Review Article

Precision cancer medicine in China: the Fudan University Shanghai Cancer Center experience

Lei-Jie Dai[1,2], Ding Ma[1,2], Zhi-Ming Shao[1,2]

[1]Department of Breast Surgery, Precision Cancer Medicine Center, Key Laboratory of Breast Cancer in Shanghai, Fudan University Shanghai Cancer Center, Shanghai, China; [2]Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

Contributions: (I) Conception and design: ZM Shao, D Ma; (II) Administrative support: ZM Shao; (III) Provision of study materials or patients: ZM Shao, D Ma; (IV) Collection and assembly of data: LJ Dai, D Ma; (V) Data analysis and interpretation: LJ Dai, D Ma; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Zhi-Ming Shao. Department of Breast Surgery, Precision Cancer Medicine Center, Key Laboratory of Breast Cancer in Shanghai, Fudan University Shanghai Cancer Center, Shanghai, China. Email: zhimingshao@yahoo.com.

Abstract: Cancer has been a major cause of death in China. Among oncologists, the concept of precision cancer medicine has been universally acknowledged. Precision cancer medicine aims to match patients to their optimum therapies. As one of the pioneers in the practice of precision cancer medicine in China, Fudan University Shanghai Cancer Center (FUSSC) has accumulated abundant practical experience that might benefit our peers and patients. Additionally, as the leading cancer center in eastern China and one of the top health providers for cancer patients across the whole county, FUSCC has been trying to generalize precision cancer medicine, continuing its mission to elevate the overall level of cancer treatment in China. Considering the discrepancy between the Chinese population and others, research on precision cancer medicine must focus on our compatriots. The closed-loop system of precision cancer medicine requires inclusive and timely translation of scientific discoveries into clinical applications. Precision cancer medicine is not merely limited to genomics but can include comprehensive management of cancer patients from all aspects. Finally, some perspectives on the future development of precision cancer medicine in FUSCC are proposed. The system of precision cancer medicine in China has not been fully established. The prognoses of Chinese patients are not satisfactory compared with those in developed countries. We hope that our efforts in constructing communication platforms, providing precision cancer medicine tools and launching large-scale clinical trials can promote the development of precision cancer medicine in China and benefit more patients.

Keywords: Precision cancer medicine; genomics; target therapy; clinical trials

Received: 07 July 2021; Accepted: 28 October 2021; Published: 30 December 2021.

doi: 10.21037/pcm-21-26

View this article at: https://dx.doi.org/10.21037/pcm-21-26

Introduction

Cancer is one of the major causes of death worldwide (1). In China, the incidence and mortality of cancer have also been increasing rapidly with the development of the country in recent decades (2). Founded in 1931, Fudan University Shanghai Cancer Center (FUSCC) was the first cancer center in China. Since its establishment, FUSCC has witnessed the development of oncology in China. And currently, FUSCC is one of the leading entities in the field of precision cancer medicine.

Clinicians have been seeking treatments to cure cancer for centuries. However, therapies for cancer may not only benefit patients but also result in concerning side effects. Chemotherapy, which still outperforms all other systematic medications in the management of cancer, is a representative treatment. As a less precise therapy, chemotherapy has demonstrated its efficacy but also produces unfavorable toxicity. Currently, clinicians are pursuing chemotherapy-free management for cancer patients to improve the

therapeutic effect while reducing adverse events. Nevertheless, the lack of a thorough understanding of cancer and disjointedness between research and industry are still restricting this aspiration.

Modern cancer care has entered the era of precision cancer medicine, which has been one of the common views among oncologists. Many specific interpretations of precision cancer medicine exist, but precision cancer medicine is universally acknowledged to consider the optimal medication for patients (3,4). However, the heterogeneity of cancer constantly challenges its diagnosis and treatment. The combination of genetics, environment and lifestyle that induces cancer is unique for each patient (5-8). Among these three aspects, genetics is the most pivotal in tumor biology and the most targetable by clinical treatment. Thus, narrowly speaking, precision cancer medicine focuses on revealing the genetics of cancer and then treating it with targeted drugs (3,4).

Broad application of precision cancer medicine has demonstrated its clinical value in improving survival and reducing untoward effects. Taking breast cancer as an example, ERBB2 (erb-b2 receptor tyrosine kinase 2) is one of the major genes amplified in breast cancer, which indicates an unfavored prognosis (9,10). Before the development of monoclonal antibodies, patients with ERBB2 amplifications could only receive chemotherapy for systemic treatment, and the outcome was rather poor. Currently, with the establishment of a diagnostic system combining immunohistochemistry (IHC) and fluorescence *in situ* hybridization (FISH), these patients can be identified and benefit from targeted therapy such as Herceptin (11,12). With further research, more treatments targeting ERBB2, such as tyrosine kinase inhibitors (TKIs) and antibody-drug conjugates (ADCs), have been developed (13), which can further improve the prognosis of patients. Similar findings have also been reported in other malignancies, thus benefiting more patients (14-16).

As one of the major cancer centers across the country and the leading center in eastern China, FUSCC was one of the first to introduce the idea of precision cancer medicine in China. Since the new century, especially in the last 10 years, precision cancer medicine at FUSCC has entered a new stage, receiving acknowledgment both domestically and internationally. With continuous efforts, FUSCC has established a mature layout of precision cancer medicine covering some major kinds of cancers and has accumulated abundant practical experience that might substantially benefit our peers.

Focusing on the Chinese population

Nationality and race are both important factors in oncology research because they are related to populations' different genetic backgrounds and unique behaviors (17).

For a long time, we have noticed a potential disparity in cancer patients' genetics between China and the Western world, and we have been exerting constant effects in the Chinese population. BRIP1/BACH1 mutation is an important mechanism in disordered BRCA1-mediated DNA double-strand break repair in breast cancer among Western populations (18). In 2009, after analyzing genetic data collected from 357 Chinese breast cancer patients and 864 normal controls, we revealed that germline mutations in BRIP1/BACH1 were so rare in the Chinese population that, unlike in Western populations, BRIP1/BACH1 testing is not recommended (19). Then, we launched a larger program to screen BRCA mutations in 2,991 patients and 1,043 controls by next-generation sequencing (NGS) and ultimately established a comprehensive spectrum of BRCA1/2 mutations in the Chinese population. Based on this spectrum, we further proposed that breast cancer patients in China who are at high and moderate risk are strongly advised to undergo BRCA1/2 mutation testing (20).

Solid work has also been completed in the field of prostate cancer. The difference in the incidence of prostate cancer between Asia and the Western world is massive. In Europe and the US, prostate cancer accounts for nearly one-third of solid tumors in humans (21). In China, although the past two decades have witnessed a surge in its incidence, prostate cancer is still widely considered a low-incidence malignancy (22). This discrepancy indicates the disparity in innate characteristics of prostate cancer between Asian patients and Western patients (23). Based on data collected from the Chinese population, our Department of Urology has established a stromal immunotype suitable for Chinese muscle-invasive bladder cancer patients to predict their prognosis and chemotherapy response (24).

Sequencing techniques represented by NSG are core tools in precision cancer medicine research (25). The large-scale practice of precision cancer medicine relies on a series of sequencing products with high reliability, feasibility and practicability. However, mainstream sequencing tools such as MSK-IMPACT (Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets) are rarely adopted for the Chinese population (26,27). To support precision medicine research and application in Chinese patients, FUSCC and CHGC (Chinese National Human

Genome Center at Shanghai) cooperatively established the Precision Cancer Medicine Center (PCMC) in 2018. Based on the genetics of the Chinese population, the PCMC has developed diverse gene testing panels for prevailing malignancies, which show outstanding technical performance and impressive cost performance and are subject to independent intellectual property rights. Currently, PCMC is one of the leading providers in genetic testing, aiming to boost the translation of research advances and industrialize precision cancer medicine.

The establishment of the PCMC first facilitated our research in breast cancer, which has topped the list of women's cancers in terms of incidence in major cities of China such as Shanghai (27). Breast cancer is highly heterogeneous and can be coarsely divided into several molecular subtypes (28). For a long time, no large-scale domestic genetic profiles were available for research, and we had to rely on foreign datasets. Thus, we categorized 484 genes closely related to precision therapy for breast cancer and established the first large-scale mutation landscape of Chinese breast cancer patients with more than 1,000 paired samples (29). Furthermore, we focused on TNBC (triple-negative breast cancer), which accounts for 15% of all breast cancer cases and has a poor prognosis due to a lack of specific targets, and established the world's largest single-center multiomic cohort of TNBC patients (30).

From bench to bedside

We insist that research in precision cancer medicine should be a closed-loop system starting from patients (clinical problems) and ending with patients (clinical practice). A promising research system of precision cancer medicine should be renewable and constantly accommodate new scientific discoveries.

Based on our multiomic TNBC cohort, we proposed the Fudan Subtyping System to subdivide TNBC into four distinct molecular subtypes: luminal androgen receptor (LAR), immunomodulatory (IM), basal-like immune-suppressed (BLIS), and mesenchymal-like (MES) (30). To verify potential targets identified by data mining in each subtype, we launched a phase Ib/II, open-label, umbrella study named FUTURE to evaluate the efficacy and safety of multiple targeted treatments in patients with refractory metastatic TNBC. The outcomes of the study showed an impressive response of patients to the designated treatment (31).

During the follow-up of the FUTURE trial, we discovered that heavily pretreated patients in the C arm or the IM arm who received anti-PD-1 with nab-paclitaxel showed a significant increase in the ORR (objective response rate) compared with those who received traditional chemotherapy (31). Thus, we further tried to introduce the same medication as a first-line treatment for patients with unresectable locally advanced or metastatic IM TNBC (FUTURE-C-PLUS trial) (32). Additionally, we found that famitinib, a multitarget small-molecule inhibitor, was able to promote the infiltration of $CD8^+$ cells and enhance PD-L1 expression without further increasing adverse events in a preclinical model (unpublished result). Thus, famitinib was also added to the treatment regimen. Recently, the FUTURE-C-PLUS trial reported exciting confirmed ORRs of 81.3% in the intention-to-treat population (n=48) and 84.8% in the per-protocol population (n=46) (32).

We are also investigating our largest original multiomics dataset of TNBC from more diverse perspectives to create a well-rounded system. The tumor microenvironment was reported to exert a profound effect on prognosis and immunotherapy (33). Therefore, we conducted an extensive immunogenomic analysis to explore the heterogeneity and prognostic significance of the microenvironment (34). We also sought to interpret TNBC metabolically. We investigated TNBC from a metabolic-pathway-based view and found that TNBC actually consists of three heterogeneous subtypes with distinct metabolic features (35). Of course, these preclinical results require further clinical verification, which is our current research objective.

Precision cancer medicine beyond genomics

Although genomics plays an essential role in precision cancer medicine, precision cancer medicine can never be restricted to pure genomics (3). Through extensive efforts, FUSCC has established several precise management systems for cancer patients.

Pancreatic cancer is widely considered "the king of carcinoma" due to its poor prognosis (36). Our Department of Pancreas Surgery has made constant efforts to revolutionize the management of pancreatic cancer patients requiring surgical therapy. The contradiction between the staging systems of European Neuroendocrine Tumor Society (ENETS) and American Joint Committee on Cancer (AJCC) once caused chaos in the field of pancreatic neuroendocrine tumors. In addition, we discovered loop holes in the AJCC and ENETS staging systems. Thus, we proposed our own staging system for pancreatic cancer, which was assessed as the Best of *Journal of Clinical Oncology*

(JCO) and was among JCO's Most-Accessed Articles (37,38). To solve the inability of the single biomarker CA19-9 to identify Lewis-negative patients, we established the triple CA19-9/CA125/CEA serum tumor marker system, which can discriminate patients who would have been missed. In addition, this system can help us identify patients who cannot benefit from surgery, which promotes personalized management of pancreatic cancer patients (39). We also explored mechanisms in patients unable to benefit from surgery from diverse molecular aspects, including the essential role of the KRAS/MEK/ERK axis (40-43), abnormal glucose metabolism (44-46) and the structure of caveolae (47,48). Through collective efforts, the PFS of pancreatic cancer patients after surgery in FUSCC has markedly improved from 14.4 to 23.6 months.

Lung cancer has long been the leading cause of death among all tumors (1). Ground-glass opacity (GGO), a hazy cloudiness observed on computed tomography (CT) images that does not obscure underlying bronchial structures or pulmonary vessels, is considered a possible sign of lung adenocarcinoma (49). With the increasing popularity of low-dose CT in lung cancer screening, proper management of GGO is rather challenging. Our Department of Thoracic Surgery developed a versatile system to address GGO comprehensively. We first proposed "minimally invasive thoracic surgery 3.0" worldwide, which pointed out the necessity of reducing systemic damage through comprehensive efforts (50). For instance, we demonstrated that facilitated by interoperative fresh-frozen pathology examination, not all peripheral small-sized lung adenocarcinomas require radical treatment (51,52). In 2017, this momentous result was introduced into the guidelines released by the European Society for Medical Oncology (ESMO) (53). Furthermore, we established "surgical strategies for pre- and minimally invasive lung adenocarcinoma 3.0" for the selection of optimal surgical timing, which include three rules, namely, (I) benign disease should not be treated as malignancy, (II) pre- and minimally invasive disease should not be treated as invasive disease, and (III) indolent malignancy should not be treated as aggressive malignancy (54). Guided by these strategies, we recommend a minimum follow-up of 4–6 months to avoid overtreatment for newly identified GGOs (55). We also demonstrated that lung adenocarcinoma with GGO cannot benefit from conventionally recommended examinations such as bronchoscopy, PET/CT, bone scanning or brain MRI, which can alleviate unfavorable physical, mental and economic impacts on patients (56-59).

Future development of precision cancer medicine at FUSCC

Guided by the idea of precision cancer medicine, FUSCC has substantially promoted the diagnosis and treatment of cancer. However, further efforts are required improve our practice and benefit a larger population.

More effective integration of industry, education and research is needed to boost precision cancer medicine. Our PCMC has had a good start, but we need to do more. Collaboration mechanisms must be established to facilitate the sharing of all kinds of medical datasets, which will facilitate the thorough utilization of such information. In addition, greater collaboration with pharmaceutical enterprises can realize rapid translation of scientific discovery into clinical application.

Precision cancer medicine should cover the stages of the human life cycle, including cancer consultation, prevention, diagnosis, treatment, recovery and hospitalization. For a long time, we limited precision cancer medicine to cancer diagnosis and treatment, which is not sufficient. For instance, with increasing attention from both physicians and patients and decreasing screening costs, precision cancer prevention (e.g., predictive genetic testing) will likely be more prevalent or even routine in the near future.

As the leading cancer center in eastern China and one of the pioneers of precision cancer medicine in the country, FUSCC is obliged to advocate this idea among other oncologists and cancer centers in China.

In China, the practice of precision cancer medicine still faces some setbacks. Although precision cancer medicine is a future trend, not all clinicians have realized the tremendous hit that it will cause to the current cancer management system. Meanwhile, with no systemic theories for reference, some entities diverged in the research and application of precision cancer medicine, causing colossal waste. Additionally, the disparity in health care levels among different regions and institutions is another major predicament. In top cancer centers such as FUSCC, where precision cancer medicine resources are more abundant, the prognoses of patients have approximately equaled international advanced standards. However, in some districts or regional hospitals, precision care is less accessible due to restrictions in testing equipment, and sometimes, even standard treatment guidelines are not sufficiently followed.

Collective efforts must be made to advance precision cancer medicine across the country. We will create platforms on which clinicians can communicate their practices

and experiences, such as promoting the operation of the journal *Precision Cancer Medicine*, holding symposiums, and organizing visiting programs. In addition, we aim to provide public gene diagnostic tools and evidence-based guidelines to standardize the practice of precision cancer medicine. Finally, we hope to launch more large-scale multicenter studies to put precision cancer medicine into practice and cure more cancer patients.

Acknowledgments

Funding: This work was sponsored by Shanghai Sailing Program for Youth S&T Talents (20YF1408700).

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Precision Cancer Medicine*, for the series "Eastern and Western Perspectives on Precision Cancer Medicine". The article has undergone external peer review.

Peer Review File: Available at: https://dx.doi.org/10.21037/pcm-21-26

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at: https://dx.doi.org/10.21037/pcm-21-26). The series "Eastern and Western Perspectives on Precision Cancer Medicine" was commissioned by the editorial office without any funding or sponsorship. Dr. ZMS serves as an unpaid Executive Editor-in-Chief of *Precision Cancer Medicine* and served as unpaid Guest Editor of the series. Dr. DM received sponsorship from Shanghai Sailing Program for Youth S&T Talents (20YF1408700). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects for the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Chen W. Cancer statistics: updated cancer burden in China. Chin J Cancer Res 2015;27:1.
3. Letai A. Functional precision cancer medicine-moving beyond pure genomics. Nat Med 2017;23:1028-35.
4. Tsimberidou AM, Fountzilas E, Nikanjam M, et al. Review of precision cancer medicine: Evolution of the treatment paradigm. Cancer Treat Rev 2020;86:102019.
5. McGranahan N, Swanton C. Clonal Heterogeneity and Tumor Evolution: Past, Present, and the Future. Cell 2017;168:613-28.
6. Marusyk A, Polyak K. Tumor heterogeneity: causes and consequences. Biochim Biophys Acta 2010;1805:105-17.
7. Wolf Y, Bartok O, Patkar S, et al. UVB-Induced Tumor Heterogeneity Diminishes Immune Response in Melanoma. Cell 2019;179:219-235.e21.
8. Olver IN. Prevention of breast cancer. Med J Aust 2016;205:475-9.
9. Slamon DJ, Clark GM, Wong SG, et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science 1987;235:177-82.
10. Ullrich A, Coussens L, Hayflick JS, et al. Human epidermal growth factor receptor cDNA sequence and aberrant expression of the amplified gene in A431 epidermoid carcinoma cells. Nature 1984;309:418-25.
11. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med 2001;344:783-92.
12. Waks AG, Winer EP. Breast Cancer Treatment: A Review. JAMA 2019;321:288-300.
13. Dieci MV, Miglietta F. HER2: a never ending story. Lancet Oncol 2021;22:1051-2.
14. Wang L, Qin W, Huo YJ, et al. Advances in targeted therapy for malignant lymphoma. Signal Transduct Target Ther 2020;5:15.
15. Hirsch FR, Scagliotti GV, Mulshine JL, et al. Lung cancer: current therapies and new targeted treatments. Lancet

2017;389:299-311.
16. Qian Y, Gong Y, Fan Z, et al. Molecular alterations and targeted therapy in pancreatic ductal adenocarcinoma. J Hematol Oncol 2020;13:130.
17. Ward E, Jemal A, Cokkinides V, et al. Cancer disparities by race/ethnicity and socioeconomic status. CA Cancer J Clin 2004;54:78-93.
18. Seal S, Thompson D, Renwick A, et al. Truncating mutations in the Fanconi anemia J gene BRIP1 are low-penetrance breast cancer susceptibility alleles. Nat Genet 2006;38:1239-41.
19. Cao AY, Huang J, Hu Z, et al. Mutation analysis of BRIP1/BACH1 in BRCA1/BRCA2 negative Chinese women with early onset breast cancer or affected relatives. Breast Cancer Res Treat 2009;115:51-5.
20. Lang GT, Shi JX, Hu X, et al. The spectrum of BRCA mutations and characteristics of BRCA-associated breast cancers in China: Screening of 2,991 patients and 1,043 controls by next-generation sequencing. Int J Cancer 2017;141:129-42.
21. Culp MB, Soerjomataram I, Efstathiou JA, et al. Recent Global Patterns in Prostate Cancer Incidence and Mortality Rates. Eur Urol 2020;77:38-52.
22. Liu X, Yu C, Bi Y, et al. Trends and age-period-cohort effect on incidence and mortality of prostate cancer from 1990 to 2017 in China. Public Health 2019;172:70-80.
23. Zhu Y, Mo M, Wei Y, et al. Epidemiology and genomics of prostate cancer in Asian men. Nat Rev Urol 2021;18:282-301.
24. Fu H, Zhu Y, Wang Y, et al. Identification and Validation of Stromal Immunotype Predict Survival and Benefit from Adjuvant Chemotherapy in Patients with Muscle-Invasive Bladder Cancer. Clin Cancer Res 2018;24:3069-78.
25. Kumar KR, Cowley MJ, Davis RL. Next-Generation Sequencing and Emerging Technologies. Semin Thromb Hemost 2019;45:661-73.
26. Cheng DT, Mitchell TN, Zehir A, et al. Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT): A Hybridization Capture-Based Next-Generation Sequencing Clinical Assay for Solid Tumor Molecular Oncology. J Mol Diagn 2015;17:251-64.
27. Timms KM, Abkevich V, Hughes E, et al. Association of BRCA1/2 defects with genomic scores predictive of DNA damage repair deficiency among breast cancer subtypes. Breast Cancer Res 2014;16:475.
28. Yeo SK, Guan JL. Breast Cancer: Multiple Subtypes within a Tumor? Trends Cancer 2017;3:753-60.
29. Lang GT, Jiang YZ, Shi JX, et al. Characterization of the genomic landscape and actionable mutations in Chinese breast cancers by clinical sequencing. Nat Commun 2020;11:5679.
30. Jiang YZ, Ma D, Suo C, et al. Genomic and Transcriptomic Landscape of Triple-Negative Breast Cancers: Subtypes and Treatment Strategies. Cancer Cell 2019;35:428-440.e5.
31. Jiang YZ, Liu Y, Xiao Y, et al. Molecular subtyping and genomic profiling expand precision medicine in refractory metastatic triple-negative breast cancer: the FUTURE trial. Cell Res 2021;31:178-86.
32. Chen L, Zhimin S, Wang Z, et al. Combination of famitinib with camrelizumab plus nab-paclitaxel as first-line treatment for patients with immunomodulatory advanced triple-negative breast cancer (FUTURE-C-PLUS): A prospective, single-arm, phase 2 study. J Clin Oncol 2021;39:abstr 1007.
33. Wu T, Dai Y. Tumor microenvironment and therapeutic response. Cancer Lett 2017;387:61-8.
34. Xiao Y, Ma D, Zhao S, et al. Multi-Omics Profiling Reveals Distinct Microenvironment Characterization and Suggests Immune Escape Mechanisms of Triple-Negative Breast Cancer. Clin Cancer Res 2019;25:5002-14.
35. Gong Y, Ji P, Yang YS, et al. Metabolic-Pathway-Based Subtyping of Triple-Negative Breast Cancer Reveals Potential Therapeutic Targets. Cell Metab 2021;33:51-64.e9.
36. Vincent A, Herman J, Schulick R, et al. Pancreatic cancer. Lancet 2011;378:607-20.
37. Luo G, Javed A, Strosberg JR, et al. Modified Staging Classification for Pancreatic Neuroendocrine Tumors on the Basis of the American Joint Committee on Cancer and European Neuroendocrine Tumor Society Systems. J Clin Oncol 2017;35:274-80.
38. Halperin DM, Yao JC, Dasari A. What's in a Name? Steady Progress in Staging Pancreatic Neuroendocrine Tumors. J Clin Oncol 2017;35:265-7.
39. Luo G, Liu C, Guo M, et al. Potential Biomarkers in Lewis Negative Patients With Pancreatic Cancer. Ann Surg 2017;265:800-5.
40. Liang C, Qin Y, Zhang B, et al. Oncogenic KRAS Targets MUC16/CA125 in Pancreatic Ductal Adenocarcinoma. Mol Cancer Res 2017;15:201-12.
41. Liang C, Qin Y, Zhang B, et al. ARF6, induced by mutant Kras, promotes proliferation and Warburg effect in pancreatic cancer. Cancer Lett 2017;388:303-11.
42. Fan Z, Fan K, Yang C, et al. Critical role of KRAS mutation in pancreatic ductal adenocarcinoma. Transl

Cancer Res 2018;7:1728-36.
43. Ji S, Qin Y, Shi S, et al. ERK kinase phosphorylates and destabilizes the tumor suppressor FBW7 in pancreatic cancer. Cell Res 2015;25:561-73.
44. Ji S, Qin Y, Liang C, et al. FBW7 (F-box and WD Repeat Domain-Containing 7) Negatively Regulates Glucose Metabolism by Targeting the c-Myc/TXNIP (Thioredoxin-Binding Protein) Axis in Pancreatic Cancer. Clin Cancer Res 2016;22:3950-60.
45. Meng Q, Xu J, Liang C, et al. GPx1 is involved in the induction of protective autophagy in pancreatic cancer cells in response to glucose deprivation. Cell Death Dis 2018;9:1187.
46. Ji S, Zhang B, Liu J, et al. ALDOA functions as an oncogene in the highly metastatic pancreatic cancer. Cancer Lett 2016;374:127-35.
47. Liang C, Shi S, Meng Q, et al. MiR-29a, targeting caveolin 2 expression, is responsible for limitation of pancreatic cancer metastasis in patients with normal level of serum CA125. Int J Cancer 2018;143:2919-31.
48. Chen T, Liu L, Xu HX, et al. Significance of caveolin-1 regulators in pancreatic cancer. Asian Pac J Cancer Prev 2013;14:4501-7.
49. Hansell DM, Bankier AA, MacMahon H, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008;246:697-722.
50. Cheng X, Onaitis MW, D'amico TA, et al. Minimally Invasive Thoracic Surgery 3.0: Lessons Learned From the History of Lung Cancer Surgery. Ann Surg 2018;267:37-8.
51. Liu S, Wang R, Zhang Y, et al. Precise Diagnosis of Intraoperative Frozen Section Is an Effective Method to Guide Resection Strategy for Peripheral Small-Sized Lung Adenocarcinoma. J Clin Oncol 2016;34:307-13.
52. Donington JS. An Additional Step Toward Personalization of Surgical Care for Early-Stage Non-Small-Cell Lung Cancer. J Clin Oncol 2016;34:295-6.
53. Postmus PE, Kerr KM, Oudkerk M, et al. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28:iv1-iv21.
54. Zhang Y, Chen Z, Hu H, et al. Surgical Strategies for Pre- and Minimally Invasive Lung Adenocarcinoma 3.0: Lessons Learned From the Optimal Timing of Surgical Intervention. Semin Thorac Cardiovasc Surg 2021. [Epub ahead of print].
55. Zhang Y, Fu F, Chen H. Management of Ground-Glass Opacities in the Lung Cancer Spectrum. Ann Thorac Surg 2020;110:1796-804.
56. Zhuge L, Huang Y, Wang S, et al. Preoperative brain MRI for clinical stage IA lung cancer: is routine scanning rational? J Cancer Res Clin Oncol 2019;145:503-9.
57. Zhang Y, Zhang Y, Chen S, et al. Is bronchoscopy necessary in the preoperative workup of a solitary pulmonary nodule? J Thorac Cardiovasc Surg 2015;150:36-40.
58. Li B, Li N, Liu S, et al. Does [18F] fluorodeoxyglucose-positron emission tomography/computed tomography have a role in cervical nodal staging for esophageal squamous cell carcinoma?. J Thorac Cardiovasc Surg 2020;160:544-50.
59. Li H, Ye T, Li N, et al. Is 99m Tc bone scintigraphy necessary in the preoperative workup for patients with cT1N0 subsolid lung cancer? A prospective multicenter cohort study. Thorac Cancer 2021;12:415-9.

doi: 10.21037/pcm-21-26
Cite this article as: Dai LJ, Ma D, Shao ZM. Precision cancer medicine in China: the Fudan University Shanghai Cancer Center experience. Precis Cancer Med 2021;4:34.