Curative Medicine to Control Cancer

Curative Medicine to Control Cancer:

Redressing Malignancy by Ameliorating the Gut Microbiome

By

Shu-Lin Liu

Cambridge Scholars Publishing

Curative Medicine to Control Cancer:
Redressing Malignancy by Ameliorating the Gut Microbiome

By Shu-Lin Liu

This book first published 2026

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

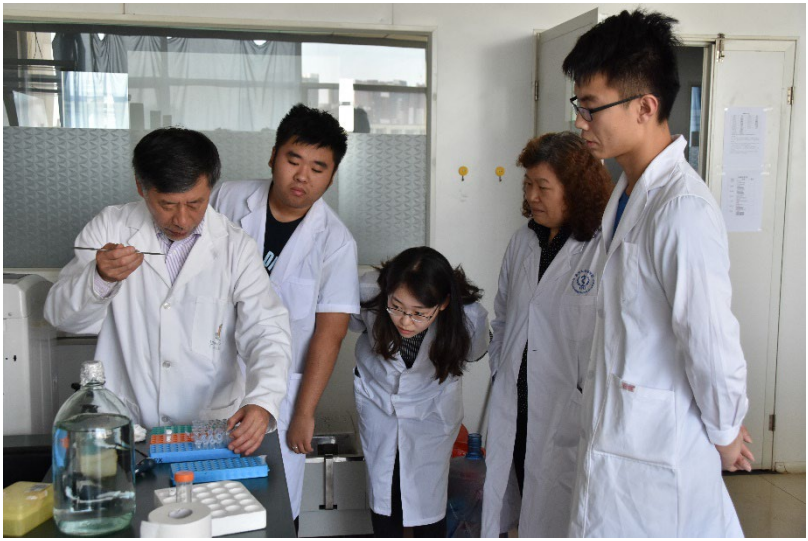
British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN: 978-1-0364-6982-5
ISBN (Ebook): 978-1-0364-6983-2

This book is dedicated to my students
and my patients

正直 善良 修己 利人

After so many years…



Time in the lab

TABLE OF CONTENTS

PREFACE

As a microbiologist and a clinical practitioner, I have instinctively combined the two areas of my expertise to explore curative therapies for diseases; this book focuses on cancer. By the word *curative*, I mean to cure, not merely alleviate, diseases. In the first few chapters, I present the principles of curative therapies and successful outcomes of cancer patients receiving such therapies, and then in the later chapters I narrate my journey toward the building-up and clinical application of curative therapies.

I began my medical career in the clinical laboratory in 1971, when I was going to be 17 years old, with Grade 5 education followed by another 5 school years with little classroom education. Among my elementary school years, Grade 6 was a totally idle period of time, no lectures were taught to us, since no teacher or school was allowed to teach. After another one and half years following the end of "Grade 6", we were en mass sent to middle schools without admission exams as usual to continue the idle school life. Beginning from 1966 to the following many years, no formally educated students graduated from universities or high schools. As a result, by the end of 1970, the whole society had desperate human power shortage, so we were assigned directly from high school to all kinds of job positions. I was allocated to Fujin Central Hospital, the largest local hospital in east Heilongjiang Province, to be trained for laboratory work.

I had to learn many things, starting from my Grade 5 education background: bacterial isolation from clinical specimens and bacterial culture, bone marrow cytology to diagnose leukemia or other blood disorder, needle biopsy to diagnose solid tumors, serum analysis to diagnose hepatitis and other systemic diseases, microscopic examination of stool to find eggs of

parasites, urine protein or glucose detection to diagnose glomerulonephritis or diabetes, *etc*., in addition to the curricula of Grade 6 and junior/senior high schools, all by self-teaching.

Once in the clinical lab, I was immensely fascinated with medical sciences and indulged in learning everything I had a chance to. I had greatest interest in bacteria: so many of them occupy the human gut, and what do they do? What is their relevance to human health and diseases? At that time, no answer was available to me. I had nobody to ask and no book to read for an answer. In the bookstores, one could hardly find books on science, technology, art, literature or philosophy.

In 1977, after all schools of the entire country had stopped formal educational operations for a straight 11 years, universities reopened to accept students by exams. The entrance exams were not easy – only a little more than four percent of the youngsters who took the exams were admitted to a university or college. I was enrolled to Harbin Medical University, which had been my dream university for quite a long time. During the campus years, my 6 years clinical laboratory experience was a great asset to facilitate my understanding and synthesizing the medical sciences. The university set up an official "student research club", the first one in the history of the university, and called for applications. Hundreds of enthusiastic students showed enormous interest and eventually four students, including me, were accepted for the club. We attended lectures or went to the hospitals according to curriculum schedules and in the weekends, holidays and evenings, we did experiments under the supervision of professors. The activities sound like those of the nowadays summer students, but there were fundamental differences in nature, as narrated in the book.

When my clinical medicine education ended, I continued my medical research at Beijing Medical College, now Peking University Health Sciences Center, as a Master of Immunology student. Here my pre-

university experience on laboratory medicine with a focus on microbiology, my clinical medicine education, and my formal research training in a basic medical research discipline, immunology, came together and formed the foundation of my proposed *Curative Medicine*, which was to come true several decades later. After graduation with an MSc degree from Beijing Medical College, I moved to Japan to do my PhD study at Gifu University, on a project of bacterial pathogenesis.

My independent research began at the University of Calgary, Canada after my PhD graduation, where I initiated comparative bacterial genomics studies, to know how phylogenetic evolution of bacteria might take place and why very closely related bacteria could have sharply different pathogenicity to humans. I obtained the answers I had been seeking from some key findings deep in the bacterial genomes. Then I felt it high time the new discoveries were transformed to health applications.

I focused on cancer. Previous studies had revealed that dysbiosis of the gut microbial environment was closely associated with cancer pathogenesis and that amelioration of the gut microbiome was correlated with better prognosis. A question has often been asked: is gut dysbiosis the cause or consequence of cancer? It might be an interesting question but I had never strived to distinguish whether it is the cause or consequence – the question of my own is how to fine-tune the community structure of the gut bacteria to rebalance the relative ratios in population size of the microbes or in terms of functions to bring cancer under better control. I believed that certain natural products may have the effect of ameliorating the gut microbiome and redressing the gut dysbiosis to achieve the therapeutic and preventive goals against diseases.

Lignans have long been known to have great health values. So I put my research focus on lignans and their potential influence on the gut bacteria in relation to cancer progression or recession. Lignans are ubiquitous in a

broad range of edible plants, such as flaxseed, sesame seed, crops, nuts, fruits, vegetable, etc.; collectively, lignans in plants are called plant lignans. Plant lignans have to be transformed to mammalian lignans, such as enterolactone and enterodiol, by bacteria for example, in order to play gut microbiome-amelioration and cancer-suppression roles. Enterolactone and enterodiol available on the market are both too expensive to be used for clinical treatment of cancers. To solve the price issue, we have successfully established a biotransformation system to convert plant lignans into mammalian lignans, making the compounds affordable in clinical application.

Our research findings and clinical work have continuously demonstrated that cancer is mostly avoidable, if appropriate constitutions in daily life and work routines, such as diet structure and mental/physical activities, can be observed. Even if cancerous tumors do form in the body, they should be controllable by curative therapies. This is our first time to put forward the concept of curative medicine, with much remaining to be explored. I therefore sincerely welcome suggestions and criticisms to make this book an increasingly better reference and hope that curative medicine will be increasingly be recognized as a definite solution to cancer and many other health problems.

ACKNOWLEDGMENTS

In the process of manuscript preparation for this book, I have been keeping the communications with my patients or their families. I am extremely pleased with their encouraging outcomes and sincerely thank them for their trust in me. In the meantime, I thank my family, mentors, friends, colleagues and students for their support and encouragement, without which the concept and practice of *Curative Medicine* would not have been possible.

In 1961, my parents sent me to elementary school and they tried their best to support my education at an extremely difficult time for them. I remember, once my teacher sternly ordered me and some of my classmates to write down a time indicating whenever we could bring the terribly delayed tuition to her. My classmates all provided a definite date, but not me. Two months after that, the teacher opened the notes to check the promised dates with each of us, one by one. Most of my classmates failed to live up to their promised dates and the teacher was furious, asking "Why?!" Silence with my classmates, as the specified dates were black on white there but the tuition money was nowhere. While looking at my note, she appeared to be quite flabbergasted to read "my father's next payday" and she showed a cold and blue face, and silence, this time, with her.

I thank my wife, my son and my grandsons for their unconditional understanding, support and assistance for my work. I have spent too little time with them in daily life and even holidays. They are, however, very happy with my curative medicine concept and its successful application in clinical practice.

As a member of the "student research club", I was supervised by Professor Shao-Xian Li, who converted me from a virtually zero research background

layman to a budding researcher, showing me how to read literature, how to design research projects, how to conduct experiments, and how to analyze and summarize the results for publication. The training by Prof. Li helped me to quickly adapt to the full time research environment at Beijing Medical College, where I conducted my graduate studies for the MSc degree, supervised by Profs. Zhen-Zhou Long and Wei-Feng Chen. I worked on a project of immunology, with a focus on the functions of T lymphocytes. I am grateful to Profs. Zhen-Zhou Long and Wei-Feng Chen for their supervision.

I spent four and a half unforgettable years at Gifu University for my PhD studies, where my supervisors Profs. Eiko Yabuuchi and Takayuki Ezaki led me to the scientific disciplines of bacterial pathogenesis and systematics. I left Japan with the PhD degree and went to Canada to start a new research area, comparative bacterial genomics, initially as a postdoctoral fellow with Dr. Kenneth Sanderson at University of Calgary. I joined Dr. Randy Johnston in late 1996 to work on a cancer therapeutics project using genomics methods. Dr. Johnston and I used to have long discussions on bacterial evolution and the origin of pathogenic bacteria. Over the past two decades, after my return to China, we did not work directly together, but we have continued the communications.

In 2002, I moved to Peking University and later to Harbin Medical University, where I received great support from Dr. Qi-De Han and Dr. Bao-Feng Yang, respectively, and from many colleagues of the two institutions and I am indebted to them. I also heartily thank all my students in Calgary, Beijing and Harbin. Every year, some students graduate to leave and new ones come to join me, and we celebrate the achievements of our research team, mostly on Teachers' Day, which is September 10 of every year.

My special thanks go to Profs. Randal Johnston, Karl Riabowol and Frans van der Hoorn for their considerate advices and invaluable suggestions on the manuscript.

Finally, I express my sincere gratitude to all of my patients and their families for their trust in me. I wish to continually receive their message on their active life activities and to hear from my colleagues and my readers for comments on the curative medicine strategy and any specific points on the concept and practice.

Liu lab at a New Year gathering

My research has been supported by funding from the Natural Sciences and Engineering Research Council of Canada, the Medical Research Council of Canada, the Canadian Institutes of Health Research of Canada, the University of Calgary, Peking University, Harbin Medical University, and the National Natural Science Foundation of China (NSFC). This book was financed by

NSFC grants 82020108022 and by a special funding from the College of Pharmacy, Harbin Medical University.

INTRODUCTION

At an international symposium organized by the Genomics Research Center, Harbin Medical University, with the theme of cancer treatment, Prof. Karl Riabowol from the University of Calgary, Canada, delivered an excellent presentation on his research. After his talk, I asked a question: “Thank you Karl for your superb talk! Cancer treatment is now precisely in the precision medicine category of scientific research, involving so many and so diverse molecular events and biochemical pathways to target the cancer for a deathblow to it, but few targeting methods can eventually achieve curative effects. Do you think it’s possible to come up with a one-for-all method against all kinds of cancers without hurting the patient?” Karl was extremely interested in this question and we had a good discussion. It was my first time to propose a novel cancer treatment method, though in the exact opposite direction from the precision medicine ideas. After that conference, I continued thinking about this, combining my previous research expertise in areas of microbiology, herbs of health and medical values, bacterial fermentation, and clinical practice. Eventually, together with my students, we developed the curative therapeutic strategies as presented in this book. I will begin with a couple of cancer cases with successful outcomes by ingesting dietary lignans without the use of chemo- or radio-therapies.

PART I

CANCER AS A DEVASTATING DISEASE: IS CURE POSSIBLE?

Cancer is among the deadliest diseases. Many modern measures to control cancer intend direct destruction of cancer cells, which however will inevitably destruct also normal cells, especially immune cells, making the already vulnerable immune functions to further fade quickly, and gastrointestinal cells, making nutrition ingestion insufficient and difficult. Even worse is the resistance caused by chemotherapy, which will lead to the relapse of the disease and, eventually, death of the patient. Gut microbiome amelioration by administrating lignans has shown unprecedented benefit in cancer treatment as a truly curative strategy.

Group meeting

1

CANCERS UNDER CONTROL BY CURATIVE THERAPIES

I started my medical career in 1971, working in the clinical laboratory of Fujin Central Hospital. At that time, hospitalized cancer patients were those diagnosed at relatively early stages of the disease, waiting for or recovering from surgery while suffering from the severe side effects of chemotherapy. Patients at middle or late stages of the malignancy would not have an opportunity to be admitted to the hospital. The patients would cry or even lie down in front of the hospital gate, hoping to get a chance to be treated. It was impossible. Few patients, even those treated by the hospital at a rather early stage, would survive for a couple of months. They would die of bleeding, infection or organ failure.

Clinical lab personnel, 1972. I was second from right.

Decades later, chemo- and radio-therapies became greatly advanced and more widely used, significantly extending survival of the patients. Nevertheless, many patients still die eventually, after remarkably extended event-free-survival, due in many cases to metastasis and relapse. Therefore, curative therapies, which stop the growth of the tumor and block its metastatic behaviors rather than head on destroy cancer cells, are urgently desirable. We have looked into the curative potential of natural products and found that lignans have the ideal therapeutic effects that can potently suppress the cancerous growth of the tumor and in the meantime do not impose adverse effects on the immune system or other physiological functions. Below are some cancer cases with successful outcomes of treatment by the lignan therapy.

Pancreatic cancer under control in a senior patient

An 83-year-old female was admitted on November 8th, 2021, presenting with deep jaundice and gross hematuria. Initial examinations showed that she had two tumors at the same time – one in the pancreas and one in the right kidney. A gadolinium-enhanced total abdomen magnetic resonance imaging scan revealed enlarged gallbladder and dilated intrahepatic bile duct, common hepatic duct and bile duct, image of which was truncated by the head of the pancreas. A nodule was found in the pancreas (Figure 1-1A). In the meantime, a right renal pelvis nodule was also found (Figure 1-1B).

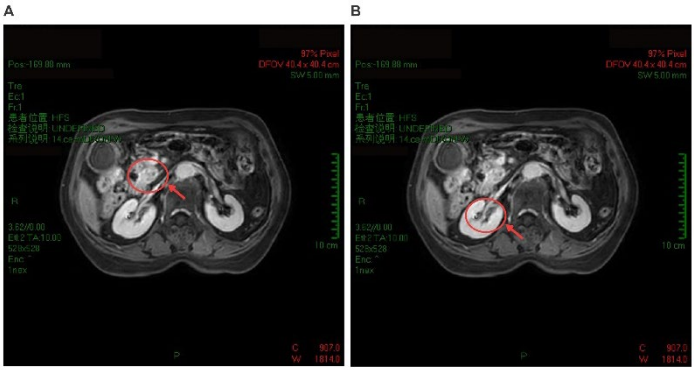


Figure 1-1. A gadolinium-enhanced total abdomen magnetic resonance imaging scan of the patient on November 15th, 2021. A: The pancreatic nodule over the head of pancreas. B: The right renal pelvis nodule [1].

The results of three-dimensional ultrasound images showed enlarged gallbladder, dilated intrahepatic bile duct, and widened common bile duct (Figure 1-2A, B). The main pancreatic duct was dilated (Figure 1-2C) and coupled with low biliary obstruction (Figure 1-2D). The patient had no family history of malignant tumors.

The patient was diagnosed with pancreatic cancer and renal pelvic cancer.

The patient underwent bile duct dilation operation on November 26th 2021, and then the jaundice became alleviated. She did not receive the conventional treatment for pancreatic or kidney cancer, such as surgery, chemo- or radio-therapy, or targeted therapy. She agreed to start oral administration of dietary lignans starting on January 12th, 2022. On January 17th, 2022, the patient felt substantial improvement of overall physical state and, particularly, her sleep status became fully recovered from severe insomnia.

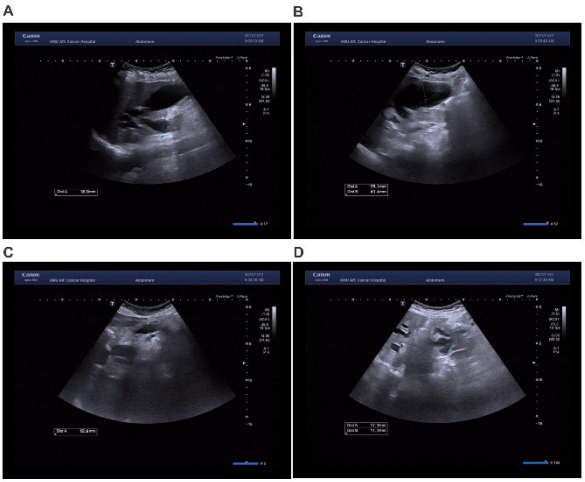


Figure 1-2. Three-dimensional ultrasound image of the whole abdomen on November 12th, 2021. A, B: The dilated bile ducts. C: The dilated main pancreatic duct. D: The low biliary obstruction [1].

After 3 months of oral lignans administration, the frequency of macroscopic hematuria decreased from daily to less than once a week, and her general condition kept showing improvement. MRI scan images showed decreased sizes of both tumors compared with the MRI results of November 15th 2021 (Figure 1-3), unambiguously demonstrating effective control of both tumors.

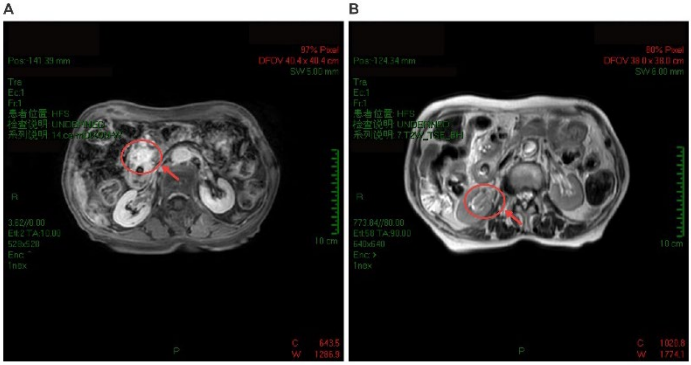


Figure 1-3. A gadolinium-enhanced total abdomen magnetic resonance imaging (MRI) scan of the patient on November 7th, 2022. A: The pancreatic nodule over the head of pancreas. B: The right renal pelvic nodule [1].

Whole blood and serum examination results showed a general trend of improvement from April to November, 2022, particularly reflected by the rapid and dramatic dropping of several biomarkers, such as CEA, CA199, CA724, CA125, and HE4. The hematuria became microscopic upon examination on November 24th, 2022; in the meantime, urine protein and glucose both kept being negative. The patient was well up to the last follow-up on September 3rd, 2023.

The way lignans work to bring cancer under control is briefly illustrated in Figure 1-4 and details will be given later in the book; the case report has been published [1].

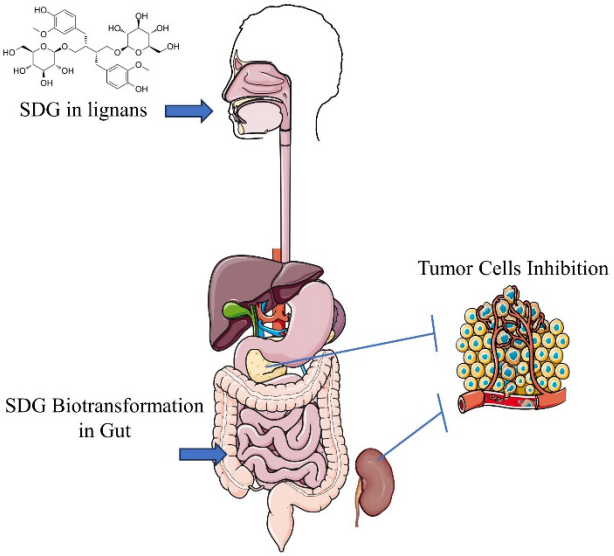


Figure 1-4. Schematic illustration of the procedure to use lignans in the treatment of cancer. SDG is the main ingredient of dietary lignans, which is converted by the gut bacteria into mammalian lignans through the biotransformation process to inhibit cancer [1].

Additional cases of malignancies with >5-year event-free survival after treatment by the curative therapies

We started the application of lignans to treat cancer in late 2019. The majority of the cancer patients who received the lignans treatment have shown evident alleviation or do not feel the disease on them anymore. The earliest cancer patients have had event-free survival for more than 5 years since the treatment with lignans. Below is a case of malignant gastrointestinal stromal tumor (GIST).

The patient was a 56-year-old male, complaining of intermittent hematochezia for over one month. The abdominal enhancement CT showed a jejunal mass in the left abdomen (Figure 1-5).

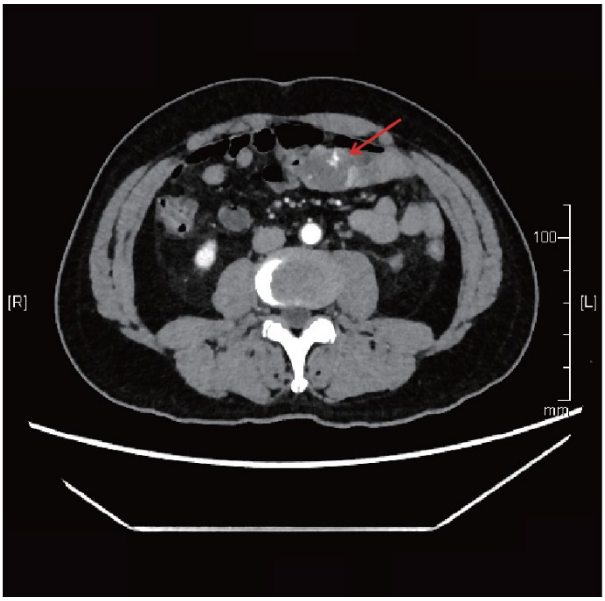


Figure 1-5. Abdominal enhancement CT. There was a jejunal mass (red arrow, high-density) in the left abdomen [2].

By laparoscopic surgery, the mass was resected and diagnosed to be gastrointestinal stromal tumor (Figure 1-6).

The patient did not receive any chemotherapy and he recovered well after the operation. In a follow-up one year after GIST resection, his carbohydrate antigen CA72-4 reached a very high serum level, >300 U/ml (the upper limit of detection; reference value: <6.9 U/ml), strongly indicating recurrence or metastasis of the tumor. The patient then was treated with dietary lignans, 15 g a dose twice a day. One month later, he

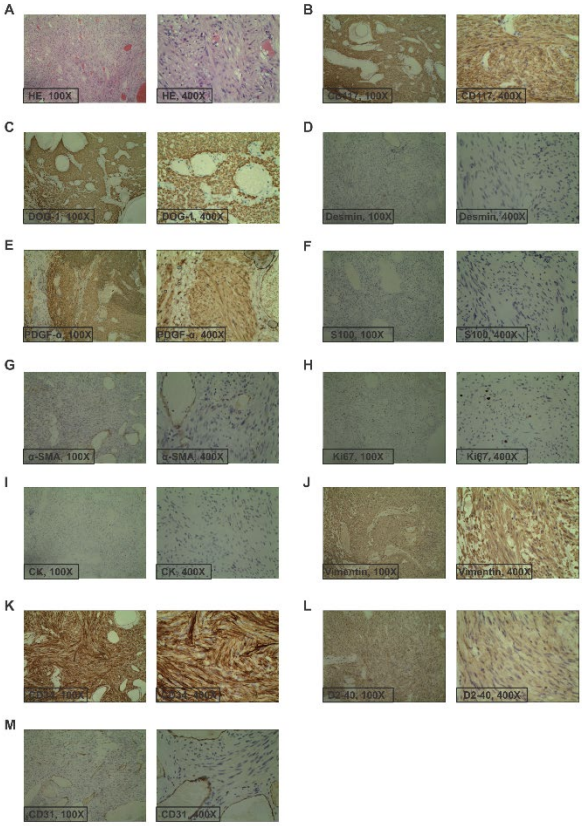


Figure 1-6. HE and IHC images of the tumor. A, HE staining. B-M, IHC images: B, CD117(+); C, DOG-1(+); D, Desmin(-); E, PDGFR-α(+); F, S-100 (-); G, α-SMA(-); H, Ki67(2 %+); I, CK (AE1/AE3; -); J, vimentin (+); K, CD34(+); L, D2-40 (+); and M, CD31 (-) [2].

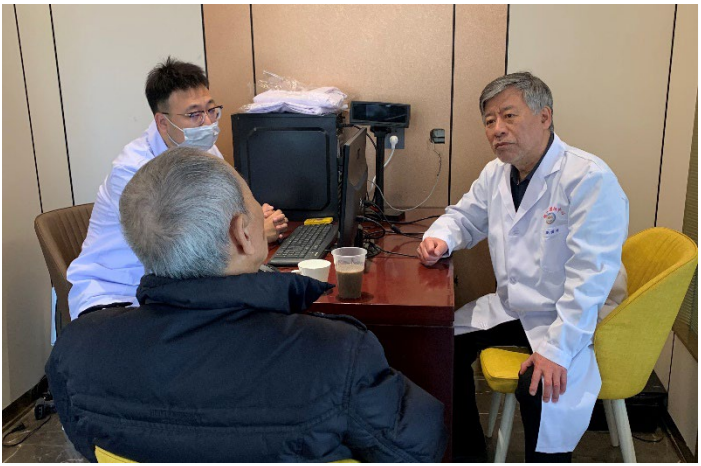
had another CA72-4 test and the level was 1.39 U/ml. He continued to take dietary lignans and had CA72-4 tested again 3 months after the previous reexamination and it remained as normal (3.99 U/ml or lower). During the period of dietary lignans administration, the patient kept reporting good

physical conditions. He felt much stronger and regained normal routine activities including aerobics, better mood and good sleep quality. This case was reported in accordance with the SCARE 2018 standard [2].

We have also achieved successful outcomes of treatment with lignans in several other cancer types, including lung cancer and colorectal cancer. The general efficacy primarily depends on the stages of the cancer. Whether malignancy of different histological or molecular types may respond differently to the treatment with lignans remains to be evaluated by systematic analyses of clinical, histological, pharmacological, microbiological, transcriptomic and all other relevant data. However, evidence accumulated to date in our institution supports our “one-for-all” curative medicine concept for cancer treatment.

Many cancer patients, or their family members when the patients themselves were too sick to come, visit us just to seek our *curative* therapies that they had heard about. They are curious and eager to know everything about the novel therapy. Ultimately, they want to know whether the *curative* therapy could really *cure* their disease, not merely extend their lifespan for another couple of years. Many of them believe that some modern therapies will not extend but rather shorten their life. They have information and good knowledge on cancer, so they would dissect your sentences into single words to judge whether your description of curative medicine would be trustable. Occasionally, I invite them to attend my lectures, case discussions, or lab meetings.

I give lectures on curative medicine to undergraduate students, assign research projects on curative medicine to my MSc and PhD students, encourage my postdoctoral research fellows to think about curative medicine in their research and clinical work, and mentor young physicians and junior faculty to understand curative medicine. I seek all



In the outpatient department

possible chances to enhance their understanding on curative medicine and elicit their enthusiasm in the research and application of curative medicine. When I see a particular new patient, for instance, I tend to gather some of my staff and students together – it is a good time to introduce the curative medicine concept deep to them. I usually take time to communicate with the patients or their relatives to understand their disease and for my young staff to understand curative medicine. Most if not all of the patients or their relatives came with great piles of laboratory and imaging examination documents, as they usually had visited one or more tumor hospitals before but were not satisfied with the treatment plans given, especially chemo- or radio-therapies. Patients increasingly deny the various therapies that directly destruct cancer cells. As a result, most required laboratory and imaging examinations had already been done when they first presented and therefore much time is saved. I would then encourage the patients or their relatives to provide the history of the current disease when I review their lab examination results, asking them to provide precise information on the onset

of the symptoms of the disease, the profession and general work environment of the patient, socio-psychological factors and specifics of the lifestyle, hobbies and free time activities, any medication used recently, and what made them come to this institution. After such brief communications, comes my time of lengthy, though not boring, explanations and remarks on the disease, followed by my treatment plans under curative medicine.

Proactive cancer prevention

In addition to the treatment of cancer that has been diagnosed, I strongly advocate proactive disease prevention for people who are exposed to high risks of cancer or have neoplasms in an organ without the nature known yet, such as pulmonary nodules. Since the occurrence of the COVID-19 pandemics, CT has been more widely used for lung examination, leading to the discovery of astonishing prevalence of pulmonary nodules, some of which having diameters exceeding 10 mm. There has been enormous panic in the population, as people know that some individuals having pulmonary nodules have eventually been diagnosed with lung cancer. As physicians, we often tell the patients that the great majority of lung nodules are benign, but we do not rule out the possibility that some of them are cancerous or may become cancerous. To the patients, my principle advice is that they have a lung CT check at intervals of 2-4 months. In the meantime, we advise the patients that proactive measures should be taken, such as well-balanced dietary structure and healthy daily routines including good sleep, appropriate aerobics and optimal social activities. We provide personalized recommendations for proactive cancer prevention. If the patient would like to receive the curative therapies as a prevention action, we agree and emphasize that the recommended proactive measures be taken at the same time. In most of the cases that we have treated with lignans, the pulmonary nodules keep decreasing in size and cancer molecular markers remain at high levels for some time and then decline gradually.