shu for a long time and seriously asked him a question in the end, "Doctor, why the 'little noon' (lunula) on my fingers disappear?" Though the question seems to be quite childish, it had bothered the patient for a long time. The higher the lunula on the nail is, the better the organ reserve function is. If a tumor is growing, "little noon" will fall down. Doctors won't pay attention to this kind of detail in the daily consultation. However, Prof. Shu can always find the symptoms of disease in the common talk and notice the changes of patients' conditions. Prof. Shu always says, *"In fact, patients teach doctors when they consult doctors. Patients can teach doctors. Therefore, patients are not just patients but also teachers and friends of doctors."*

Conversation with Yongqian Shu

AME: *Chemotherapy has always been the main treatment for lung cancer and almost irreplaceable. However, chemotherapy brings more side effects. Then, what are the side effects of targeted therapy?*

Prof. Shu: The side effects of chemotherapy are mainly myelosuppression and damage to the immune function of the body. For targeted therapy, it is mainly interference in signal transduction, leading to some slow damage on normal cells. In conclusion, the side effect of molecular targeted drug is lighter than of chemotherapy, and has a much better impact on the patient's tolerance and acceptance.

AME: *You have been working on individualized new therapeutic target for the diagnosis and treatment of non-small cell lung cancer, targeting therapy for tumor microenvironment, including angiogenesis, immunotherapy, vaccination and immunological blockade of lung cancer. Which one do you think is more promising?*

Prof. Shu: Cell-based immunotherapy. I think anti-PD-1 monoclonal antibody, PD-L1 monoclonal antibody, and CTLA4 monoclonal antibody will still be popular for treating non-small/small cell lung cancer and are expected to change the NSCLC treatment guidelines.

AME: *What's your next development plan for Division of Oncology, Jiangsu Province Hospital?*

Prof. Shu: I would like to lead medical oncology team of Division of Oncology, Jiangsu Province Hospital, to become the best tumor medical team in Jiangsu Province, and achieve a status in the whole nation. By establishing subspecialty in the Division of Oncology, Jiangsu Province Hospital, every team is sure to have a certain level of influence in the whole nation.

AME: *As the academic leader of Oncology, what's your expectation to young doctors in this field?*

Prof. Shu: I hope they have love in Oncology, and can do better than me in the future. I also hope young doctors can put more efforts to learn the basic research, know more about the international frontier research, and learn from others' successful experiences. By listening, learning widely, and studying hard, young doctors can prevent themselves from going to a dead-end.

AME: *When getting along with patients, what should be noticed?*

Prof. Shu: Listen to patients with patience, constantly encourage them, and help them face disease positively.

AME: *In these years, you have always fought in the front line. Do you feel stressful sometimes? How do you relieve the pressure from work and science study?*

Prof. Shu: Sure, I do. What I do to relieve pressure is to stay away from medical business and go out with some

childhood friends, talking interesting things happening in our expertise. And sometimes I drive to suburban areas alone and enjoy beautiful scenery along the road.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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