

A visual analysis of NSF thesis research in biosafety from 2001 to 2022

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Abstract. This paper aims to conduct a literature visualization analysis of Chinese papers published by National Natural Science Foundation (NSFC)-funded projects in the field of biosafety in China from the year 2001 to the year 2022. Methods: From the China Knowledge Network database, we set the time period from 1 January 2001 to 31 October 2022 and the Chinese journal literature funded by NSFC projects. The association between the authors of the papers was analyzed using VOSviewer1.6.18. Moreover, CiteSpace6.1.R3 was used to visualize the paper's institutional collaboration, the keywords and the timeline of the papers. Results: It revealed that a few teams, including Tong Yigang, Zhou Yusen, Yang Ruifu and Cao Wuchun as the core, were involved in the NSFC-funded biosafety field. The State Key Laboratory of Biosafety of Pathogenic Microorganisms was the main institutional undertaking unit, and inter-institutional collaboration was more dispersed. Research frontiers are focused on the prevention and management of major emerging and emergent infectious diseases, biotechnology development, application, identification, evaluation and management of unknown risks, etc. Conclusion: From year 2000 to year 2022, the biosafety field focused on funding infectious diseases and epidemiology, and the research direction concentrated on the hot events of society, the development trend of science and technology and national strategic needs. However, there was a trend toward financing being excessively focused in a small number of units and teams and away from the field of microbial drug resistance. It is suggested that the NSFC guidelines and directions should include special projects related to microbial drug resistance, and the selection of projects should be appropriately enriched in terms of research teams, research institutions and research directions.

Keywords: biosafety; NSFC; dissertation; visualization.

Biosafety refers to the harm or potential risk of biological factors to the country's social, economic, public health and ecological environment. With the anthrax mail incident in the United States in 2001 [1], the SARS incident in 2003 [2], the 2019 novel coronavirus pandemic that killed nearly 7 million people in 2019 [3], Derrickburg in 2021 was controversial due to the disclosure of fatal strains such as anthrax, the loss of strains, and the traceability of the novel coronavirus in its history. Biosecurity has become one of the global security issues of international concern. Biological threats can have a greater impact than nuclear threats and chemical threats, and pose a huge threat to global human life and health, social and economic development, and are directly related to the country's political security, economic security and other security. Research on biosafety has become a hot spot and focus in academia, National Natural Science Foundation of China As one of the most important sources of funding for scientific research, the 14 th Five-Year Plan of the National Natural Science Foundation of China (NSFC) clearly focuses on the epidemiological characteristics, pathogenesis and new prevention and treatment strategies of emerging and major infectious diseases. Through the analysis of NSFC papers published in the field of biosafety from 2001 to October 2022, the correlation analysis of publishing institutions, authors and research contents is carried out to provide guidance and reference for the direction of National Natural Science Foundation of China, further optimize the technological innovation in the field of

national biosafety, and provide support for comprehensively improving the national biosafety governance capacity.

1. Data sources and methods

1.1 Data source

China National Knowledge Infrastructure (CNKI) is the largest database of Chinese literature, covering more than 1600 journals and more than 8.5 million articles. By setting ' National Natural Science Foundation ' and ' Chinese Journal ' as the screening conditions, the time span is set from January 2001 to October 31,2022, and a total of 461 articles are obtained after deleting invalid documents.

1.2 Methods

VOSviewer 1.6.18 was used to analyze the correlation between the authors. CiteSpace6.1.R3 is used to visualize the cooperation of institutions, keywords and timelines of papers. The time span is from January 1,2001 to October 31,2022, the time division interval is 1 year, TOPN is set to 50, and the nodes select time, institutions and keywords respectively. R 4.2.2 was used to process the annual number of documents.

2. Results

2.1 Analysis of the basic situation of the paper

The number of NSFC papers in the field of biosafety from 2001 to 2022 is shown below (Fig.1). Overall, 2006,2008,2011,2012,2015 and 2021 are the peaks of publication. It basically reached the peak within 1-2 years after the anthrax incident in the United States in 2001, SARS in 2003, avian influenza in 2005, African swine fever in 2008, influenza A in 2009, the invasion of *Solidago canadensis* in 2010, the Middle East respiratory syndrome in 2013, the gene editing event in 2018, and the new coronavirus pneumonia in 2019.

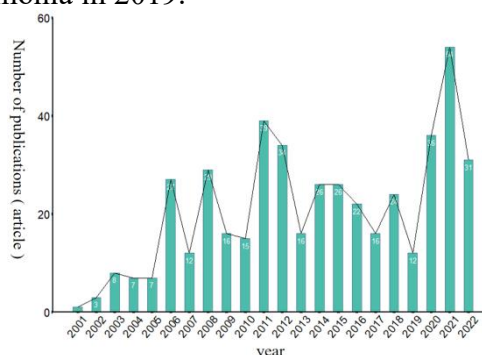


Figure 1 Annual number of NSFC papers on biosafety from 2001 to 2022

2.2 Analysis of research institutions

The statistical results show. The top 10 institutions with the highest number of NSFC papers in the field of biosafety from 2001 to 2022 were the State Key Laboratory of Pathogenic Microbial Biosafety (58 papers), Institute of Bioengineering, Academy of Military Medical Sciences (29 papers), Institute of Microbial Epidemiology, Academy of Military Medical Sciences (26 papers), Institute of Microbial Epidemiology, Academy of Military Medical Sciences (8 papers), School of Economics and Management, Nanjing Agricultural University (7 papers), Institute of Basic Medicine, Academy of Military Medical Sciences (7 papers), Wuhan Literature and Information Center, Chinese Academy of Sciences (6 papers), Anhui Medical University (5 papers),

Department of Microbiology, Second Military Medical University (5 papers) and School of Economics and Management, Beijing Agricultural University (5 papers).

The visualization map of institutional cooperation is drawn with the author institution as the node type (Figure 2). There are 412 nodes and 286 connections in the map, and the network density is 0.0034. The size of nodes in the map represents the number of documents issued by institutions, and each node represents one institution. The thicker the connection between nodes, the closer the cooperation between institutions. It can be seen from the cooperative relationship shown in the map that there is a clear cooperative relationship between the State Key Laboratory of Pathogenic Microbial Biosafety and the Institute of Microbial Epidemiology, Academy of Military Medical Sciences, and between the State Key Laboratory of Pathogenic Microbial Biosafety and the Institute of Bioengineering, Academy of Military Medical Sciences. The State Key Laboratory of Pathogenic Microorganism Biosafety ranked first in the number of publications has more cooperation with other institutions. The School of Economics and Management of Nanjing Agricultural University has issued a large number of papers but has not shown a fixed and obvious cooperative relationship. Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan Literature and Information Center of Chinese Academy of Sciences and Wuhan Branch of National Science Library of Chinese Academy of Sciences have not published many papers, but they have obvious cooperative relationship. In addition, there are some institutions scattered around the map, but their cooperative relationship is not obvious.

From the perspective of time (the darker the color of the institution, the earlier the paper was published), the National Key Laboratory of Pathogenic Microbial Biosafety, the Institute of Microbial Epidemiology of the Academy of Military Medical Sciences, the Institute of Bioengineering of the Academy of Military Medical Sciences, the Department of Microbiology of the Second Military Medical University, the Institute of Health and Environmental Medicine of the Academy of Military Medical Sciences, the School of Biosafety Science and Technology of Hunan Agricultural University, the Library of Foshan University, and the School of Environmental Science and Engineering of Tongji University started earlier in the field of biosafety. The National Key Laboratory of Pathogenic Microorganism Biosafety, Institute of Microbial Epidemiology, Academy of Medical Sciences, Military Academy of Sciences, School of Economics and Management, Nanjing Agricultural University, Anhui Medical University, University of Chinese Academy of Sciences, Chinese Academy of Agricultural Sciences, School of Economics and Management, Beijing Agricultural University and other biosafety fields started late.



Figure 2 Visualization map of institutional cooperation of NSFC papers in the field of biosafety from 2001 to 2022(*According to the author labeling unit)

According to the key words of the main authors of NSFC papers in the field of biosafety from 2001 to 2022, it can be seen that the research of the State Key Laboratory of Pathogenic Microorganism Biosafety mainly focuses on epidemiology and genetic technology. The Institute of Bioengineering, Academy of Military Medical Sciences focuses on biosafety capacity building. The School of Economics and Management, Nanjing Agricultural University focuses on invasive biosafety management. The Institute of Basic Medicine, Academy of Military Medical Sciences focuses on the construction of biological defense capabilities.

unit	keywords
State Key Laboratory of Pathogenic Microbial Biosafety	Dengue virus (5), replicon (4), expression (4), sequence analysis (3), anthrax toxin (3), prokaryotic expression (3)
Institute of Bioengineering, Academy of Military Medical Sciences	Biosecurity (25), bioterrorism (8), biological defence (5), anthrax (3), infectious diseases (3), capacity-building (3), symptom surveillance (3), early warning (3)
School of Economics and Management, Nanjing Agricultural University	Safety management (2)
Institute of Basic Medicine, Academy of Military Medical Sciences	Biosecurity (5), bioterrorism (3), biological defence (2), capacity-building (2), situation (2)

Table 1 Key words of NSFC papers in the field of biosafety from 2001 to 2022 (part)

2.3 Analysis of the author

Using VOSviewer software to detect functional analysis, it can be seen that Zheng Tao has the highest number of articles, a total of 29 articles. From 2001 to 2022, the main author research field of NSFC papers in the field of biosafety. From the perspective of authors and their units, the units and individuals with a large number of papers are mainly Zhou Yusen, Yang Ruifu, Cao Wuchun, Liu Wei and other scholars from the Institute of Microbial Epidemiology, Academy of Military Medical Sciences, and Tong Yigang, School of Life Science and Technology, Beijing University of Chemical Technology. From the perspective of research direction, epidemiology is the most important direction in the field of NSFC-funded biosafety and the field with the most papers.

Table 2 NSFC papers on biosafety from 2001 to 2022 Main authors ' research fields (part)

Name	Unit	Research Direction
Yang Ruifu	State Key Laboratory of Pathogenic Microorganisms,	Microevolution and pathogenic mechanism of pathogenic bacteria, pathogenic microorganism detection technology (biosensors and biochips) and microbial forensic medicine
Zhou Yusen	Institute of Microbial Epidemiology,	Studies on etiology and immunology of hepatitis virus and emerging infectious diseases
Cao Wuchun	Academy of Military Medical Sciences	Epidemiology and Control of Infectious Diseases, Application of Spatial Information Technology in Public Health and Molecular Epidemiology
Zhou Dongsheng		Research on Medical Microorganisms and Biosafety
Tong Yigang	School of Life Science and Technology, Beijing University of Chemical Technology	Biosafety, microbiology, genomics, bioinformatics, high-throughput sequencing, super resistant bacteria, bacteriophage
Fan Huahao		Drug screening of emerging infectious diseases (coronavirus, enterovirus) and molecular mechanism of virus infection in host
Liu Wei	Institute of Microbial Epidemiology,	Epidemiology of new vector-borne infectious diseases
Zuo Shuqing	Academy of Military Medical Sciences	Molecular epidemiological studies
Song Yajun		Basic Medicine
Chen Bin	Yunnan Agricultural University	Study on Integrated Pest Management

* All authors ' research directions are based on public data query.

2.4 Research hotspots and frontier trend analysis

2.4.1 High frequency keywords

Using CiteSpace software, nodes select ' keywords ' and draw a keyword co-occurrence network map (Figure 3). The frequency of each keyword is derived, and the frequency of high-frequency keywords can reflect the research hotspots in a certain subject field. There are 525 nodes and 708 connections in the map, and the network density is 0.0051. Each circle in the map represents a keyword. The size of the circle represents the number of occurrences of the keyword. The color of the circle and the line represents the distance of time. Red indicates that in recent years, gray indicates that the time is long. Because the theme of this study is biosafety, excluding the keyword ' biosafety ', the top 10 keywords are bioterrorism, laboratory, safety management, gene drift, dengue virus, identification, ecological risk, infectious disease and biotechnology.

From the perspective of the relationship between keywords, bioterrorism mainly focuses on the early warning, monitoring and evaluation of biological attacks and the establishment of corresponding security management mechanisms. Gene drift mainly focuses on its impact on the ecological environment and risk assessment. Dengue virus mainly focuses on its viral sequence analysis. Biotechnology mainly focuses on the application of genetic engineering, metabolic engineering and other technologies.

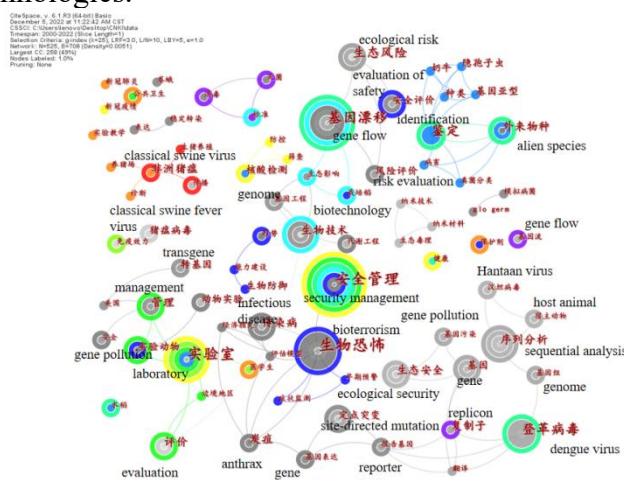


Figure 3 Keyword co-occurrence graph of NSFC papers in the field of biosafety from 2001 to 2022

The larger the betweenness centrality value of the keyword node, the greater its influence in the entire network and the more important it is. The analysis showed that the top five keywords of betweenness centrality were biosafety (0.46), gene (0.05), bioterrorism (0.03), safety management (0.03), and dengue virus (0.03). See Table 3 for details.

Table 3 Keyword clustering of biosafety NSFC papers from 2001 to 2022

Cluster	Clustering words	Keywords	Silhouette value
#0	Biosafety	Protective agents, climate change, gene flow, ultrafine particles	1
#1	Bioterrorism	Anthrax, defense mechanisms, symptom surveillance, terrorist attacks	1
#2	Replicator	Translation, dengue virus, genome, sequence analysis	0.978
#3	Experimental animals	Knowledge, America, Occupational Exposure, Veterinary	0.994
#4	Sunshine	Antiprotease peptides, histopathology, feeding behavior, bioassay	1
#5	Evaluation	Genetic engineering, public health emergencies, border areas, laboratories	0.961
#6	Ecological risk	Risk assessment, introgression hybridization, transgenic escape, plant growth	0.993

The emergence of keywords can detect the development frontier and research trend of a certain research field. The high-frequency keywords emerging in different years represent the research direction that emerged in this period and received widespread attention, thus further reflecting its evolution process. The greater the strength of the burst, the more obvious the frontier trend of research in this field. Using CiteSpace to draw the keyword emergence map, see Figure 7. The length of the red bar indicates the age of the keyword, which is the research frontier of this period. It can be seen that the research frontiers of NSFC papers in the field of biosafety from 2003 to 2012 mainly involve ecological risk, swine fever virus, ecological safety, sequence analysis, anthrax toxin, gene, dengue virus, infectious diseases, transgenic, risk assessment and anthrax. From 2015 to 2022, the research frontiers in this field mainly focus on identification, alien species, safety management, laboratory and medical examination. The top six keywords were bioterrorism (intensity of 3.39), identification (intensity of 3.25), dengue virus (intensity of 2.97), laboratory (intensity of 2.91), ecological security (intensity of 2.19), and ecological risk (intensity of 2.15).

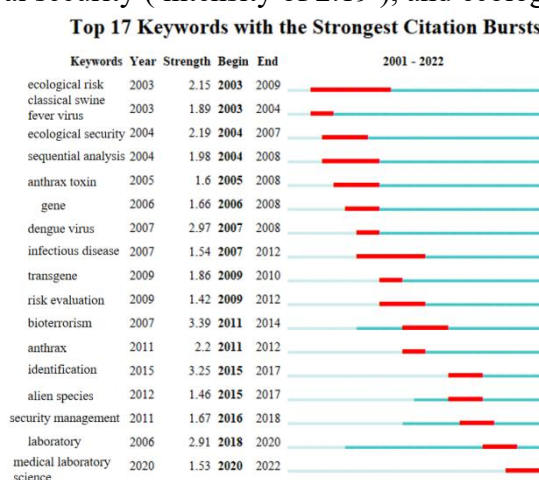


Figure 4 Keywords map of NSFC papers on biosafety from 2001 to 2022

3. Discussions

3.1 Research funding

From the publication of NSFC papers in the field of biosafety from 2001 to 2022, it can be seen that the overall number of publications is on the rise. Under the background of the interweaving of traditional and non-traditional security at home and abroad and the frequent occurrence of biosafety incidents, it is necessary for the NSFC to continue to guide scholars to pay attention to the field of biosafety, which is inseparable from the social attention and the domestic security situation. It also indirectly shows that one of the tendencies of NSFC support fund projects is to focus on the actual needs of social development and public attention.

From the perspective of research institutions, There are relatively few NSFC-funded institutions in the overall biosafety research field, and the links between institutions are insufficient. It shows that the NSFC funded projects generally focus on whether the previous research foundation of the undertaking unit is deep and whether the undertaking unit can complete the project on schedule. At the same time, it also shows that the NSFC funding unit in the field of biosafety is too concentrated in the National Key Laboratory of Pathogenic Microbial Biosafety, and the unit focuses on the research and development of infectious diseases and biotechnology, which is not conducive to the comprehensive development and diversified research of the whole biosafety discipline and field.

From the perspective of the authors, a research team with Tong Yigang, Yang Ruifu, Zhou Yusen and Cao Wuchun as the core has been basically formed. From the perspective of the research direction of its core members, it mainly focuses on the epidemiology of infectious diseases. From the perspective of the author 's cooperation map, Tong Yigang 's team members have the most

contacts with Cao Wuchun and Zhou Yusen 's team at the same time, forming a certain degree of interaction and strong combination.

3.2 Research hotspots and frontiers

3.2.1 Research focus

From the perspective of research keywords, in addition to microbial resistance, bioterrorism, laboratory, safety management, gene drift, dengue virus, identification, ecological risk, infectious diseases, biotechnology and other biosafety fields are basically covered. From the keyword clustering ranking, the proportion of funding for biosafety and bioterrorism is large. Specific to the subdivision field, prevent major emerging infectious diseases such as new corona and other emerging infectious diseases, establish evaluation models and estimate their impact ; the research, development and application of biotechnology focus on the research and development of new technologies such as genetic engineering and metabolic engineering. The biosafety management of pathogenic microorganism laboratory focuses on experimental animals, risk assessment and management. The safety management of human genetic resources and biological resources focuses on genes, gene pollution, replicons, species variation caused by gene drift, the impact on the ecological environment and the ecological risks and safety assessment. Prevention of Alien Invasion and Biodiversity Conservation focuses on the identification of alien species, fungal taxonomy and disease ; prevention of bioterrorism attacks and prevention of biological weapons threats focus on establishing a security management system, monitoring related symptoms, and early warning. However, there is a lack of papers on funding projects related to microbial resistance, and no relevant keywords have been found, indicating that NSFC should increase its support for research related to microbial resistance.

3.2.2 Research hotspots

Key words around biosafety are mainly such as protective agents, climate change, gene flow, etc., focusing on technology research and development and the interpretation of a phenomenon under certain conditions. The key words of bioterrorism are anthrax, defense mechanism, etc., indicating that the anthrax incident in the United States is the starting point for people to pay attention to biosafety, and the focus is on the research of security mechanism and early warning mechanism. Replicon keywords include translation, genome, sequence analysis, etc., focusing on DNA molecular technology research. Focusing on the key words of experimental animals, such as knowledge, occupational exposure, etc., the focus tends to be on risk management in animal experiments. Around the sunshine keywords, there are anti-protease peptides, histopathology, bioassay, etc., focusing on biodiversity technology research. The evaluation keywords include genetic engineering, public health emergencies, etc., focusing on the risk assessment of technology and emergencies. Around the ecological risk keywords, there are analysis and evaluation, Zhejiang infiltration hybridization, etc., focusing on the impact of biotechnology application on ecology.

3.2.3 Research changes and frontiers

It can be seen from the changes in keyword density and timeline that biosafety has always been the focus of NSFC funding. According to the time sequence and intensity, 2003-2009 focused on ecological risks, 2004-2007 focused on ecological security, 2007-2008 focused on dengue virus, 2011-2014 focused on anthrax incidents, 2011-2014 focused on bioterrorism, 2015-2017 focused on identification, 2018-2020 focused on laboratories.

In contrast, the duration or intensity of CSFV, sequence analysis, anthrax toxins, infectious diseases, risk assessment, and exotic species were shorter or lower, indicating that close to social hot events, attention to technological development trends and national strategic needs is one of the prerequisites for NSFC funding.

4. Summary

It is found that the NSFC-funded institutions are concentrated in the National Key Laboratory of Pathogenic Microorganism Biosafety and a few influential teams, and the funded fields are funded in addition to microbial resistance. The research direction focuses on social hot events, technological development trends and national strategic needs. However, the current NSFC funding in the field of biosafety is concentrated with a few institutions and teams, which is not conducive to the diversified development of the entire biosafety research field. Secondly, the funding for microbial resistance is insufficient. At present, microbial resistance is one of the major problems that need to be solved urgently in the field of global public health. It is urgent and serious to curb microbial resistance. Therefore, it is suggested that the NSFC project guidelines and directions should increase the special projects related to microbial resistance and increase the funding for microbial resistance technology research. In the selection of projects, we should appropriately enrich the research team, research institutions and research directions, and give preference to young talents and multi-agency joint application projects.

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