Original Article

Analysis of the differences in lung cancer research trends between China and the United States based using project funding data

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Background: Lung cancer is the leading cause of cancer-related death, and countries all over the world have given considerable support to lung cancer research. However, analysis on the status of funding in the field of lung cancer is still lacking.

Methods: We visited the National Natural Science Foundation of China (NSFC) and National Institutes of Health (NIH) official websites to gather lung cancer research information between 2008 and 2020. RSTCM6 software was used to extract the keywords of funded projects which were then imported into CiteSpace software for visual analysis of word frequency.

Results: A total of 1,745 and 5,939 search results were finally obtained from the NSFC and NIH websites, respectively. The amount of NSFC funding for projects in the field of lung cancer increased steadily from 2008 to 2012, while the NIH funding for lung cancer was significantly higher in even years than in odd years between 2008 to 2018. The Shanghai Jiaotong University, Sun Yat-sen University, and Guangzhou Medical University were the top three research institutions that had received the most projects funded by the NSFC. Apoptosis, proliferation, invasion, metabolism, the pathogenesis of lung cancer, cell signal transduction, epithelial-mesenchymal transformation (EMT), and immune-related research were the most frequently funded research areas by the NSFC. Biomarkers, targeted therapy, signal pathway, genomics, and immune-related research were funded most the most frequently funded research areas by the NIH. Both the NIH and NSFC funding for lung cancer immune-related research has increased in recent years.

Conclusions: NIH funding in the United States is decreasing year by year, whereas NSFC funding is increasing in China. There are some differences in research focus in lung cancer research funding between China and the United States. However, both countries have increased the support for immune-related research in recent years.

Keywords: Lung cancer; research trends; National Natural Science Foundation of China (NSFC); National Institutes of Health (NIH)

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Introduction

Lung cancer is the leading cause of cancer-related death. Approximately 1.8 million people are diagnosed with lung cancer and 1.6 million people die from lung cancer on average each year (1). The 5-year survival of lung cancer patients varies from 5% to 57% depending on the cancer stage and regional differences (2-5). Among the common subtypes of lung cancer, non-small cell lung cancer (NSCLC) accounts for 85% of lung cancer cases (6).

In recent years, cancer immunotherapy has made significant progress with the support of a significant amount of funding (7-11). A study, funded by AstraZeneca reported that the clinical activity of durvalumab in patients with epidermal growth factor receptor (EGFR) + NSCLC with ≥25% of tumor cells expressing programmed death-ligand 1 (PD-L1) produced encouraging results (12,13). Results like the one above demonstrate how immunotherapy has fundamentally changed the treatment of patients with metastatic NSCLC (14). Research shows that PD-L1 is often highly expressed in NSCLC, which is a promising sign for patients with advanced lung cancer (15). The efficacy of immunotherapy alone, however, is considered to be limited, and many immunotherapy programs combined with targeted drug therapy have been included in clinical trials (16). The research goal for advanced NSCLC is to understand and solve the mechanism of drug resistance and refractory diseases and ultimately improve the cure rate.

All of the above-mentioned studies, and the issues they attempt to resolve, require considerable funding. The National Natural Science Foundation of China (NSFC) is the primary channel providing support for basic scientific research. The analysis of NSFC funding has become a valuable method for measuring the competitiveness in the basic research field, and can provide useful insights for researchers who wish to apply for scientific research funding. As the most advanced country in medical research, the United States, along with its primary medical agency, the National Institutes of Health (NIH), was also included in this analysis to enable a comparison of lung cancer research funding between China and the United States.

Methods

Study design

The information on the NSFC was retrieved from the network information system of the NSFC (https://isisn.nsfc.gov.cn/egrantindex/funcindex/prjsearch-list), the MedSci Natural Science Fund inquiry system (https://www.medsci.cn/sci/nsfc.do), and the inquiry system for scientific funding results in LetPub (https://www.letpub.com.cn/index.php?page=grant), with the keywords of "lung" and "lung cancer" for the period between 2008 and 2019. We wrote the corresponding web crawler code to integrate the search results into an excel table, and combined this with manual screening to obtain accurate project funding information. NIH funding information for the United States was downloaded from the NIH official website (https://report.nih.gov) with the keywords of "lung cancer" for the period between 2008 and 2020. We manually removed some items with incomplete information. The project name, person in charge, amount of funding, approval time, subject code, project approval number, application institution, and project type were included in our information table. Our study was conducted in accordance with the Declaration of Helsinki, and the Institutional Review Committee of Zhongshan Hospital (Fudan University, Shanghai, China) allowed this study to be exempt from ethical considerations because our study did not involve any patient's information or animal experiment. The relationship between the frequency of corresponding keywords was analyzed by CiteSpace (5.3.R 8.12.30.2018).

Statistical analysis

The keywords of NSFC- and NIH-funded projects were obtained by using ROSTCM6 software to preprocess the data. They were successively imported into CiteSpace (5.3.R 8.12.30.2018) software for cluster analysis and word frequency analysis.

Results

A total of 1,745 and 5,939 search results were finally obtained from the NSFC and NIH respectively. First, we analyzed the trend in the annual total funds and the number of projects funded by the NSFC and NIH in the field of lung cancer from 2008 to 2020. It can be seen from *Figure 1* that the funding including funding amount and funding number of lung cancer between China and the United States is significantly different. *Figure 1A* shows the NSFC funding situation in China. The amount of NSFC funding projects in the field of lung cancer increased steadily from 2008 to 2012, but did not change much after 2012. The proportion of the number of projects funded in lung cancer among the number of all medical science projects between

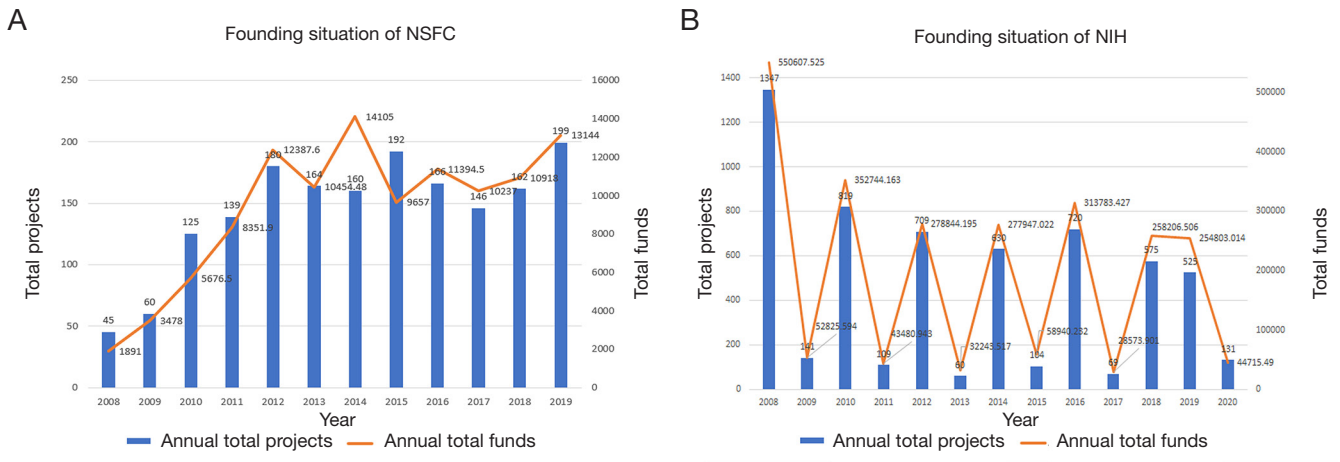

Figure 1 Founding situation of NSFC and NIH from 2008 to 2019. (A) Histogram of the total amount of the NSFC funding for lung cancer-related research between 2008 and 2019. (B) Histogram of the total amount of the NIH funding for lung cancer-related research between 2008 and 2020. NSFC, National Natural Science Foundation of China; NIH, National Institutes of Health.

2008 to 2019 was 1.72%, 1.49%, 1.03%, 1.81%, 2.09%, 1.89%, 1.92%, 2.17%, 1.86%, 1.47%, 1.94%, and 2.01%, respectively. NIH funding for lung cancer was significantly higher in even years than in odd years in the period between 2008 to 2018. Generally speaking, NIH funding in the United States decreased each while the opposite trend was seen for the NSFC in China.

As the respective scientific research institutions obtained the total amount of funding capital, the total number of projects could indirectly reflect the research level of institution in the field of lung cancer. We conducted a comparative analysis of the top 10 institutions that received the most funds between China and the United States, as shown in *Tables 1* and *2*, respectively. Shanghai Jiaotong University, Sun Yat-sen University, and Guangzhou Medical University were the top three research institutions in the field of lung cancer research in mainland China, receiving a total of 66.386, 57.140, and 43.195 millions CNY, respectively. The top three institutions that received the most number of funds were Shanghai Jiaotong University, Sun Yat-sen University, and Fudan University. Among the scientific research institutions in the United States, the top three scientific research institutions with the largest amount of funding received in the field of lung cancer were Leidos Biomedical Research, Inc., the University of Texas MD Anderson Cancer Center, and the University of Pennsylvania. The corresponding amount of funding was 71.484, 53.405, and 52.862 million USD, respectively. The top three institutions that received the most number of funded were the University of Texas MD Anderson Cancer Center, the University of Pennsylvania, and Stanford University.

We also analyzed the trends in lung cancer research for the NSFC's General Program and National Science Foundation for Young Scientists. As shown in *Table 3* and Figure S1, both the General Program and the Foundation for Young Scientists have received an increasing amount of funding. Between 2008 and 2019, the year in which the General Program received the most funding was 2014, with the funding amount reaching 11.335 million CNY, while the Foundation for Young Scientists received the most funding in 2019, with the funding amount reaching 25.475 million CNY.

To explore the differences between China and the United States in the field of lung cancer research in the past 12 years, we analyzed the frequency of corresponding keywords and their relationship using the CiteSpace. We found that the basic experimental research of lung cancer in the past 12 years in the Chinese mainland included topics such as apoptosis, proliferation, invasion, metabolism, pathogenesis, cell signal transduction, epithelial-mesenchymal transformation (EMT), and immune-related research. In the clinical study of lung cancer, EGFR and KRAS gene mutations were the most frequently studied (*Figure 2A*, Table S1). Throughout the studied time period, the occurrence of lung cancer, EMT, and apoptosis were the main hotspots of research. Since 2011, the research on immunity-related to lung cancer, cancer cell metabolism, and EGFR inhibitors began to increase, while the research

Table 1 Research institution's rank and bid amount for lung cancer projects funded by the NSFC between 2008 and 2019

Institution	Number of projects		Bid amount	
	n	Rank	Millions CNY	Rrank
Shanghai Jiao Tong University	74	1	66.386	1
Sun Yat-sen University	62	2	57.140	2
Guangzhou Medical University	31	9	43.195	3
Fudan University	56	3	39.175	4
Sichuan University	44	4	34.680	5
Zhejiang University	42	6	33.600	6
Third Military Medical University	38	7	33.440	7
Shanghai Institute of Life Sciences, Chinese Academy of Sciences	23	10	33.040	8
Peking University	43	5	32.797	9
The Second Military Medical University	34	8	29.730	10

NSFC, National Natural Science Foundation of China.

Table 2 Research institution's rank and bid amount for lung cancer projects funded by the NIH between 2008 and 2020

Institution	Number of projects		Bid amount	
	n	Rank	Millions USD	Rank
Leidos Biomedical Research, Inc.	14	10	71.484	1
University of Tx Md Anderson Can Ctr	142	1	53.405	2
University of Pennsylvania	139	2	52.862	3
Stanford University	119	3	48.993	4
Massachusetts General Hospital	97	9	47.956	5
Sloan-Kettering Inst Can Research	107	6	47.029	6
Dana-Farber Cancer Inst	100	8	41.934	7
University of Pittsburgh At Pittsburgh	110	5	40.561	8
University of California, San Francisco	101	7	39.608	9
Johns Hopkins University	116	4	38.020	10

NIH, National Institutes of Health.

on long non-coding RNA (lncRNA), genomics, and KRAS gene mutations has started to grow in the past several years (*Figure 2B*).

Similarly, the basic experimental research of lung cancer founded by NIH in the United States has focused on the mechanism of lung cancer, biomarkers, targeted therapy, signal pathways, genomics, and immune-related research. In contrast, clinical research has focused on the diagnosis, treatment methods, and clinical risk factors of lung cancer, drug testing, and imaging (*Figure 2C*, Table S2). Recently, the United States has also begun to focus on funding immunotherapy-related research on lung cancer (*Figure 2D*).

Discussion

In recent years, significant progress has been made in lung

Table 3 NSFC's funding for the General Program and NSFC for Young Scientists between 2008 and 2019

Year	Number of the general projects		Number of youth science foundation programs	
	n	Millions CNY	n	Millions CNY
2019	90	7.486	64	2.548
2018	91	7.514	37	9.460
2017	81	6.124	37	1.725
2016	91	6.855	22	1.254
2015	113	7.295	39	0.708
2014	101	11.335	20	1.426
2013	81	6.916	23	0.920
2012	100	8.823	25	1.068
2011	72	5.510	28	0.599
2010	68	3.414	36	1.759
2009	32	1.596	15	0.294
2008	23	1.259	14	0.463

NSFC, National Natural Science Foundation of China.

cancer research, screening, and personalized treatment (precision medicine). Several diagnostic methods can be used to diagnose NSCLC, including X-ray, computed tomography (CT), and positron emission tomography (PET) imaging, and histological examination of tumor biopsy. Recent evidence suggests that low-dose CT screening can reduce lung cancer-specific mortality by 62 per 100,000 people per year (17). These methods have been improved through years of in-depth research on the clinical diagnosis and treatment of lung cancer. As our results show, in the past 12 years, both China and the United States have funded lung cancer imaging research, which is an essential support for the progress of the diagnostic imaging of lung cancer (18).

With the improvement and popularization of imaging examination, an increasing number of early-stage lung cancer patients are being identified. The predominant treatment of early-stage lung cancer is surgery. Many retrospective clinical studies funded by the NSFC and NIH have proven that the surgical treatment on early-stage lung cancer has an appreciable effect (19,20). Data show that patients diagnosed with early-stage lung cancer (T1a-cN0) have a high probability of remission (T1a =92%, T1b =86%, T1c =81%) (21). The support for clinical research has enabled us to see new viewpoints and experiences of lung cancer treatment in time, and has provided a platform through which clinicians can learn from one another.

Patients with advanced lung cancer are usually not suitable for surgical treatment, and so both the NSFC and NIH have given considerable funding support to the exploration of other treatment methods for lung cancer (22-24). Radiotherapy and chemotherapy can still improve the survival of patients with advanced lung cancer. However, according to our analysis, traditional treatment methods for advanced lung cancer, such as radiotherapy and chemotherapy, are still somewhat funded, but the relative proportion of the funding has declined. Abandoning chemotherapy and using molecular targeted therapy or immunotherapy is the standard first-line treatment for about 50% of patients with advanced NSCLC (25). A greater understanding of the pathogenic genomic changes of NSCLC and the development of new drugs represent the progress that has been made in NSCLC treatment. A variety of targeted drugs have been proven to be effective in improving the long-term survival of patients. Several driving gene mutations have been identified, including EGFR and anaplastic lymphoma kinase (ALK), and research has begun to tackle the problems of acquired drug resistance (26-28). Curiously, NIH funding for lung cancer was significantly higher in evenly numbered years, but we have no convincing explanation for this phenomenon. We speculate that it may represent a balancing adjustment

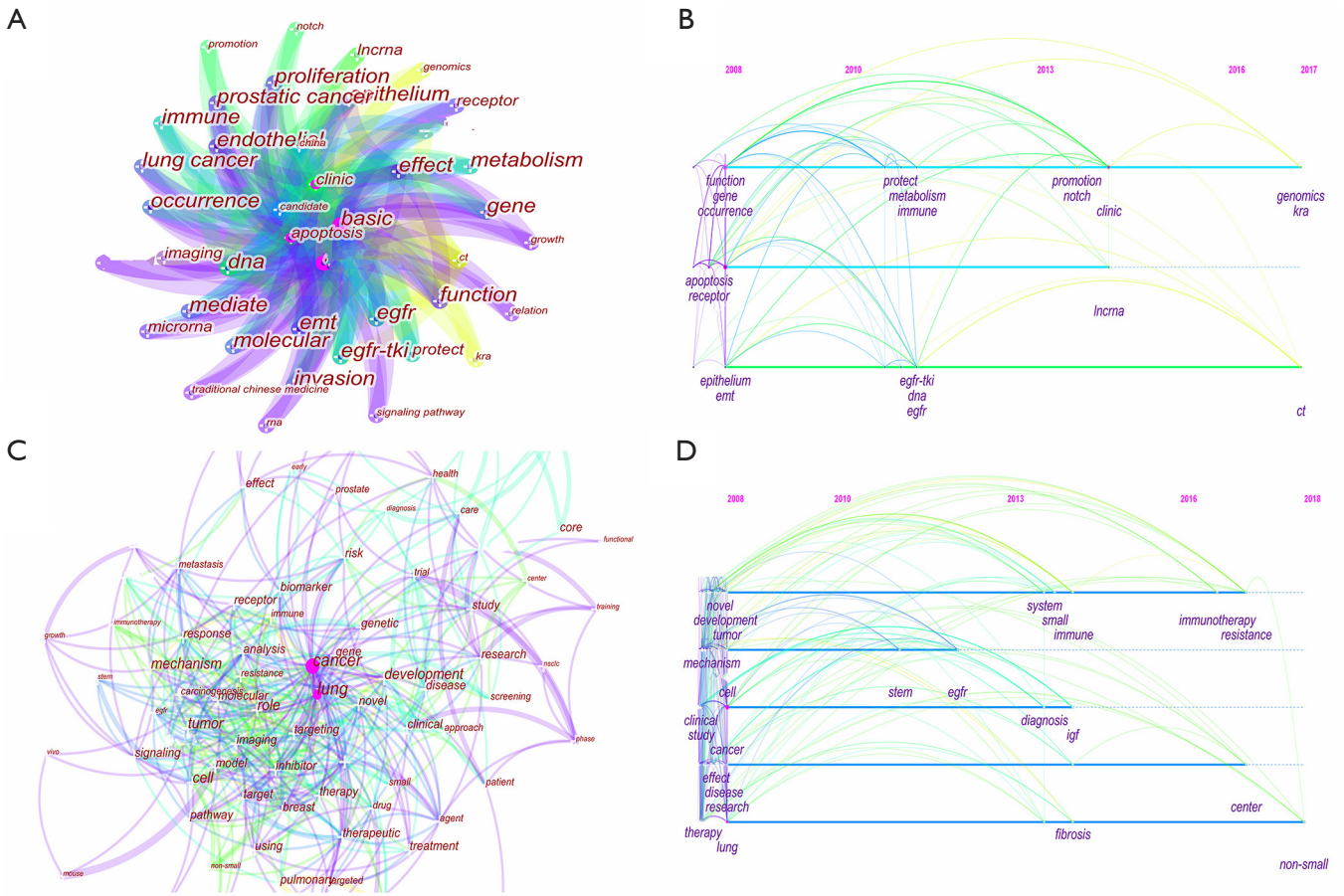

Figure 2 Founding projects trends in non-small cell lung cancer between China and America. (A) Clustering analysis of word frequency of projects supported by the National Natural Science Foundation of China (NSFC) in lung cancer-related research over the years. (B) Trend chart of the critical projects supported by the NSFC in lung cancer-related research between 2008 and 2019. (C) Clustering analysis of the word frequency of projects supported by the NIH in lung cancer-related research over the years. (D) Trend chart of critical projects supported by the NIH in lung cancer-related research between 2008 and 2020.

across different fields or the product of the response to feedback from the preceding year.

In the past 2 years, one of the most popular research areas in cancer treatment has been immunotherapy. Our results indicate that both the NSFC and NIH have provided significant funding to immunotherapy research in recent years. Because of the remarkable curative effect of immunotherapy targeting programmed cell death protein 1 (PD1)/PD-L1, it has attracted the interest of relevant researchers, and studies related to tumor immunotherapy have exploded in number in recent years (29,30). However, immunotherapy has some limitations. For example, immunotherapy is only applicable to a portion of patients and may involve adverse reactions (31,32). To solve these issues, considerable funding is required.

Our analysis of NSFC and NIH lung cancer research funding may inform those researchers who wish to apply for scientific research funding through a better understanding of their research environment. However, there may be some limitations to this study. For one, some funded projects were excluded, which might have led to some deviation in the results. Also, we did not track the research results of these funded projects, as this would have required an intensive workload, but this is worth exploring further.

In conclusion, while some differences may exist in the funding trends in lung cancer research between China and the United States, both countries have increased their support for immune-related research in recent years.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-3957). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Our study was conducted in accordance with the Declaration of Helsinki, and the Institutional Review Committee of Zhongshan Hospital (Fudan University, Shanghai, China) allowed this study to be exempt from ethical considerations because our study did not involve any patient's information or animal experiment.

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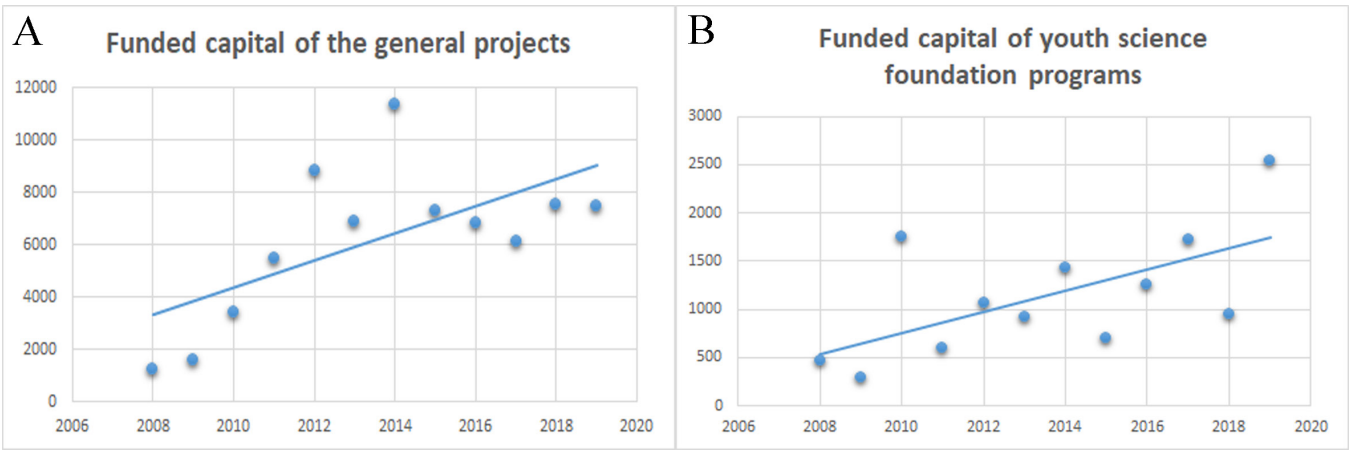

Figure S1 Founding situation of youth scientists between China and America. (A) Scatterplot of the trend for total funding of the China Youth Scientists Fund from 2008 to 2019. (B) Scatterplot of the trend for total funding of the United States National Youth Science Foundation from 2008 to 2019.

Table S1 Word frequency analysis results of NSFC-funded projects in lung cancer

Freq	Centrality	Sigma	PageRank	Keyword
12	0	1	0.96	EMY
12	0	1	0.78	Epithelium
12	0	1	0.6	Invasion
12	0	1	0.6	Lung cancer
12	0	1	0.6	Occurrence
9	0.01	1	1.34	DNA
9	0	1	0.87	EGFR-TKI
9	0	1	0.87	EGFR
9	0	1	0.69	Endothelial
9	0	1	0.6	Metabolism
9	0	1	0.6	Immune
9	0	1	0.6	Prostate cancer
9	0	1	0.6	Proliferation
6	0.33	1	3.66	Apoptosis
6	0.22	1	3.17	Clinic
6	0	1	0.51	lncRNA
6	0	1	0.51	Imaging
6	0	1	0.51	microRNA
6	0	1	0.51	Receptor
3	0	1	0.97	CT
3	0	1	0.97	China
3	0	1	0.51	Growth
3	0	1	0.42	Promotion
3	0	1	0.42	Genomics
3	0	1	0.42	Traditional Chinese Medicine
3	0	1	0.42	Notch
3	0	1	0.42	KRAS
3	0	1	0.42	Signaling Pathway
3	0	1	0.42	RNA

NSFC, National Natural Science Foundation of China.

Table S2 Word frequency analysis results of NIH-funded projects in lung cancer

Freq	Burst	Centrality	Sigma	PageRank	Keyword
1,718		0.59	1	0	Cancer
1,174		0.31	1	0	Lung
283		0.03	1	0	Mechanism
275		0.03	1	0	Development
219		0.03	1	0	Therapy
197	4.24	0.07	1.31	0	Targeting
179	2.68	0	1	0	Treatment
178		0.03	1	0	Research
176		0.06	1	0	Imaging
171		0.02	1	0	Signaling
162		0.07	1	0	Clinical
158		0.01	1	0	Pulmonary
139		0.02	1	0	Breast
133		0.01	1	0	Inhibitor
111		0.01	1	0	Receptor
108		0.03	1	0	Therapeutic
100	3.82	0.03	1.12	0	Biomarker
94		0.04	1	0	Risk
89	2.89	0.01	1.02	0	Metastasis
78		0.02	1	0	Drug
75	10.5	0.03	1.36	0	Trial
69	15.7	0	1.08	0	Immune
66	4.8	0.02	1.1	0	Health
64		0	1	0	Screening
57	3.91	0	1.01	0	Injury
53	4.76	0.03	1.14	0	Care
53	10.14	0	1.01	0	Fibrosis
52	12.12	0	1.01	0	Small
50	11.06	0.03	1.38	0	Agent
48	12.32	0.01	1.16	0	Targeted
45	3.73	0.01	1.02	0	Tissue
40	13.05	0	1.05	0	Prostate
36	16.42	0.01	1.1	0	Resistance
35	16.67	0	1.08	0	IGF
35	16.67	0	1.08	0	OT
34	11.09	0	1	0	Carcinogenesis
31	10.1	0	1.02	0	Growth
29	9.45	0	1.02	0	Mouse
28	9.12	0.01	1.12	0	Phase
27	8.8	0	1.01	0	NSCLC
27	8.8	0	1.04	0	Training
27	11.63	0	1.01	0	Early
27	11.63	0.02	1.31	0	Diagnosis
26	8.47	0	1.02	0	Delivery
24	7.81	0	1.02	0	Vivo
24	7.81	0	1.02	0	Exposure
23	7.49	0	1	0	Smoking
23	11.14	0	1	0	Non-small
21	9.92	0	1.01	0	Immunotherapy
16	9.05	0	1	0	Stem
16	9.27	0	1.02	0	EGFR

NIH, National Institutes of Health.

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