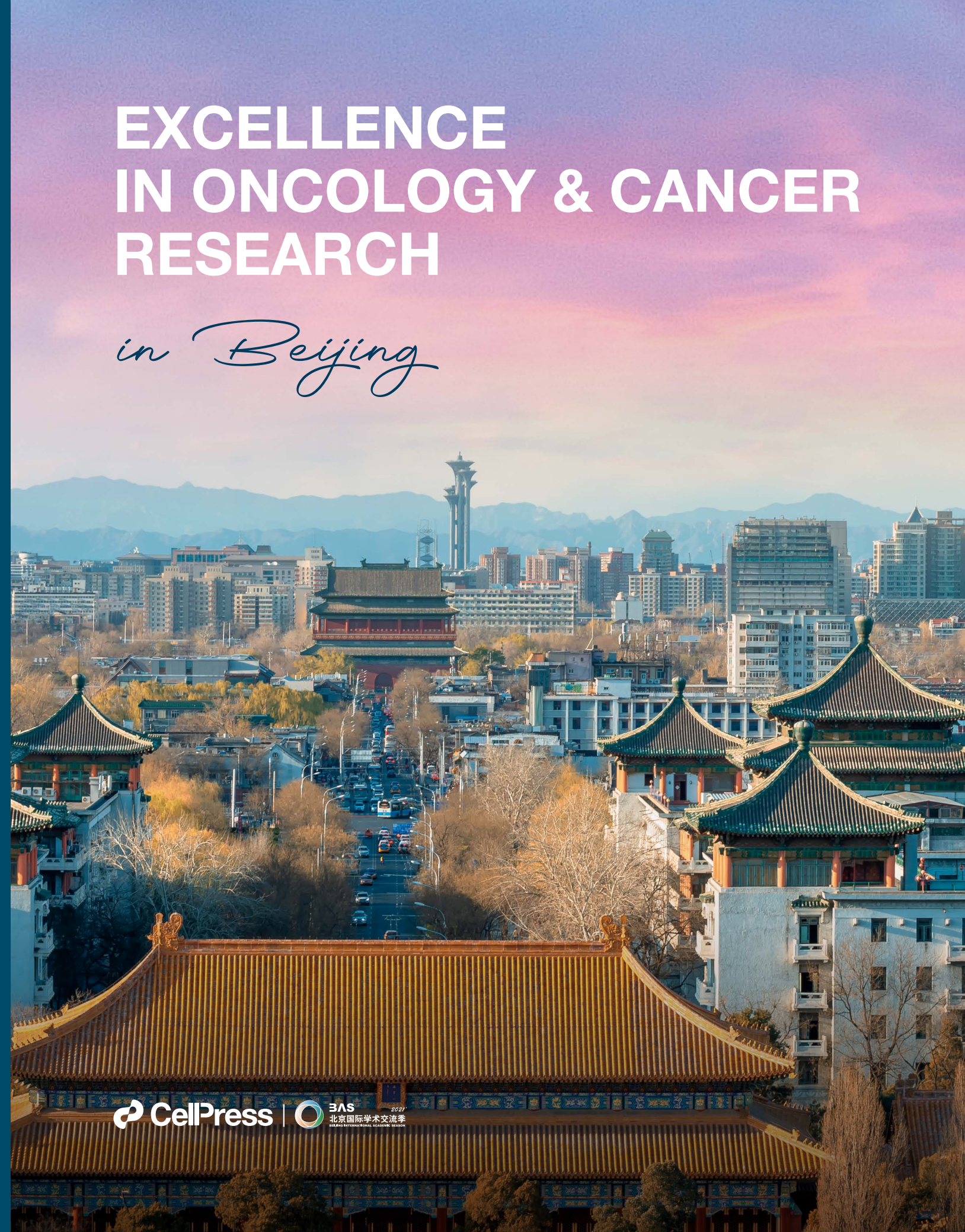


EXCELLENCE IN ONCOLOGY & CANCER RESEARCH

in Beijing



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Jie He

Director of National Cancer Center
Director of Cancer Hospital of Chinese
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Foreword

Cancer research in China has advanced rapidly and achieved exciting results in the past 10 years, especially in Beijing. The city has always been a cancer research hub, which contributed innovative ideas to many hot topics at the research frontier, playing a leading role in international and domestic studies.

According to statistics from Elsevier, the National Natural Science Foundation of China (NSFC) awarded \$155 million in grants to cancer research in Beijing in the years 2010-2018. In the past 10 years, 100 institutions in Beijing have published within the disciplines of oncology and cancer research. The top 15 collaborating institutions with co-authored oncology and cancer publications in Beijing between 2010 and 2019 are:

- Chinese Academy of Medical Sciences
- Peking University
- Capital Medical University
- University of Chinese Academy of Sciences
- Chinese Academy of Sciences
- Ministry of Education, China
- Ministry of Health of People's Republic of China
- General Hospital of People's Liberation Army
- CAS-Institute of Biophysics
- Academy of Military Medical Sciences
- Tsinghua University
- CAS-Institute of Automation
- CAS-Institute of Zoology
- Chinese Center for Disease Control and Prevention
- Beijing University of Chinese Medicine

Oncology and cancer research output in Beijing grew 277% from 873 publications in 2010 to 3,287 in 2019. Between 2010 and 2019, Beijing's publication and citation performance were also outstanding, with 22,468 published papers, 95,364 participating authors worldwide, 17.1 citations per publication, and 1.05 field-weighted citation impact.

The number of patents globally citing Beijing's oncology research reached 1,480, accounting for 28% of China citing-patent count. A total of 519 published oncology research from Beijing were cited by patents, accounting for 22% of China patent-cited output. The count of oncology or cancer-related patents filed in Beijing with the USPTO or WIPO reached 362, accounting for 14% of China patent output. According to Elsevier's indicators, such as field-weighted citation index, international collaboration rate, and the publications in the top 10% journals, Beijing's performance in oncology and cancer research has surpassed international and domestic averages and the city has climbed the ranks and taken the lead.

Researchers in Beijing have excelled in tumor genetics and genomics research, proteomics research, single-cell sequencing, tumor immunity

and immunotherapy, tumor epidemiology, and big data research and application. In the field of tumor genetics and genomics research, Chinese Academy of Medical Sciences led studies in esophageal cancer, lung cancer, pancreatic cancer, and colorectal cancer; Peking University piloted hepatocellular and intrahepatic cholangiocarcinoma research; Beijing Tiantan Hospital steered secondary glioblastoma studies; and recently, the Cancer Hospital of Chinese Academy of Medical Sciences and National Protein Science Center (Beijing) have combined genomics and proteomics to analyze the characteristics of lung adenocarcinoma in the Chinese population.

For the first time, these studies systematically revealed the inherited genetic mutations that correlated to common solid tumors in the Chinese population and discovered molecules related to tumor occurrence, development, and clinical prognosis. The research provided a theoretical and practical basis for revealing pathogenesis, molecular typing, molecular markers, determining and developing clinical drug targets, and formulating precise diagnosis and treatment plans.

In the field of single-cell sequencing, a research team at Peking University identified distinct myeloid populations through combined scRNA-seq analyses on the tumor microenvironment in human colorectal cancer and murine tumor models. They found heterogeneity and interactions in key cells that regulate tumor immunity, revealing a new mechanism for myeloid-targeted immunotherapy in colorectal cancer. In tumor immunity and immunotherapy, scientists at Tsinghua University have made breakthroughs in the basic research of tumor immunology and discovered new targets for vaccine adjuvants.

In the field of clinical research, according to numbers from the US clinical trial website (www.clinicaltrials.gov), there have been 7,001 cancer-related clinical trials across China since January 1, 2010, and 2,121 of those were carried out in Beijing, accounting for nearly one-third (30.3%) of the total. Tumor immunotherapies that are currently in the spotlight include T cell immunomodulators and cell therapy. The immune checkpoint regulators PD-1 and PD-L1 are the most common targets, of which eight related products are already on the market in China. Under the leadership of the Cancer Hospital of the Chinese Academy of Medical Sciences, the first China-developed PD-1 monoclonal antibody and HPV vaccine was approved by NMPA. Since 2011, when the National Cancer Center was established in Beijing,

the center has set up a series of cohort studies on cancers, such as lung cancer and esophageal cancer, and multiple population-based cancer screening projects for the early detection of upper gastrointestinal cancer, lung cancer, and esophageal cancer.

These efforts not only took the initial step in characterizing risk factors for common cancers in the Chinese populations, but also evaluated the efficacy of current strategy on cancer screening, diagnosis, and treatment in China. With the aid of big data, the National Cancer Center is continuously expanding and updating the national cancer registration and monitoring network, the national cancer prevention and control platform, the national cancer quality control platform, the national anti-tumor drug monitor system, and the national cancer data platform. The center aims to build a comprehensive and multi-dimensional network for cancer prevention, treatment, and control in the whole country, with the purpose of promoting the construction of national cancer biobank and sharing of the national cancer resource while laying a solid foundation for the nation's clinical research on malignant tumors in the future.

This introduction mentions only a few Beijing scientist research results due to word limits. Please refer to www.cell.com for other related papers.

Cell Press and the Beijing Municipal Science and Technology Commission have collected 10 representative papers published by Chinese scholars in the Cell Press journals, conducted in-depth interviews with extraordinary scientists in Beijing, and analyzed cancer research development in the area. The editors have organized a special issue, "Excellence in Oncology & Cancer Research in Beijing", to demonstrate the advancement of cancer research in the past 10 years and to reflect the work and effort of Chinese scientists in the field from a new angle.

2020 has been a challenging year, but China has overcome hardship through hard work. At the beginning of the new year, I would like to extend my highest respect and best wishes to all of you who care about and support cancer research, to colleagues who are fighting at the front line of cancer research, cancer prevention, and control, and to my retired friends who have contributed to the field! 2021 is the first year of the "14th Five-Year Plan", so let us continue to strive with faith and courage to work towards a healthy China and contribute to the innovation and development of cancer research worldwide!

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PEOPLE

THE MINDS THAT DRIVE DISCOVERIES

As a prominent talent hub, Beijing attracts brilliant minds in oncology and cancer research. These experts have propelled the advance in scientific discoveries and clinical care, both as their personal endeavour and through collaborative efforts in the community.



MIND IN SCIENCE HEART IN ART

Qimin Zhan

To Qimin Zhan, a true physician has a wealth of medical knowledge, superb skills, and a love for humanity. As a physician-scientist who has his mind in science, Zhan often finds comfort in the arts, which inspires him with innovative ideas and motivates him amid difficulties. At Peking University, he studies pathogenesis and gene mutations in esophageal cancer, a disease that is uniquely prevalent in the Chinese population. With a hope of a "healthier China", he is leading domestic and international efforts to find solutions.

Who sent the summer breeze on a cold winter night
Melting the ice sealed bleak winter
Who lit the candle in the dark
Shining in people's desperate hearts
...

It may come as a surprise that the lyric writer and singer behind the song is Qimin Zhan, a scholar of the Chinese Academy of Engineering and President of the Peking University Health Science Center.

"As a physician-scientist, you need not only a wealth of medical knowledge and superb medical skills, but also a love for humanity," says Zhan. He says that only when a physician has both "wings" can one fly higher and farther.

At work and in life, Zhan has his mind in science and his heart in art. He became the "charming role model" in his students' eyes while leading and promoting the rapid development of China's molecular oncology research.



Shouldering the research of prevalent cancers in China ■

In academia, Zhan focuses on tumor molecular biology and tumor translational medicine research. Zhan's research team mainly targets esophageal squamous cell carcinoma, a malignant tumor with the highest morbidity and mortality in China compared to the rest of the world. "Facing cancers with 'Chinese traits', biomedical scientists in China are duty-bound," he says.

By collaborating with domestic research teams and combining esophageal squamous cell carcinoma samples and clinical information from patients, Zhan's team discovered eight significant mutated genes that correlate with the disease's occurrence in 2014. Among the mutated genes, FAM135B is a newly discovered tumor-related gene. Meanwhile, they also collected vital data on gene copy number variants in esophageal squamous cell carcinoma. These gene mutations and copy number variations are essential factors in the occurrence and development of the disease. The findings can provide new insights for diagnosis, treatment, and drug development. This discovery was published in the journal *Nature*.

Zhan has emphasized that besides the most prevalent esophageal squamous cell carcinoma, other cancers such as liver cancer, gastric cancer and nasopharyngeal cancer are malignant tumors with the highest morbidity and mortality in China compared to the rest of the world, compelling Chinese scientists and physicians to focus on research and prevention of these cancers. "Developed countries in Europe and the United States invest not so much research efforts into these cancers with 'Chinese traits', and thus if we don't initiate inno-

vative research, there will be no effective treatment for these patients. Even if there were, the high treatment costs and mortality rate will continue to burden the people of China," he says.

To understand the disease's pathogenesis, Zhan led his team to tackle the research from multiple angles, including molecular biology, genomics, and tumor microenvironment. The tumor microenvironment in the development of esophageal cancer and its interaction with the genome has been the focus of Zhan's team in recent years. "In our study, we have found many potential molecular markers and druggable targets. We hope that by working with pharmaceutical companies, we can translate these lab research findings into diagnosis methods and treatments for cancer," he says.

In the context of the Healthy China Initiative, the Central Committee of the Communist Party of China and the State Council have put forward a cancer prevention and control plan, "prevention first, combined with treatment and control". Zhan's team also further advanced cancer research strategy by including "pre-cancerous lesion" as a topic, focusing on controlling cancer risk factors. "Besides esophageal cancer, other gastrointestinal tumors have important physiological signals in the early stage, which can help us distinguish high-grade and low-grade lesions. If we can block the signals at the early stage, it can effectively prevent pre-cancerous lesions from becoming tumors," says Zhan. He hopes to actively promote the early detection, diagnosis, and treatment of cancer by emphasizing the importance of early diagnosis and treatment in high-risk areas.

Integrating resources, promoting health technology innovation ■

In addition to academic research, Zhan has several positions associated with cancer associations and societies: vice-chairman of the Chinese Anti-Cancer Association, vice-president of the Chinese Medical Doctor Association, vice-chairman of the Chinese Society of Microcirculation, president of the International Cancer Institute of Peking University, and more. Among them, the International Cancer Research Institute of Peking University, established in October 2019, is currently Zhan's "anti-cancer frontline".

Zhan says that in response to the country's significant need for scientific and technological innovation and cancer prevention, Peking University used its comprehensive academic advantages to establish

the Cancer Institute. "The International Cancer Institute of Peking University will make full use of high-quality resources and deploy cutting-edge discoveries in translational applications, clinical diagnosis, and treatment. It aims to nurture a group of research talents with international-leadership qualities, contributing to China's cancer research prevention and control," he says.

With more than a hundred years of history, the Peking University Health Science Center plays an essential role in China's medical field. As the center director, Zhan hopes that cancer research is not limited to the medical field. "The development in medicine has two obvious traits: one is scientific innovation, the second is interdisciplinary collaboration," he says. Zhan used the International Cancer Institute of Peking University as an academic exchange platform, inviting different universities and various fields to communicate and cooperate, building a health and technology innovation network.

In 2020, the project team formed by the International Cancer Institute of Peking University and other research institutes successfully applied for the National Natural Science Foundation of China's "Center of Basic Medicine" project. "We are the second Center of Basic Medicine in the project's history!" says Zhan. Moreover, the institute has also published landmark research in genomics and single-cell sequencing in *Cell*, *Cell Research*, and other journals. The published findings were significant and have attracted attention from scientists worldwide.

From the Chinese Academy of Medical Sciences to Peking University, Zhan was immersed in Beijing's academic environment, witnessing the golden age of cancer research in China. "With the support of China's national and Beijing's regional policies, universities in Beijing have developed a strong academic atmosphere. Beijing is also gradually growing into an international cancer research hub," he says.

Zhan's next step is to strengthen international collaborations. "We still have room for research and development improvements if we want to play a crucial role in leading and supporting the field of cancer research worldwide," he says. Zhan added that there are many research institutions and an abundant number of medical samples in Beijing, presenting as a strong foundation for international cooperation. "Cancer research is a global issue. We will continue to share our resources and make joint efforts to end cancer as soon as possible."

Tapping in science and art to cultivate innovative talents ■

Being in the cancer research field for more than 30 years, Zhan has also experienced hesitations and hardships. He is incredibly thankful for Min Wu, a tumor geneticist and cell biologist. "I served as director of the State Key Laboratory of Molecular Oncology of the Chinese Academy of Medical Sciences from 2002 to 2016. Wu, who held that title before me, gave me a lot of encouragement and guidance," Zhan recalled with sentiments. "I was standing on the shoulders of giants and climbing upward. Wu is a significant mentor in my career, and I look up to him."

Besides the help of mentors, art is also a vital support to Zhan. He sang at the graduation ceremony of the Health Science Center, played pipa on the TV lecture program "Voice", and joined NetEase Cloud Music as a musician. Zhan uploaded more than 40 songs, some of which were his original music.

"I wrote an article titled 'Science and Art Meet at the Mountain Peak'," says Zhan. He firmly believes that science and art share common grounds and can influence and nurture each other. "Art can be a key factor in motivating your research career. When you face difficulties, art helps with adjusting your mindset, allowing you to see a rich and colorful world beyond the research topic in front of your eyes."

As an educator, Zhan often encourages his students to have their "mind in science and heart in art". "The key to education is to cultivate students with the spirit for scientific innovation and sentiment for arts and humanity," he says. Every year, during student orientation at Peking University Health Science Center, Zhan faces a new generation of physicians and biomedical scientists. He hopes that these students gain a wealth of knowledge from their future study and work, view medicine as a lifelong pursuit, and experience self-cultivation through arts, nurturing

innovative thinking. "Medical skills, ethics, knowledge, and humanity are the traits that a true physician possesses."

Looking forward ■

Looking into the development of Chinese cancer research in the next decade, Zhan, a molecular oncologist and medical educator, is filled with hope and confidence. "I am optimistic about technological innovation and the growth of talents. Cancer diagnosis and treatment may evolve from data digitization to data visualization. There may also be major breakthroughs in clinical therapeutic interventions."

Zhan is looking forward to the day when cancer is no longer a "terminal illness" and becomes a "preventable, treatable, and controllable" chronic disorder with a significant decline in morbidity and mortality. He hopes to improve people's overall health and push the establishment of a "healthy China".



WHERE YOUR HEART LONGS YOUR STEPS FOLLOW

Zemin Zhang

A relative's cancer diagnosis prompted Zemin Zhang's return to China. He gave up his executive job at a renowned pharmaceutical company in the US and returned to campus in China—as a professor at the School of Life Science, Peking University. Devoting his efforts to cancer research, Zhang and his team aim to advance cancer immunotherapy and targeted therapies in the hope of curing cancer one day.



"If one of your relatives is diagnosed with cancer, how would you help?" Professor Zemin Zhang asks his graduate students this same question every year during enrollment at the School of Life Sciences, Peking University.

To him, the question isn't hypothetical. It's his real-life experience.

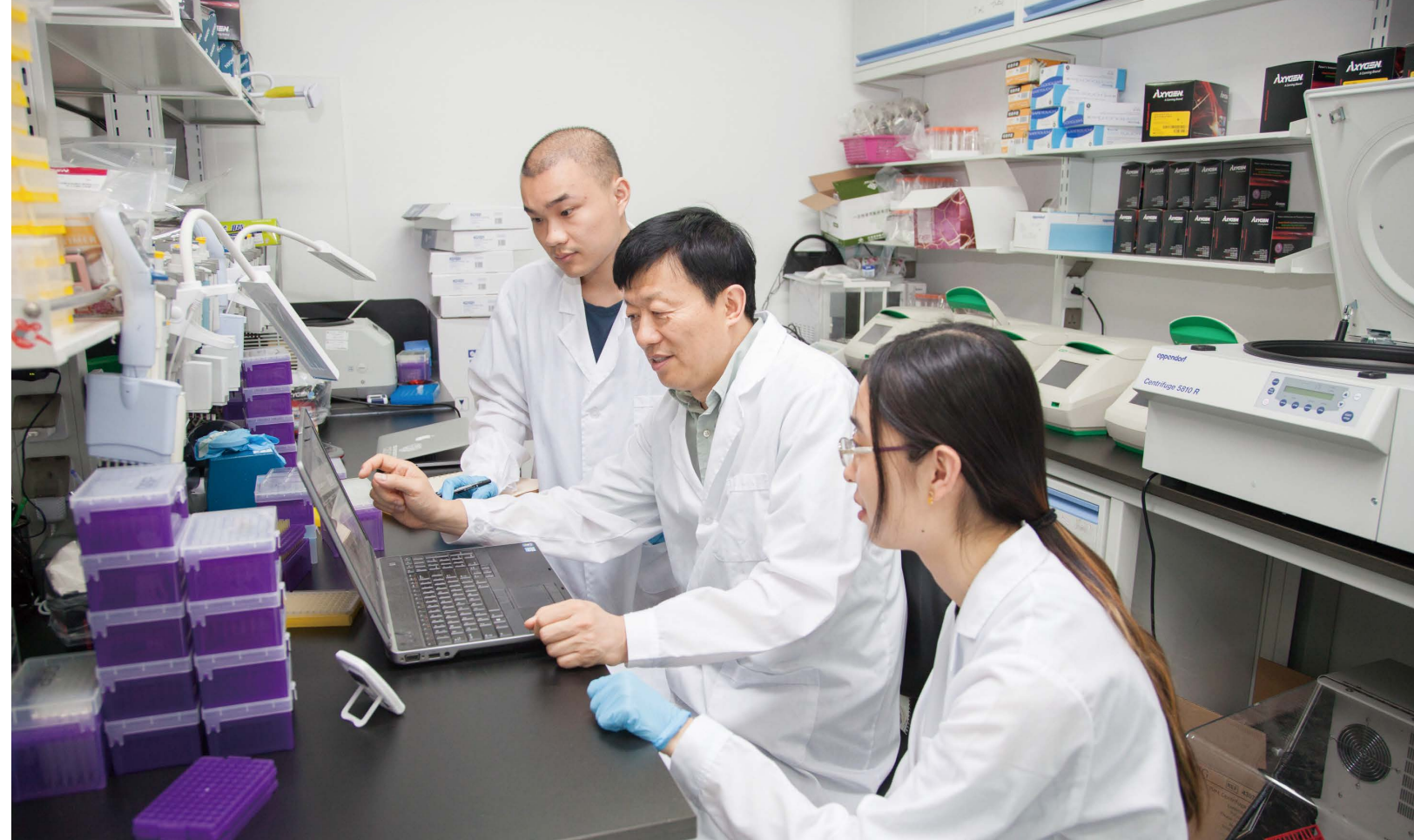
Zhang was in the United States working at Genentech, surrounded by top cancer experts, when he learned that his sister had breast cancer. He was sure that he could help her somehow, at least finding the best cutting-edge treatment for her condition. Contrary to his expectation, instead of performing pathological diagnosis and molecular typing, local physicians sent his sister straight to surgery and applied chemotherapy. The side effects of the treatment wore her out significantly.

Many years later, Zhang still feels a sense of somberness every time he recalls the event. The experience became a pivotal moment for him—with all his accomplishments overseas, what does it mean if he could not help his family?—and he started to consider returning to China.

Where your heart longs, your steps follow. "Returning to China, I wanted to devote myself to cancer research for my home country and strive towards every cancer scientist's ultimate goal—curing cancer," says Zhang.

Transitioning from an American executive to a Chinese professor ■

After graduating from Nankai University, Zhang continued his PhD study in the United States, eventually joining Genentech/Roche and focusing on discovering targeted therapies in tumors. Zhang worked at



the world-leading pharmaceutical company for nearly 17 years, becoming the director and principal scientist of bioinformatics while leading efforts in cancer genomics. He has also made direct contributions to the identification of molecular targets for multiple cancer treatment drugs.

Returning to China at the peak of Zhang's career not only means that he's giving up his cushy job, but it also pulls him away from the world's cancer research hub. Was he stepping in the wrong direction?

Standing at an intersection without navigation, you never know which road will lead you to your destination. Zhang saw scientists who returned to China early in their career seizing great opportunities and succeeding in their fields. "I wondered what facilitated their success," he says. Zhang

was curious and eager. In 2014, Zhang joined Peking University as a professor at the invitation of Xiaoliang Xie, current director of Peking University's Biomedical Pioneering Innovation Center. After returning to China, Xie's words rang true to Zhang's ears, "In Beijing, you can do research that you can't in the United States."

"Some projects are difficult to carry out in the United States but easier in China," says Zhang. He cited the alliance jointly formed by research institutions to investigate COVID-19 through single-cell research launched last year as an example. "We contacted every research unit working on single-cell and COVID-19. Of the approximately 25 entities, 20 immediately responded, forming the world's largest single-cell research alliance for COVID-19. This is completely impossible abroad!" Zhang praised the country's dynamic scientific research environment and

strong government support, making more extensive studies possible.

Changing research directions and optimism about cancer immunotherapy ■

Zhang spent over a decade studying cancer cells in the United States. Now, he and his team focus on the tumor immune microenvironment from a single-cell perspective, hoping to promote cancer immunotherapy and targeted therapy developments.

The change in research direction requires the advancement of bioinformatics technologies and reestablishing the understanding of tumors—from targeting cancer cells to stimulating and strengthening the immune system's autonomous immune defense, which is not trivial.

In an ever-changing world, people achieve excellency by meeting challenges head-on, especially for scientists like Zhang. He believes that the most crucial thing in scientific research "is intriguing and has transformational value".

"Cancer immunotherapy is destined to become a central direction in the field of cancer treatment," says Zhang. He's not the only one who thinks that. In 2018, the Nobel Prize in Physiology or Medicine was awarded to American scientist James Allison and Japanese scientist Tasuku Honjo for their contributions to cancer immunotherapy. The attention promoted immunotherapy research overnight, and it has become one of the fastest-growing and most dynamic fields in the biomedical community worldwide.

In recent years, Zhang and his team have published several studies in renowned journals *Cell* and *Nature*, bringing forth novel ideas for cancer immunotherapy development. With hard work and perseverance, Zhang, who "intruded" on the academic running track, became one of the top contestants, leading the race with confidence and talent. "In terms of studying tumor immune microenvironment from a single-cell perspective, I think our team may have done the most concentrated research and is also relatively advanced," he says.



Looking forward to discovering new cancer targets in China in the next 10 years ■

From the United States to China and from corporations to universities, Zhang was not sure whether he made the right choice before returning to China. Now, he has the answer: "From a research perspective, it has exceeded my expectation." His success is closely related to the rapid growth in China's cancer research and clinical practice.

With groups of exceptional scientists returning to China from abroad and the emergence of outstanding local scientists, the country is rapidly catching up with leading countries in cancer research and is even leading the race in some new topics.

If scientific research funding and university talents are the fuel that drives cancer research, close cooperation with clinical resources is the catalyst that accelerates this development. "Beijing has a wealth of clinical resources. On top of that, doctors and patients are highly cooperative, which helps observe the patients' immune characteristics and dynamic changes during the treatment process," says Zhang. He feels that these results are difficult to achieve abroad.

Looking at the next 10 years of cancer research development in China, Zhang hopes that the country can discover new cancer targets. "I hope that in the future, new anticancer targets that are as important as PD-1 can emerge in China."

PD-1 is a crucial immunosuppressive molecule in the cancer research field, which enables tumor cells to escape from the immune system. PD-1 inhibitor drugs have shown efficacy in various cancer treatments, prompting dozens of Chinese companies to follow up in research or production. But, unfortunately, China has yet to discover notable targets on its own. "I hope we can identify some new targets and transform them from basic research into a novel anticancer intervention," says Zhang.

In Zhang's head, he can already see the goal. All that is left to do is keep chasing and persevere until he reaches the finish line.

Chen Wu

SEIZE THE DAY AND LET YOUR DREAMS GUIDE YOU

Chen Wu is a sixth-generation scientist at the Chinese Academy of Medical Sciences studying esophageal cancer, a disease that disproportionately affects the Chinese population. As a physician-scientist studying the disease for over 15 years, she has become a bridge between her patients and science, bringing problems found by the bedside to the lab bench for solutions. Shouldering a long line of research and patients' expectations, Wu is determined to provide better care and combat esophageal cancer.

When the car drove into Henan, deep into the hills by the foot of the eastern Taihang Mountains, groups of old farmers in the fields came into Chen Wu's view.

Some of them may be cases on the patient list for her epidemiology group to follow-up. Some of them may be Dr. Wu's patients, whom she screened for esophageal cancer. Others may have relatives that passed away from esophageal cancer who were treated by Dr. Wu.

The fields are located in Linzhou, Henan, a high-risk region for esophageal cancer in China. Wu and her colleagues and students visit every month to screen the at-risk locals for tumors and to provide treatment.

Wu and her colleagues brought the most advanced screening tools and treatment plans from the laboratory at the National Cancer Center, Chinese Academy of Medical Sciences to rural areas of Linzhou. They hope to reduce the morbidity rate and alleviate the suffering of patients through early detection and intervention. At the same time, they are grateful for the volunteers and patients who allow them to dig into the disease's etiology and hopefully defeat it one day.

Seize the day and let your dreams guide you. Wu has been focusing on esophageal cancer research for 15 years. She emphasizes that her research purpose is built on her patients' needs, and "screening out early-stage patients as soon as possible and giving late-stage patients precise treatments and hope" is her goal. "We must always remember that we have to be with the patients to understand what they need first, and then return to the lab to study solutions."

Following her heart, Wu pursued her scientific research career, showing her talent and reaching for her goals.



Taking over the national mission of enlightening esophageal cancer research in China ■

At the Cancer Hospital of the Chinese Academy of Medical Sciences, Wu is a sixth-generation researcher on esophageal cancer and currently serves as a professor, researcher, and PhD advisor. "Studying esophageal cancer is a responsibility that Chinese scientists must shoulder and it's our generation's duty," Wu has said in multiple public speeches and interviews. The history of it can be traced back to Linzhou, Henan.

In 1959, the Prime Minister of China, Enlai Zhou, instructed Ritan Hospital (now Tumor Hospital) of the Chinese Academy of Medical Sciences (along with several other hospitals and research institutes) to focus on Linxian County (now Linzhou), Henan Province. The goal was to investigate the incidence of esophageal cancer. They established the first epidemiological investigation base for esophageal cancer in China, with an official mission for comprehensive prevention and treatment of the cancer.

With modern medical intervention, esophageal cancer incidence in Linzhou, Henan, and other parts of the country has been controlled and the mortality rate has gradually decreased. However, the cause of the disease has yet to be discovered and China still has the highest morbidity and mortality rate of esophageal cancer in the world. Unlike Europeans and Americans who are susceptible to esophageal adenocarcinoma, most patients in China are diagnosed with esophageal squamous cell carcinoma. Although the latter accounts for 90% of esophageal cancer cases worldwide, Chinese scientists face esophageal squa-



mous cell carcinoma on their own.

Starting from Linzhou, Henan in 1959, scientists before Wu first studied cancer from an epidemiological perspective and later introduced biochemical and genomics research approaches. The entire history of esophageal cancer study in the country is contained in six generations and more than sixty years of perseverance in scientific research.

There is a long way to go, but progress is being made, one step at a time. Wu completed her PhD studies under Dr. Dongxin Lin at the Peking Union Medical College and finished her postdoctoral training at Harvard University. Wu has been conducting genetic and

genomics research in areas with a high incidence of esophageal cancer, such as Henan and Shanxi, holding the torch that researchers from the previous generations passed down.

Moving basic and clinical research forward with benevolence ■

Today, the goal of studying esophageal cancer is not only to solve a national problem but also to relieve patients' pain. In Wu's perspective, this is the "deal" she promised her research participants without saying it out loud.

Wu's research requires collecting samples from patients with eso-

phageal cancer in addition to following up on the progression of their treatment. "The best way to map the cancer is by following the disease progression of an individual from healthy to early-stage and late-stage." In her 5 to 10 years of research collaboration with participants, Wu's not the only one who is pouring her heart into the study.

Wu says that every time her team visits Linzhou, Henan, for tumor screening, locals would meet up with them. These people don't exactly understand the research, but they know the team and trust Wu enough to become long-term volunteers for the project. To Wu, who grew up in a big city, this kind of faith means a greater responsibility. "Their hospitality makes you want to do better in cancer research!"

Majoring in clinical medicine in undergraduate studies, Wu has seen her fair share of life-or-death situations. She knows that esophageal cancer is painful for patients. Whether it's because of a physician's benevolence or her trying to return the local participants' trust, Wu wants her patients' experience to guide the research, bringing problems found by the bedside back to the lab bench for answers. She hopes to find the best solution for her patients and advance clinical research.

In recent years, she illustrated the world's most extensive esophageal cancer genome map with the help of young scientists in her lab. The team discovered tumor susceptibility and cancer-driving genes unique to the Chinese population, providing fundamental knowledge for screening and prevention in high-risk groups.

"This is also the reason and advantage for doing scientific research in the Cancer Hospital," says Wu. Her team is always thinking of ways to integrate basic research topics and clinical practices. "Basic research and clinical practice cannot be separated. They're an interdisciplinary science."

Lately, the central government in Beijing has also promoted the development of interdisciplinary research in medicine. Wu praised the central government for becoming more inclusive and showing great interest in translating basic research to clinical applications. "Beijing's push for implementing multidisciplinary research will help promote the importance of it to the rest of the country. It will also boost the momentum of medical advancement." Wu looks forward to taking this opportunity for further bench-to-bedside research endeavors.

Asserting the patient's contribution with a feminine touch ■

When asked what the advantages are of being a female scientist, Wu always says science has nothing to do with gender.

Nevertheless, Wu's feminine side, the gentleness and attentiveness, has made her more aware of the patients' needs. Even for patients with late-stage esophageal cancer who cannot undergo surgery, Wu still wants to give them hope. Years of clinical experience have made her realize "When someone is desperate, the person depends and trusts their doctors even more. They'll ask all kinds of questions because, at that moment, we're like their savior." Therefore, Wu asks her students to take extra care of late-stage patients and designs her teaching based on patients' needs, such as providing hospice care.

The sincerity and familiarity people often find in women also helped Wu gain the trust of locals. She would patiently and cordially call her patients to remind them of their tumor screening. She doesn't call her local patients during wheat-harvesting seasons because she understands that they are busy and that the harvest is critically important. "Every December, the number of surgeries in Linzhou, Henan, will drop. Why? Because people don't want to have surgery during the Chinese New Year," says Wu. However, she never presses on the question because she knows that when the Chinese New Year holiday rolls around, the locals' children will visit, and they'll have the surgery after the holiday.

However, when it comes to scientific research, gender is irrelevant. "People invite me to give lectures or participate in international conferences not because I'm a female scientist, but because they want to listen to my latest research progress," says Wu. In her view, an individual's achievement is not defined by their appearances but lies in the purpose and results of their research and their dedication to patient care.

Holding the torch of esophageal cancer research that was passed down to her and shouldering patients' expectations with a feminine touch, Wu is integrating basic research and clinical application. She will always stand by her patients-no matter how long it takes to combat esophageal cancer-with her best intentions marching forward.

FACING CHALLENGES HEAD-ON

Xin Lin

Xin Lin has dealt with cancer for many years, not only as a scientist but also as a cancer survivor. His personal experience gave him a deeper understanding of patients' expectations, which solidified his determination to explore better cancer treatments. Working as a professor at Tsinghua University, Lin developed a T cell therapy with fewer side effects that may better treat blood cancer and tumors in the future, realizing bench-to-bed-side translation to fulfill patients' hope.



In 2011, Xin Lin was diagnosed with cancer again. This time, it was lung cancer, the king of cancers.

"At that moment, I thought 'it's over. This is the second time I've got cancer,'" says Lin. Lost, helpless, and anxious, emotion surrounded him. As a professor of molecular and cellular oncology, Lin has "dealt" with cancer for many years. It wasn't until the reality of the disease struck him, twice, that he finally saw the other side of it.

"As a cancer patient, you feel very helpless. You hope to be cured, but you also have to face the fact that your life is dimming," says Lin. Before, Lin just considered his cancer research as a job, an intellectual puzzle to solve. Now, as a cancer patient himself, he has a deeper understanding of patients' expectations. The urgency and importance of cancer research become evident.

Fortunately, Lin caught the lung cancer early and recovered after surgically removing the tumor. However, after the two incidents, Lin felt a strong and clear sense of duty, which drove his devotion to cancer research.

In 2012, Lin, who was cancer-free, once again challenged the disease. This time, as a scientist, continuing his work and facing challenges in scientific research head on.

Embracing challenges, returning to China mid-career ■

Lin was the first batch of students enrolled in Shanghai University of Science & Technology after the reinstatement of China's college entrance exams in 1978. He studied chemistry for his bachelor's degree and later pursued biochemistry as a graduate student after attending his father's lecture by chance,

which kindled his interest in immunology. Lin took 13 years to switch gears from chemistry to immunology. It was not until 1995 that he finally set foot on the right path when he joined the University of California, San Francisco, as a postdoctoral fellow in immunology.

After realizing their dreams, people tend to settle down. But not Lin, he enjoys the scramble. "I think it has something to do with my personality. I like the challenge," he says.

"Life is a scramble," is Lin's motto. Between work, research, and life, everything is continuously changing and scrambling.

After 2000, Lin taught at the School of Medicine, the University of New York at Buffalo, and then the University of Texas MD Anderson Cancer Center. As his position changed, he switched from studying immune mechanisms to tumor research. Lin's determination to explore clinical treatment in cancer solidified following his cancer diagnoses in 2009 and 2011.

In 2013, Lin started to consider returning to China. The MD Anderson Cancer Center, where he worked, is a world-class cancer research, diagnosis, and treatment facility. The *US News & World Report's* "Best Hospitals" survey ranked MD Anderson Cancer Center as the top hospital for cancer care in the US for years. Many of Lin's family and friends told him not to give up his faculty position in the US and suggested that if he stayed, he'd be able to climb the academic ladder and reach achievements and fame one day.

However, Lin chose to return to China for a second career. "First, I was driven by a strong sense of belonging. I've always hoped to succeed in my field and give back to my country. Second, I have become a professor and program director at the University of Texas MD Anderson Cancer Center. My life settled and was predictable. There weren't any challenges," he says.

In 2014, Lin officially joined Tsinghua University as a medical school professor and the chairman of the Department of Basic Medical Sciences, opening a new round of challenges in his life.

Exploring and developing innovative cellular immunity interventions ■

Having accomplishments in the field of cancer research is not an easy task. When every road seems like a dead-end, how do you create your own path?



Since 2014, Lin's lab has been focusing on T cell immunotherapy application. T cell is a type of immune cell that plays a vital role in the body's immune defense. T cells kill tumor cells but can also be easily "exhausted" by tumor cells, which may prevail and win the battle.

To help the T cells make a comeback, scientists "installed" a guidance switch called CAR through genetic engineering and sent the cells back into the body to fight the cancer. Clinical studies have confirmed the CAR-T cell therapy's efficacy in blood cancers.

Lin wasn't satisfied by merely following in the footsteps of scientists before him. He redesigned CAR and invented a brand new structure called STAR, which he applied to patent. In clinical research, Lin's lab targeted tumor cells directly with STAR-T cell therapy, which effectively increased T cells' survival time in the body. Moreover, the technology reduced T cell exhaustion, which prevented tumor escaping and tumor recurrence. "Compared to conventional CAR-T cell treatment in blood cancers, STAR-T cell therapy performs better, has fewer side effects, and is easier to work with for designing multi-target variants. The new therapy also has a better effect on solid tumors," says Lin, sharing his latest results with excitement. "This project is our most important breakthrough in recent years. It will be published in *Science Translational Medicine* soon."

Lin's lab has established two independent intellectual property platforms, STAR-T and TCR-T. Besides praising his team's concerted effort, Lin also attributes his ac-

hievements to China's close integration of basic research and clinical application. "There are many clinical samples and questions in China, which increases research and clinical integration opportunities. It also opens up and boosts translational research. This is the country's unique advantage," he says.

Diligently focusing on tumor research and treatment innovation ■

To Lin, cancer research has become a career that he strives for with his life. He is happy that he chose to return to China and believes that doing research at Tsinghua University is on par with the MD Anderson Cancer Center in the US, if not better.

"The students at Tsinghua University are excellent. The ones who joined my lab not only have a wealth of knowledge, but they also have a passion for research," says Lin. "My experience has exceeded my expectations!" So far, his lab has published more than 100 research papers, including one in *Nature Medicine* in 2017 that illustrated the molecular mechanism of JNK1 negatively regulating antifungal immune responses. In 2018, his paper in *Immunity* revealed a novel mechanism of how intestinal fungi play a role in colon tumors' pathogenesis by regulating myeloid suppressor cells. In *Nature Communications*, his 2019 paper demonstrated that the K63 ubiquitination modification of RIPK1 could regulate cell death during inflammation by regulating the RIPK1 kinase activity. Now, his latest study on STAR-T cell therapy for treating tumors will be published in *Science Translational Medicine*.

Returning to China, Lin witnessed the rapid development of life sciences and basic medical sciences. Being a part of the science community, he is incredibly grateful for the country's strategy in providing strong support for precision medicine and the increase in research funding, investment and talent recruitment in the Beijing area. "Beijing has a large number of universities and research institutes. The active recruitment of talents in recent years, brought many scientists who were abroad back here. These scientists not only brought back the latest technologies and shepherded future research directions, but also drove the international collaborations through their connections worldwide," he says. "Thanks to the support of the funding and platforms, many high-tech applications have been applied to cancer research, such as single-cell sequencing, genomics, and big data research. It's all possible now. I believe, with the support, cancer research will become translational soon."

Looking at the next 10 years, Lin hopes to see breakthroughs in China's biopharmaceutical industry. "With stable investment and the active recruitment of talents, I believe that China will develop tumor immunotherapy drugs or targeted cancer therapy on its own within 10 years," he says.

The exploration of science will always be about taking the initiative and action to move towards your goal. Lin will continue to embrace challenges, investigate cancer for innovative treatments, and promote bed-to-bedside translation to bring hope to patients.

ON ONE WINDING PATH COME WHAT MAY

Yonghui Zhang

A chemist by training, Yonghui Zhang took a leap of faith and entered the unfamiliar world of tumor immunotherapy without much support. However, his love for science and perseverance for research guided him through the unconventional path. Chemistry provided him with unique perspectives on cancer research, leading him to tackle immunology from a distinctive angle—lipid metabolism. His findings demonstrated how lipid metabolism is crucial to immune cells, which may one day help boost immune responses to vaccines and act as a target for tumor immunotherapy.

In 2013, Yonghui Zhang returned to Beijing from the United States and joined the School of Pharmacy at Tsinghua University as an assistant professor. Having initially trained as a chemist, the last 7 years have taken him on a sometimes bewildering journey deep into the heart of a notoriously complex biological field: tumor immunity. This transition has been so wide ranging in scope that some of his colleagues still express frank shock that he has pulled it off; he is now publishing elite immunology papers and collaborating on clinical efforts to deploy immune-cell-based onco-therapies.

"What you have to understand is that my deep and abiding interest in isoprenoids has brought me where I am. My current research program—while now full of complex immunology experiments with various experimental models and clinical samples—is still focused dead-square on isoprenoid metabolism and on the mevalonate pathway in particular."

Upon returning to China and starting his lab at Tsinghua, he repeatedly heard colleagues express surprise about his seemingly narrow focus on a very well-studied pathway. There has been more than a half-century of groundbreaking and Nobel-prize-winning science about the mevalonate pathway (three prizes), and some folks were initially skeptical about whether he was wasting his time (and his new lab's resources) on well-trod ground. Zhang recalls, "it was difficult and challenging back then." At the time, he had never worked on protein expression and didn't understand the details, assumptions, and conventions for using various mouse models for immunology research.



Out of the wilderness ■

Happily, his "all-in" bet on that the mevalonate pathway affects tumor immunity was right. Zhang credits his stubborn perseverance for keeping him going during those early days of immunometabolism research. Five years on, he reaped some initial success with a paper in one of the top academic journals, *Cell*, which also published a Leading Edge Preview article that ventured his study might have "a potentially huge impact" for advancing both anti-infection and anti-tumor immune defenses.

The *Cell* paper from Zhang's team in 2018 demonstrated proof-of-principle for targeting the mevalonate pathway for drug development, including for new vaccine adjuvants and for improving tumor vaccine activity. Ultimately, the enabling insights for the discovery in the *Cell* paper stemmed from a clinical observation: patients with a rare immune disease developed pyrexia and fever due to a disorder in metabolizing lipids (isoprenoid synthesis pathway dysfunction). Moreover, clinicians had reported the puzzling fact that these patients generated aberrantly high antibody titers when they received vaccinations. This elevated immune response was foundational evidence lending support to Zhang's theory that "some lipid metabolism pathways can regulate immunity". This was the scientific and medical context underlying the launch of Zhang's lab at the Tsinghua School of Pharmacy, and the basic insights uncovered in the *Cell* study have helped explain how deficiency for particular lipids can directly disrupt antigen presentation in dendritic cells. This has implications well beyond a single immune disease, clearly extending to current (and emerging) onco-immunology

treatment concepts: antigen presentation is central to all of adaptive immunity.

Holding up the spirit of science ■

Taking paths that may seem unpromising is essential for innovative discoveries and breakthroughs in research. Zhang defines himself as "a scientist studying tumor immunity through the lens of chemistry". His work has emphasized the power of using chemistry to deeply probe the molecular mechanisms through which the immune system targets antigens from pathogens and from tumor cells. In particular, Zhang has used his chemistry background—he trained at the elite Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences before going to work in the US—and continually invested the time needed to develop sets of inhibitor analogs to provide multi-layered insights about how lipid metabolism affects immune responses.

Further, rather than using a single chemical agent to shut down some metabolic process, Zhang's team tries to target multiple distinct steps in metabolic pathways, and this has enabled comparisons yielding insights not evident when using a single inhibitor alone. "I get the feeling that some of my research colleagues still think it's bizarre that I spend so much time running additional sets of experiments with apparently overlapping metabolic modulations (i.e., use of bisphosphonates and statins when both types of drug would ultimately block the mevalonate pathway)."

Another big success occurred in 2019 when Zhang's team revealed the antigen-recognition mechanism of $\gamma\delta$ T cells in a study pub-

lished in the journal *Immunity*. Beyond focusing attention on the unique functions of $\gamma\delta$ T cells and using structural data to clarify a longstanding debate about "inside-out" or direct activation of $\gamma\delta$ T cells, the *Immunity* study provided theoretical support for making use of immune cells in allogeneic cell therapy.

Zhang's $\gamma\delta$ T cell work also highlights the fast-moving nature of cancer research in Beijing. Intra-Beijing collaborations between the basic researchers like Zhang and his team with medical scientists doing clinical research are really speeding up the translation of biological discoveries into medicine. "An allogeneic $\gamma\delta$ T cell treatment for solid tumors has already entered the pre-clinical research stage, and we are also working with three hospitals to carry out clinical research on both blood cancer and solid tumor treatments," says Zhang.

Teaching and mentoring ■

Zhang's persevering attitude has been shaped by his professors and research mentors. "My mentor, Eric Oldfield from the University of Illinois at Urbana-Champaign, is the most research-focused scientist in my mind. I remember my realization that this man has clearly devoted his whole being to science." Fortunately, the Zhang lab has received strong support from the Tsinghua University School of Pharmacy. In particular, Professor Xuebin Liao was a key factor in recruiting Zhang back to China to join Tsinghua University's effort in pharmaceutical research and has remained a stalwart colleague through ups and downs. With his lab now well-established at Tsinghua, Zhang is grateful for its full support. "Looking back, I'm fortunate that I chose to return to China."

The leading edge of scientific research is a very high-pressure environment, and immunotherapy is undoubtedly one of the hottest and fastest-moving research topics in cancer research. Zhang entered this increasingly crowded area because his scientific inquiries brought him there: he clearly thinks that the body's immune system holds the answers to his most personally compelling scientific questions. His advice to young researchers would be focus on asking compelling research questions with a big upside and to worry much less about defined fields or chasing hot topics. "If you are asking interesting questions, you can recruit top talent."

Zhang's team is a combination of talented scientists from biochemistry, drug design, structural biology, immunology, and other disciplines and he says these young researchers are his "right-hand man" in the lab. He remains especially grateful for the early members of the lab who had some faith in the big vision of his mevalonate-pathway-focused research program. Zhang praised his students as "hardworking" and "reliable". Amid the 2020 pandemic, they have overcome many difficulties and continue to pursue their research, and he tries to encourage his students and keep them moving towards their goals. "You must have enough passion for science and remember why

you stepped into this field. Even if you're not studying the seemingly hottest topic, you persist and devote yourself to it whole-heartedly. Don't overthink what others tell you. We must stick to the path that we believe in, even if it's non-mainstream, even if it seems unpromising," says Zhang.

A very bright future for finding cures in Beijing ■

Zhang strongly endorses Beijing as a hotspot for life science and biomedical research. "I spent many years abroad and had some achievements, but I always felt a sense of restraint back then. The research context in Beijing right now is very special; there are now opportunities that were simply not available to me or my colleagues in the USA. Provided that you have an original scientific idea to pursue, I would argue that the support available in Beijing might be peerless. There is a huge amount of creative research going on here, and the publication achievements are increasingly reflecting this."

He also praises Beijing for its investment in basic research and its major role in pushing cancer research progress. "I am especially grateful to the Beijing Municipal Science and Technology Commission for supporting the $\gamma\delta$ T cell project during the most difficult time of my research," says Zhang. The commission both provided research funding and also connected Zhang's team to Tiantan Hospital and 301 Hospital for clinical collaboration, which has dramatically accelerated the translation of basic research findings.

Zhang has also noticed multiplier effects and increasing broad opportunities as more and top teams do innovative basic and clinical cancer research in China generally and in Beijing in particular. "In the next 5 to 10 years, we can expect China's very rapid development in immunotherapy, especially with breakthroughs for new target drug development." Regarding the future of his own lab, Zhang said, "We have made a name for ourselves in the field, but this is just the beginning. There is still so much knowledge for us to uncover."

FOLLOW YOUR HEART STRIVE TOWARDS EXCELLENCY *Meng Chen*

As a cancer patient's family, Meng Chen witnessed the poise and professionalism of oncologists when she was a teenager. The experience kindled her curiosity for cancer research, a field she has been studying for 20 years now—with the help of big data. Chen is leading big data research at the Chinese Academy of Medical Science to build a national cancer clinical database for data analysis and sharing. Her work can better inform policy decisions, healthcare management, and pharmaceutical research in the future.



When Meng Chen was in junior high school, a family member was diagnosed with esophageal cancer and, fortunately, defeated the cancer after surgery and chemotherapy. The professionalism and dedication of the doctors that she witnessed had a deep impression on her. It also introduced cancer-related questions into her life.

"Why do people get cancer?"

"What is the pathological result, how should we treat it, and with what medicine?"

"How about the five-year survival rate..."

Meng kept thinking about these questions, which set her on the path of cancer research. Her curiosity about the pathogenesis of cancer and the determination to defeat cancer for the sake of the patient became the driving force in her future work. "I have deeply experienced how painful and far-reaching the impact of cancer can be on patients and their families. I hope that through my efforts, I can find practical methods for prevention, diagnosis, and treatment," she says, following her heart and striving towards excellence.

After more than 20 years of study and research, in which Meng engaged in cutting-edge big data cancer research at top cancer hospitals across China and the United States, she is approaching her goals, step by step.

Challenging emerging fields and establishing a national cancer database ■

Big data cancer research is an emerging field, which collects, transforms, and leverages data from cancer hospitals to reveal patterns or build models for assisting clinical decision-making. The method can improve the accuracy of malignant tumor diagnosis, standardize the diagnosis and treatment process, strengthen patient management, promote precision medicine development, and optimize cancer prevention and control. It also provides a digital infrastructure for clinical medicine research and national public health management.

As the deputy director of the National Cancer Data Center of the National Cancer Center/Cancer Hospital of the Chinese Academy of Medical Sciences and Peking Union Medical College, Meng focuses on organizing and promoting the "National Cancer Data Center and Cancer Big Data Platform", a major project from the National Development and Reform Commission and the National Health Commission, also called "One Data-

base, One Network". This project aims to build a nationwide remote collaboration network that aggregates clinical data from the National Cancer Center, 30 provincial cancer hospitals, 128 cancer-specialized hospitals, and more than 1,000 cancer clinics from general hospitals. The goal is to create high-value oncology data resources for accessibility and interoperability in China.

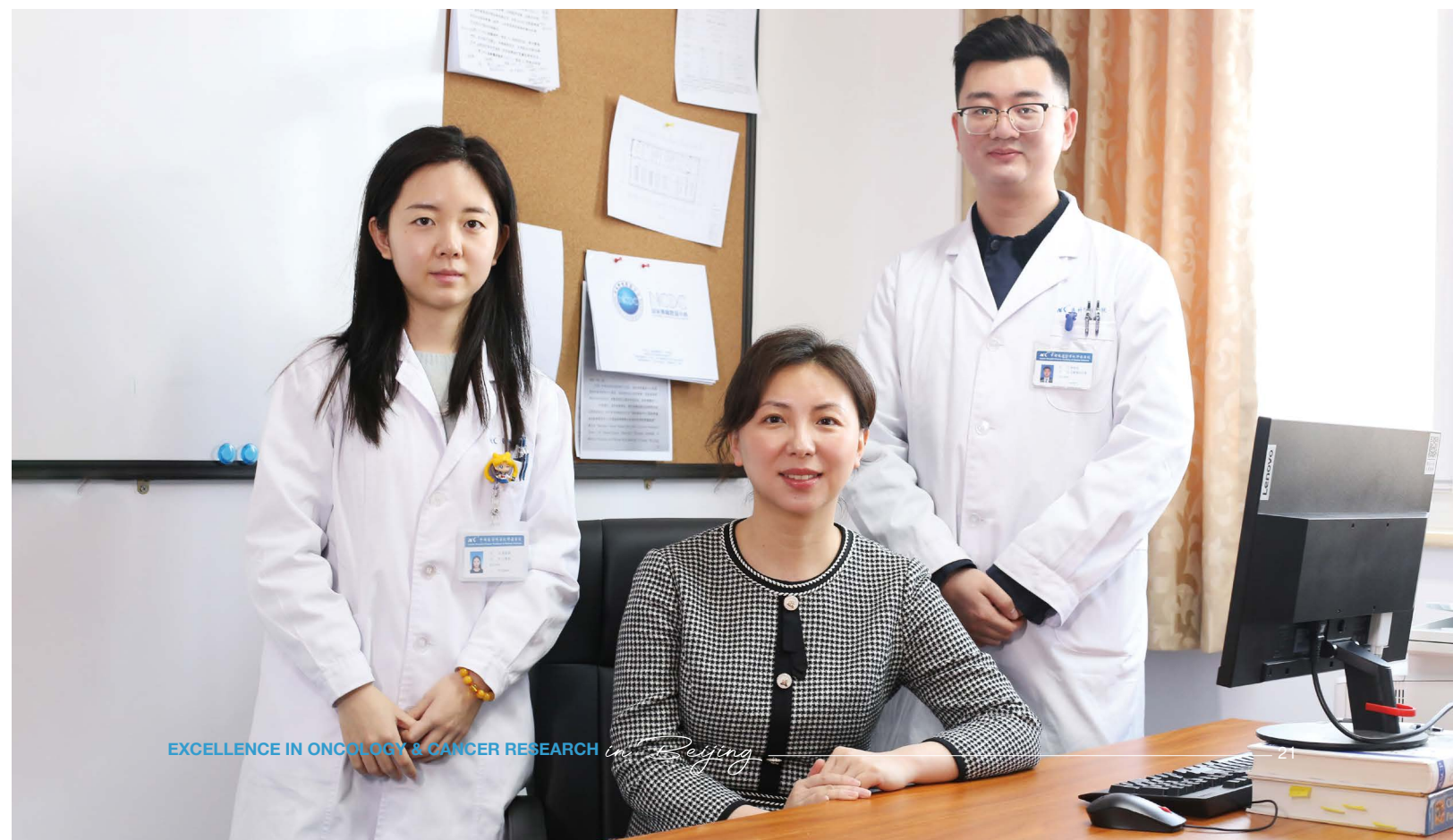
"I have been doing cancer epidemiological research since 2006. It has been always difficult to obtain data, and the data collected was often either incomplete or poor quality. These are the most common obstacles encountered in data science," says Meng. Since then, she realized that it's essential to have a high-quality database for clinical research. "The accumulation of a large amount of data does not equal big data. The development and utilization of big data relies on having

a high-quality database, which is manifested in its standardization, real-time operation, traceability, and the ability to update continuously. These are the qualities required to reflect the current clinical practice and ensure the reproducibility of biomedical research." Meng takes the ASCO Cancer Learning Intelligence Network for Quality (CancerLinQ) as an example to illustrate the importance and feasibility of real-time support for clinical decision-making. "We have recently conducted in-depth discussions with many well-known companies on how to accomplish real-time operation with big data. Moving data processing ahead to the hospital side where the data were produced could be a potential alternative to achieve T+1 and T+0 goals."

Steering research direction to break through research barriers ■

Before joining the Cancer Hospital

of the Chinese Academy of Medical Sciences, Meng studied and worked at the University of Texas MD Anderson Cancer Center in the United States for 10 years. As a cancer molecular epidemiologist, she focused on identifying and validating biomarkers for bladder cancer and kidney cancer. Her research won her several international awards including four scholar-in-training awards from American Association for Cancer Research (AACR) from 2008 to 2011. In 2012, Meng became the youngest faculty at the Department of Epidemiology of MD Anderson Cancer Center. She also won a CPRIT Innovation Fellowship by the Cancer Prevention and Research Institute of Texas (CPRIT) and a special fellowship for junior faculty from the Duncan Family Institute for Cancer Prevention. Meng wasn't satisfied with these achievements. Although she worked at the top-ranked cancer center in the United States, Meng



often stumbled in research because she "couldn't get the data to do the research I wanted to". Intending to conduct translational research, she joined the Department of Laboratory Medicine at MD Anderson and received the COMACC-certified clinical chemistry training for lab director. Meng went through residency rotations at six world-famous hospitals (Methodist Hospital, Texas Children's Hospital, St. Luke, Ben Taub, VA Hospital, and MD Anderson Cancer Center) in Texas Medical Center in Houston. During her training, Meng got to know hospital information systems, such as HIS and LIS, and participated in clinical trials. "I was responsible for the data collection and analysis for high-sensitivity troponin T to detect myocardial toxicity caused by chemotherapy. The method was later approved by the FDA and currently is the gold standard for myocardial infarction diagnosis, which can quickly save patients' lives. I thought that was really meaningful," she says. After her training ended in 2015, Meng worked as a clinical assistant professor in the Department of Biomedical Science at University of New Hampshire for three years. During that time, she trained numerous students and health professionals for partnering hospitals such as Dartmouth-Hitchcock Medical Center and Massachusetts General Hospital while honing her skills to organize, coordinate, and integrate projects across institutions.

"Over my years abroad, what supported me is the curiosity about the unknown and pursuing my research. But I've always been homesick, and the sentiment grew stronger with time," says Meng. "From being a student to an assistant professor, 16 years of experience abroad has given me a clear understanding of the prospects of my professional development." She noted that China's medical research had been rapidly growing in the past years. "My family is in China. If I can find an ideal job there, why wouldn't I go home?" The Cancer Hospital of the Chinese Academy of Medical Sciences is undoubtedly her first choice. "It is the number one cancer hospital in China and has gained international recognition for cancer diagnosis, treatment, and research. It is also a sister institute with MD Anderson Cancer Center, a professional counterpart. I hope to become a bridge between the Cancer Hospital and MD Anderson for international collaborations."

Cultivating standards informed oncology data ecosystem ■

"Big data in cancer belongs to the field of medical information, but it also requires multidisciplinary knowledge. My background in epidemiology and clinical experiences gave me an advantage," says Meng. In 2019, Meng joined the Cancer Hospital of the Chinese Academy of Medical Sciences.

The Cancer Hospital of the Chinese Academy of Medical Sciences has been gathering experience and meticulously planning for many years to welcome the arrival of big data. From China's first cancer registration site initiated in 1959 to the establishment of the National Cancer Center under Cancer Hospital of the Chinese Academy of Medical Sciences, the center has been responsible for the whole nation's cancer registry. Recently, the "National Cancer Data Center" officially launched. The Cancer Hospital of the Chinese Academy of Medical Sciences spent 15 years building a solid infrastructure in the field of clinical big data on cancer. "I see the hope of solving the two problems that have troubled the data science field—the difficulties in obtaining data and the barriers to applying it clinically. In China, there is a cancer collaboration network and government policy support, which bring all sectors of cancer community together. The findings can have an impact on the nation through macro-management, policy formulation, resource allocation, performance evaluation, and more."



Looking back on the past two years of experience, Meng appreciates this better opportunity after returning to China. "Our department was just approved as the National Cancer Data Center, which is a milestone of the National Cancer Center in the leveraging of big data in medicine. I can foresee its bright future prosperously."

Looking at the next 10 years, "big data in medicine is no longer optional, but instead is an important pillar of the whole industry. It may be a gradual process, and we're still in the early stage where different entities are investing efforts in planning strategies and redistributing data assets. Once the foundation is set, the medical industry may experience a lot of new growth," says Meng.

"Learning from other countries' experience of big data research and development, there are a variety of cancer-related data and databases from institutions at all levels now. However, a national standard for cancer data that keeps pace with the times and has clinicians' support is needed urgently.

"Collaborations among the government, industries, and academia can drive the national standards for clinical data on cancer, which will in turn impact the fields of national public health management, clinical practice, and pharmaceutical research profoundly. The high-quality standards will improve China's cancer care in clinical settings, translate cancer research to clinical applications, and provide better support and service in public policies," says Meng.

With such a grand vision, more challenges are coming Meng's way. "The technology for big data application based on artificial intelligence is yet to be developed. The balance of development and data security, ethics, and regulations are all vital elements to consider for building a healthy ecosystem for cancer big data applications," she says.

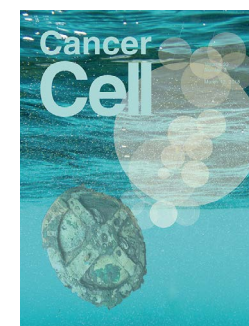
"I have received a lot of support, thanks to the national policies, the Cancer Hospital of the Chinese Academy of Medical Sciences, and the talent recruitment projects in Beijing, such as the Phoenix Project, and funding supports," says Meng.

The yearning to cure cancer and the pursuit of research drove Meng forward. Today, she has grown into a crucial asset to the National Cancer Data Center. Whether it's fate or serendipity, Meng carries the momentum, exploring knowledge and striving towards excellence.

PAPERS

THE DISCOVERIES THAT ADVANCE SCIENCE

The exceptional discoveries in oncology and cancer research made by scientists and clinicians in Beijing are captured by a suite of Cell Press journals, among which we highlight several representatives showcasing the diverse topics and broad scope of these achievements.



TUMOR-REPOPULATING CELLS INDUCE PD-1 EXPRESSION IN CD8+ T CELLS BY TRANSFERRING KYNURENINE AND AHR ACTIVATION

CANCER CELL

VOLUME 33, ISSUE 3, P480-494.E7, MARCH 12, 2018

Abstract: Despite the clinical successes fostered by immune checkpoint inhibitors, mechanisms underlying PD-1 upregulation in tumor-infiltrating T cells remain an enigma. Here, we show that tumor-repopulating cells (TRCs) drive PD-1 upregulation in CD8+ T cells through a transcellular kynurenine (Kyn)-aryl hydrocarbon receptor (AhR) pathway. Interferon- γ produced by CD8+ T cells stimulates release of high levels of Kyn produced by TRCs, which is transferred into adjacent CD8+ T cells via the transporters SLC7A8 and PAT4. Kyn induces and activates AhR and thereby upregulates PD-1 expression. This Kyn-AhR pathway is confirmed in both tumor-bearing mice and cancer patients and its blockade enhances antitumor adoptive T cell therapy efficacy. Thus, we uncovered a mechanism of PD-1 upregulation with potential tumor immunotherapeutic applications.



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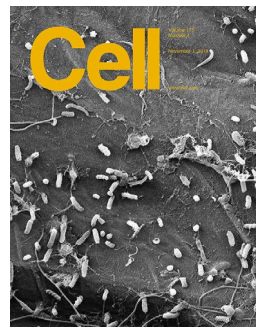
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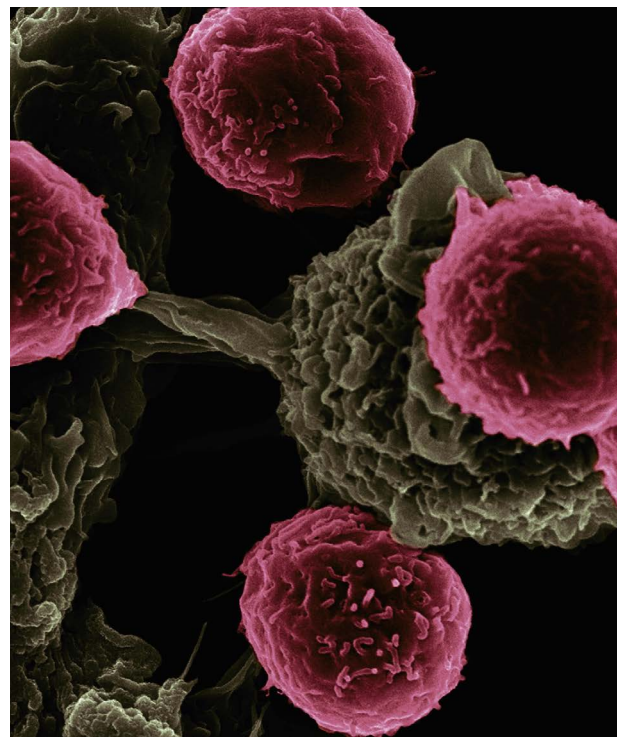


THE MEVALONATE PATHWAY IS A DRUGGABLE TARGET FOR VACCINE ADJUVANT DISCOVERY

CELL

VOLUME 175, ISSUE 4, P1059-1073.E21, NOVEMBER 01, 2018

Abstract: Motivated by the clinical observation that interruption of the mevalonate pathway stimulates immune responses, we hypothesized that this pathway may function as a druggable target for vaccine adjuvant discovery. We found that lipophilic statin drugs and rationally designed bisphosphonates that target three distinct enzymes in the mevalonate pathway have potent adjuvant activities in mice and cynomolgus monkeys. These inhibitors function independently of conventional "danger sensing". Instead, they inhibit the geranylgeranylation of small GTPases, including Rab5 in antigen-presenting cells, resulting in arrested endosomal maturation, prolonged antigen retention, enhanced antigen presentation, and T cell activation. Additionally, inhibiting the mevalonate pathway enhances antigen-specific anti-tumor immunity, inducing both Th1 and cytolytic T cell responses. As demonstrated in multiple mouse cancer models, the mevalonate pathway inhibitors are robust for cancer vaccinations and synergize with anti-PD-1 antibodies. Our research thus defines the mevalonate pathway as a druggable target for vaccine adjuvants and cancer immunotherapies.



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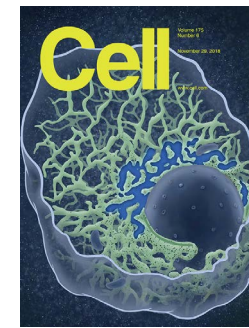
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MUTATIONAL LANDSCAPE OF SECONDARY GLIOBLASTOMA GUIDES MET-TARGETED TRIAL IN BRAIN TUMOR

CELL

VOLUME 175, ISSUE 6, P1665-1678.E18, NOVEMBER 29, 2018

Abstract: Low-grade gliomas almost invariably progress into secondary glioblastoma (sGBM) with limited therapeutic option and poorly understood mechanism. By studying the mutational landscape of 188 sGBMs, we find significant enrichment of TP53 mutations, somatic hypermutation, MET-exon-14-skipping (METex14), PTPRZ1-MET (ZM) fusions, and MET amplification. Strikingly, METex14 frequently co-occurs with ZM fusion and is present in ~14% of cases with significantly worse prognosis. Subsequent studies show that METex14 promotes glioma progression by prolonging MET activity. Furthermore, we describe a MET kinase inhibitor, PLB-1001, that demonstrates remarkable potency in selectively inhibiting MET-altered tumor cells in preclinical models. Importantly, this compound also shows blood-brain barrier permeability and is subsequently applied in a phase I clinical trial that enrolls MET-altered chemo-resistant glioma patients. Encouragingly, PLB-1001 achieves partial response in at least two advanced sGBM patients with rarely significant side effects, underscoring the clinical potential for precisely treating gliomas using this therapy.



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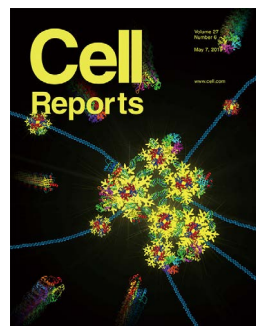
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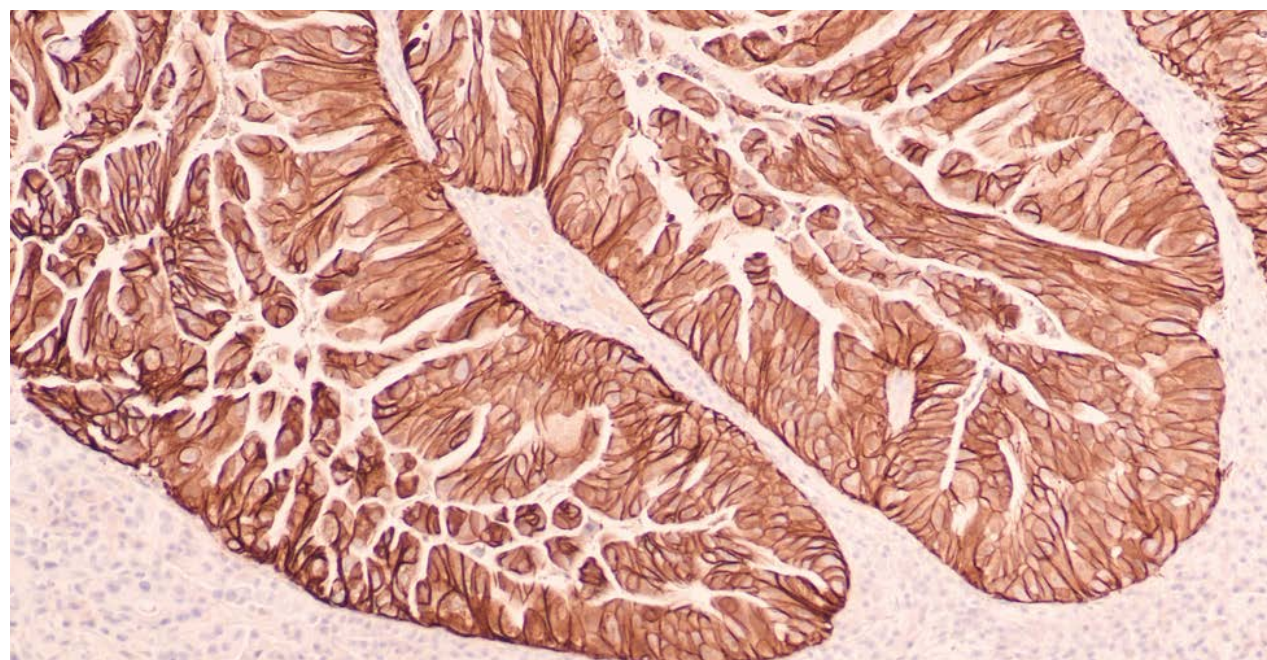


DISSECTING THE SINGLE-CELL TRANSCRIPTOME NETWORK UNDERLYING GASTRIC PREMALIGNANT LESIONS AND EARLY GASTRIC CANCER

CELL REPORTS

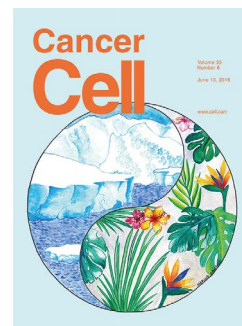
VOLUME 27, ISSUE 6, P1934-1947.E5, MAY 07, 2019

Abstract: Intestinal-type gastric cancer is preceded by premalignant lesions, including chronic atrophic gastritis and intestinal metaplasia. In this study, we constructed a single-cell atlas for 32,332 high-quality cells from gastric antral mucosa biopsies of patients spanning a cascade of gastric premalignant lesions and early gastric cancer (EGC) using single-cell RNA sequencing. We then constructed a single-cell network underlying cellular and molecular characteristics of gastric epithelial cells across different lesions. We found that gland mucous cells tended to acquire an intestinal-like stem cell phenotype during metaplasia, and we identified OR51E1 as a marker for unique endocrine cells in the early-malignant lesion. We also found that HES6 might mark the pre-goblet cell cluster, potentially aiding identification of metaplasia at the early stage. Finally, we identified a panel of EGC-specific signatures, with clinical implications for the precise diagnosis of EGC. Our study offers unparalleled insights into the human gastric cell atlas in premalignant and early-malignant lesions.



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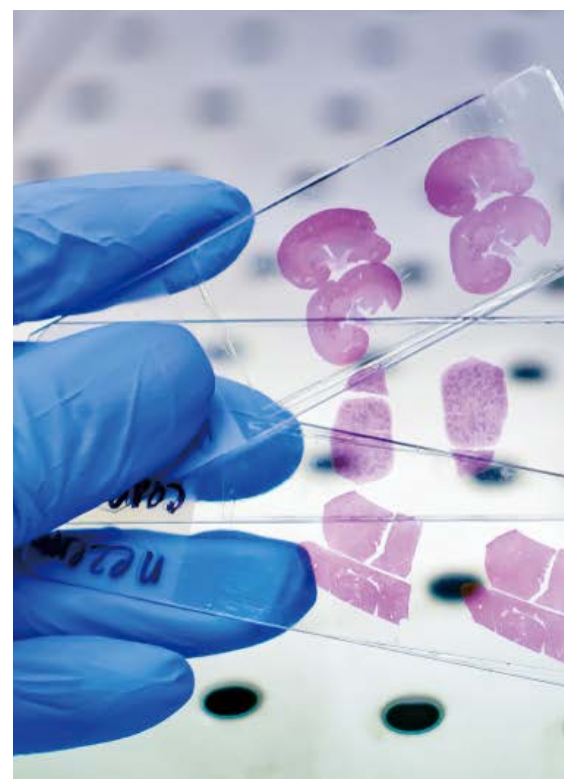


GENOMIC AND TRANSCRIPTOMIC PROFILING OF COMBINED HEPATOCELLULAR AND INTRAHEPATIC CHOLANGIOCARCINOMA REVEALS DISTINCT MOLECULAR SUBTYPES

CANCER CELL

VOLUME 35, ISSUE 6, P932-947.E8, JUNE 10, 2019

Abstract: We performed genomic and transcriptomic sequencing of 133 combined hepatocellular and intrahepatic cholangiocarcinoma (cHCC-ICC) cases, including separate, combined, and mixed subtypes. Integrative comparison of cHCC-ICC with hepatocellular carcinoma and intrahepatic cholangiocarcinoma revealed that combined and mixed type cHCC-ICCs are distinct subtypes with different clinical and molecular features. Integrating laser microdissection, cancer cell fraction analysis, and single nucleus sequencing, we revealed both mono- and multiclonal origins in the separate type cHCC-ICCs, whereas combined and mixed type cHCC-ICCs were all monoclonal origin. Notably, cHCC-ICCs showed significantly higher expression of Nestin, suggesting Nestin may serve as a biomarker for diagnosing cHCC-ICC. Our results provide important biological and clinical insights into cHCC-ICC.



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SECRETED PYRUVATE KINASE M2 PROMOTES LUNG CANCER METASTASIS THROUGH ACTIVATING THE INTEGRIN BETA1/FAK SIGNALING PATHWAY

CELL REPORTS

VOLUME 30, ISSUE 6, P1780-1797.E6, FEBRUARY 11, 2020

Abstract: Cancer cell-derived secretomes have been documented to play critical roles in cancer progression. Intriguingly, alternative extracellular roles of intracellular proteins are involved in various steps of tumor progression, which can offer strategies to fight cancer. Herein, we identify lung cancer progression-associated secretome signatures using mass spectrometry analysis. Among them, PKM2 is verified to be highly expressed and secreted in lung cancer cells and clinical samples. Functional analyses demonstrates that secreted PKM2 facilitates tumor metastasis. Furthermore, mass spectrometry analysis and functional validation identify integrin β 1 as a receptor of secreted PKM2. Mechanistically, secreted PKM2 directly bound to integrin β 1 and subsequently activated the FAK/SRC/ERK axis to promote tumor metastasis. Collectively, our findings suggest that PKM2 is a potential serum biomarker for diagnosing lung cancer and that targeting the secreted PKM2-integrin β 1 axis can inhibit lung cancer development, which provides evidence of a potential therapeutic strategy in lung cancer.



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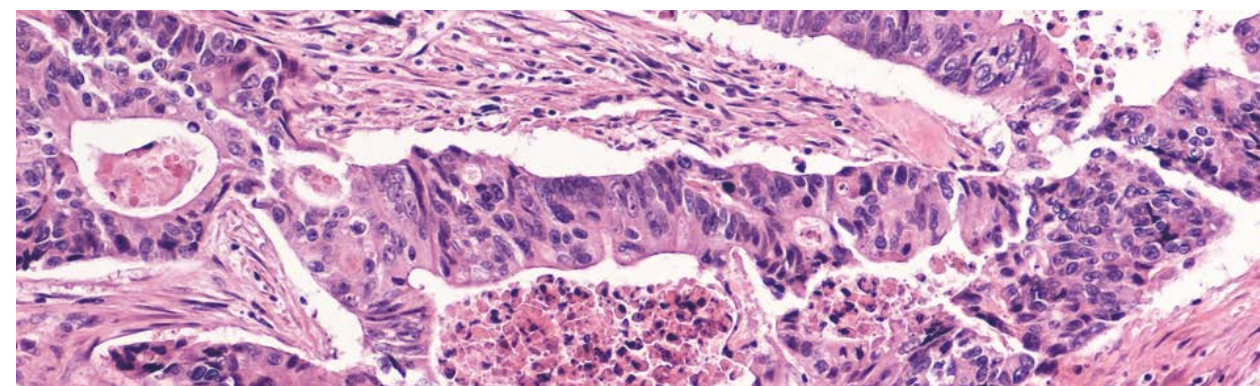


SINGLE-CELL ANALYSES INFORM MECHANISMS OF MYELOID-TARGETED THERAPIES IN COLON CANCER

CELL

VOLUME 181, ISSUE 2, P442-459.E29, APRIL 16, 2020

Abstract: Single-cell RNA sequencing (scRNA-seq) is a powerful tool for defining cellular diversity in tumors, but its application toward dissecting mechanisms underlying immune-modulating therapies is scarce. We performed scRNA-seq analyses on immune and stromal populations from colorectal cancer patients, identifying specific macrophage and conventional dendritic cell (cDC) subsets as key mediators of cellular cross-talk in the tumor microenvironment. Defining comparable myeloid populations in mouse tumors enabled characterization of their response to myeloid-targeted immunotherapy. Treatment with anti-CSF1R preferentially depleted macrophages with an inflammatory signature but spared macrophage populations that in mouse and human expresses pro-angiogenic/tumorigenic genes. Treatment with a CD40 agonist antibody preferentially activated a cDC population and increased Bhlhe40 + Th1-like cells and CD8 + memory T cells. Our comprehensive analysis of key myeloid subsets in human and mouse identifies critical cellular interactions regulating tumor immunity and defines mechanisms underlying myeloid-targeted immunotherapies currently undergoing clinical testing.



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INTEGRATIVE PROTEOMIC CHARACTERIZATION OF HUMAN LUNG ADENOCARCINOMA

CELL

VOLUME 182, ISSUE 1, P245-261.E17, JULY 09, 2020

Abstract: Genomic studies of lung adenocarcinoma (LUAD) have advanced our understanding of the disease's biology and accelerated targeted therapy. However, the proteomic characteristics of LUAD remain poorly understood. We carried out a comprehensive proteomics analysis of 103 cases of LUAD in Chinese patients. Integrative analysis of proteome, phosphoproteome, transcriptome, and whole-exome sequencing data revealed cancer-associated characteristics, such as tumor-associated protein variants, distinct proteomics features, and clinical outcomes in patients at an early stage or with EGFR and TP53 mutations. Proteome-based stratification of LUAD revealed three subtypes (S-I, S-II, and S-III) related to different clinical and molecular features. Further, we nominated potential drug targets and validated the plasma protein level of HSP 90 β as a potential prognostic biomarker for LUAD in an independent cohort. Our integrative proteomics analysis enables a more comprehensive understanding of the molecular landscape of LUAD and offers an opportunity for more precise diagnosis and treatment.



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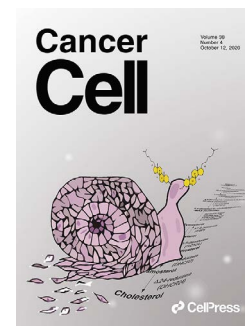
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HEMATOPOIETIC PROGENITOR KINASE1 (HPK1) MEDIATES T CELL DYSFUNCTION AND IS A DRUGGABLE TARGET FOR T CELL-BASED IMMUNOTHERAPIES

CANCER CELL

VOLUME 38, ISSUE 4, P551-566.E11, OCTOBER 12, 2020

Abstract: Ameliorating T cell exhaustion and enhancing effector function are promising strategies for the improvement of immunotherapies. Here, we show that the HPK1-NF κ B-Blimp1 axis mediates T cell dysfunction. High expression of MAP4K1 (which encodes HPK1) correlates with increased T cell exhaustion and with worse patient survival in several cancer types. In MAP4K1 KO mice, tumors grow slower than in wild-type mice and infiltrating T cells are less exhausted and more active and proliferative. We further show that genetic depletion, pharmacological inhibition, or proteolysis targeting chimera (PROTAC)-mediated degradation of HPK1 improves the efficacy of CAR-T cell-based immunotherapies in diverse preclinical mouse models of hematological and solid tumors. These strategies are more effective than genetically depleting PD-1 in CAR-T cells. Thus, we demonstrate that HPK1 is a mediator of T cell dysfunction and an attractive druggable target to improve immune therapy responses.



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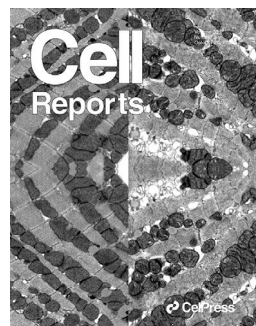
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PPAR α INHIBITION OVERCOMES TUMOR-DERIVED EXOSOMAL LIPID-INDUCED DENDRITIC CELL DYSFUNCTION

CELL REPORTS

VOLUME 33, ISSUE 3, 108278, OCTOBER 20, 2020

Abstract: Dendritic cells (DCs) orchestrate the initiation, programming, and regulation of anti-tumor immune responses. Emerging evidence indicates that the tumor microenvironment (TME) induces immune dysfunctional tumor infiltrating DCs (TIDCs), characterized with both increased intracellular lipid content and mitochondrial respiration. The underlying mechanism, however, remains largely unclear. Here, we report that fatty acid-carrying tumor-derived exosomes (TDEs) induce immune dysfunctional DCs to promote immune evasion. Mechanistically, peroxisome proliferator activated receptor (PPAR) α responds to the fatty acids delivered by TDEs, resulting in excess lipid droplet biogenesis and enhanced fatty acid oxidation (FAO), culminating in a metabolic shift toward mitochondrial oxidative phosphorylation, which drives DC immune dysfunction. Genetic depletion or pharmacologic inhibition of PPAR α effectively attenuates TDE-induced DC-based immune dysfunction and enhances the efficacy of immunotherapy. This work uncovers a role for TDE-mediated immune modulation in DCs and reveals that PPAR α lies at the center of metabolic-immune regulation of DCs, suggesting a potential immunotherapeutic target.



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PERFORMANCE

THE SCIENCE THAT ACCELERATES PROGRESS

Celebrating Beijing's role as a global center of impactful oncology and cancer research. The diagrams below chart the city's scholarly outputs and activities across this critical medical discipline.



BEIJING METROPOLITAN REGION

EXCELLENCE IN ONCOLOGY AND CANCER RESEARCH

ONCOLOGY AND CANCER RESEARCH OUTPUT IN BEIJING

**GREW
277%**

from 873 publications in 2010 to 3,287 in 2019



**100
INSTITUTIONS**

IN BEIJING HAVE PUBLICATIONS WITHIN THE DISCIPLINES OF ONCOLOGY AND CANCER RESEARCH

BETWEEN 2010 AND 2018, THE NSFC AWARDED

**\$155
MILLION**

in grants to cancer research in Beijing



PUBLICATION AND CITATION PERFORMANCE 2010-2019

SCHOLARLY OUTPUT*

22,468

CITATIONS PER PUBLICATION

17.1

AUTHORS (GLOBALLY)

95,364

FIELD-WEIGHTED CITATION IMPACT**

1.05

*Number of publications indexed in Scopus

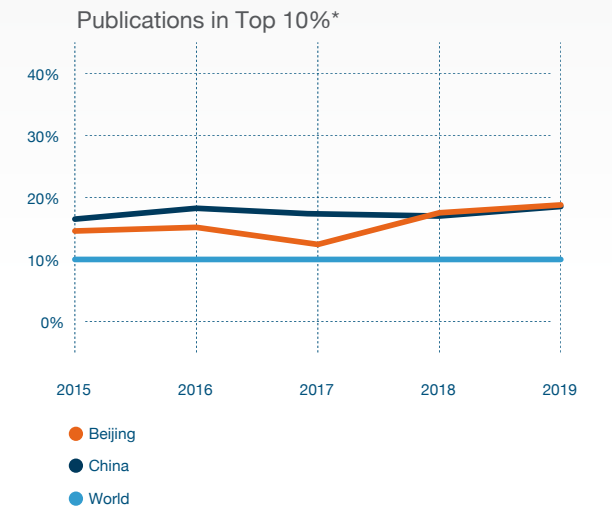
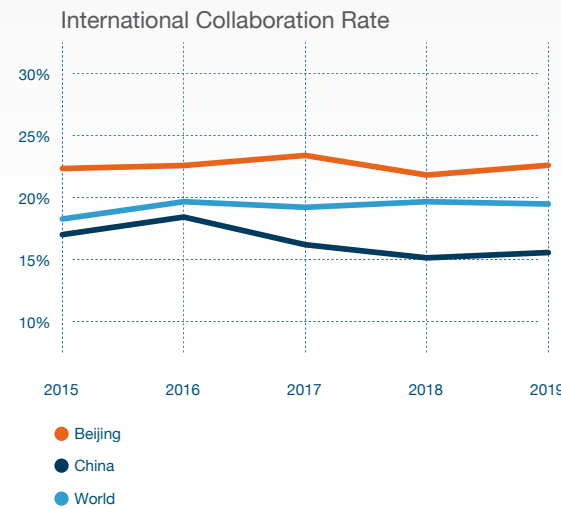
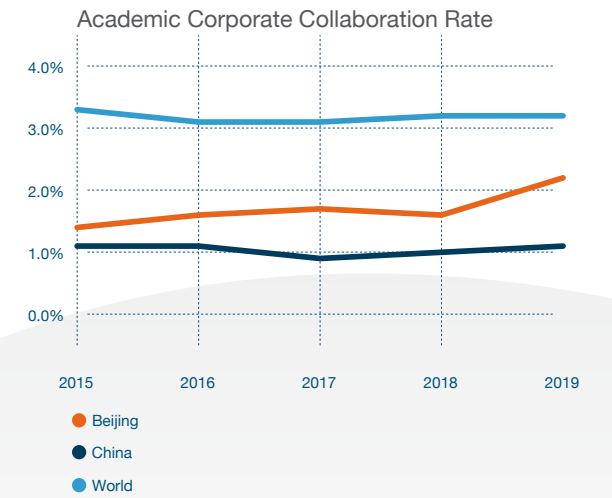
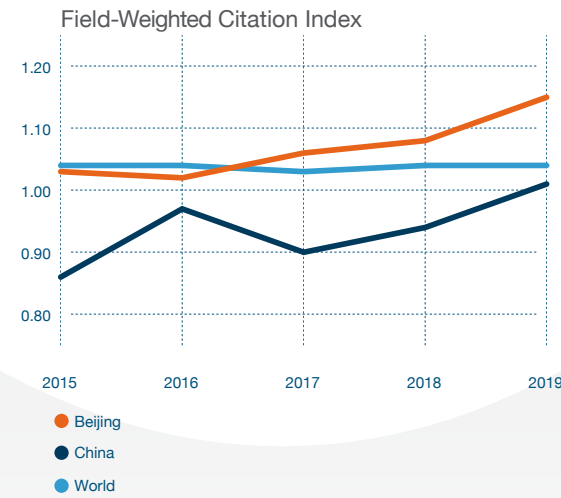
**The ratio of the total citations received by the denominator's output, and the total citations that would be expected based on the average of the subject field

CO-AUTHORED ONCOLOGY AND CANCER PUBLICATIONS WITHIN THE TOP 15 COLLABORATING INSTITUTIONS IN BEIJING 2010-2019



- Chinese Academy of Medical Science
- Peking University
- Capital Medical University
- University of Chinese Academy of Sciences
- Chinese Academy of Sciences
- Ministry of Education, China
- Ministry of Health of People's Republic of China
- General Hospital of People's Liberation Army
- CAS-Institute of Biophysics
- Academy of Military Medical Science China
- Tsinghua University
- CAS-Institute of Automation
- CAS-Institute of Zoology
- Chinese Center for Disease Control and Prevention
- Beijing University of Chinese Medicine

BEIJING'S ONCOLOGY AND CANCER RESEARCH TRENDS



*The extent to which publications are present in the top 10% of the most-viewed publications

INDUSTRY IMPACT: PATENTS AND PATENT CITATIONS 2010-2019



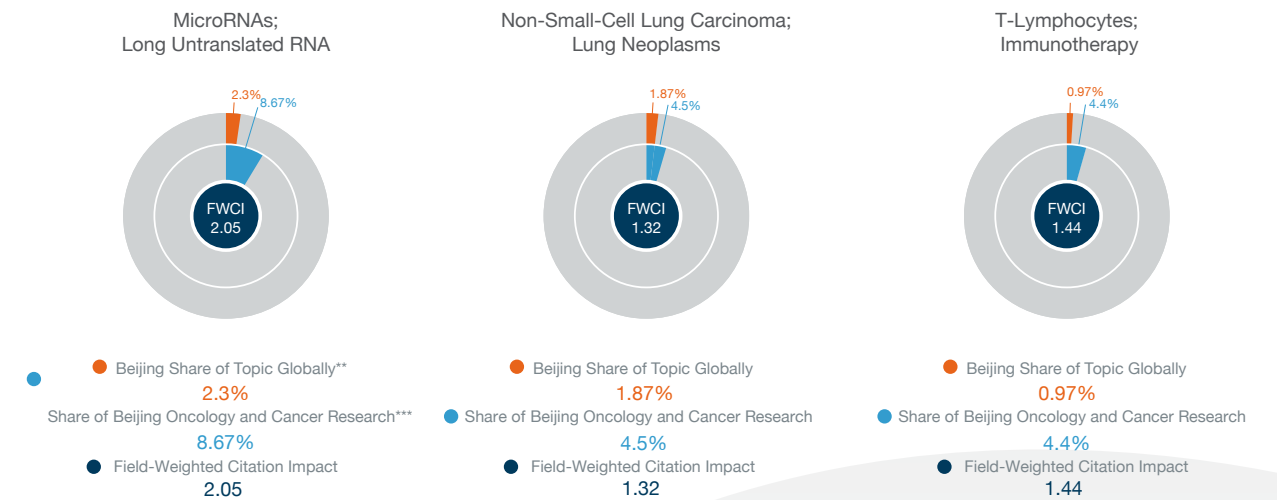
*patft.uspto.gov; All patents with Applicant or Inventor City from Beijing, and Title or Abstract with keywords "cancer" or "oncology" from 2010-2019
 **patentscope.wipo.int; All patents with Applicant Address from Beijing, and Title or Abstract with keywords "cancer" or "oncology" from 2010-2019
 Results from search queries not de-duplicated.

INDUSTRY IMPACT: TOP CORPORATE COLLABORATORS 2010-2019

Institution	Co-Authored Publications
SINOPEC	54
AstraZeneca	33
Novartis	31
Merck	27
GlaxoSmithKline	24
Pfizer	23
Leidos Inc	23
Bayer AG	15

BEIJING'S OUTSIZED CONTRIBUTION TO HIGH PROMINENCE* TOPICS IN ONCOLOGY

Top 3 Largest Topic Clusters in Oncology by Beijing's Output (2010-2019)



*An indicator of momentum among the nearly 96,000 global, unique research topics, based on citation patterns
 **Total Beijing Topic Publications Divided by Total Global Topic Publications
 ***Total Beijing Topic Publications Divided by Total Beijing Oncology and Cancer Publications

NEXT 6 TOPIC CLUSTERS BY OUTPUT 2010-2019

OUTPUT	SHARE OF GLOBAL TOPIC OUTPUT	FWCI****	PROMINENCE
Lymphoma; Diffuse Large B-Cell Lymphoma			
466	0.9%	0.68	89.558%
Hepatocellular Carcinoma; Liver			
457	1.2%	0.79	84.270%
Acute Myeloid Leukemia; Precursor Cell Lymphoblastic Leukemia-Lymphoma			
441	1.0%	0.61	89.625%
Breast Neoplasms; Mammography			
405	0.8%	1.15	88.220%
Stomach Neoplasms; Esophageal Neoplasms; Gastrectomy			
352	1.3%	1.17	72.088%
DNA Methylation; Epigenomics			
328	2.1%	1.13	80.589%

****Field-weighted Citation Impact