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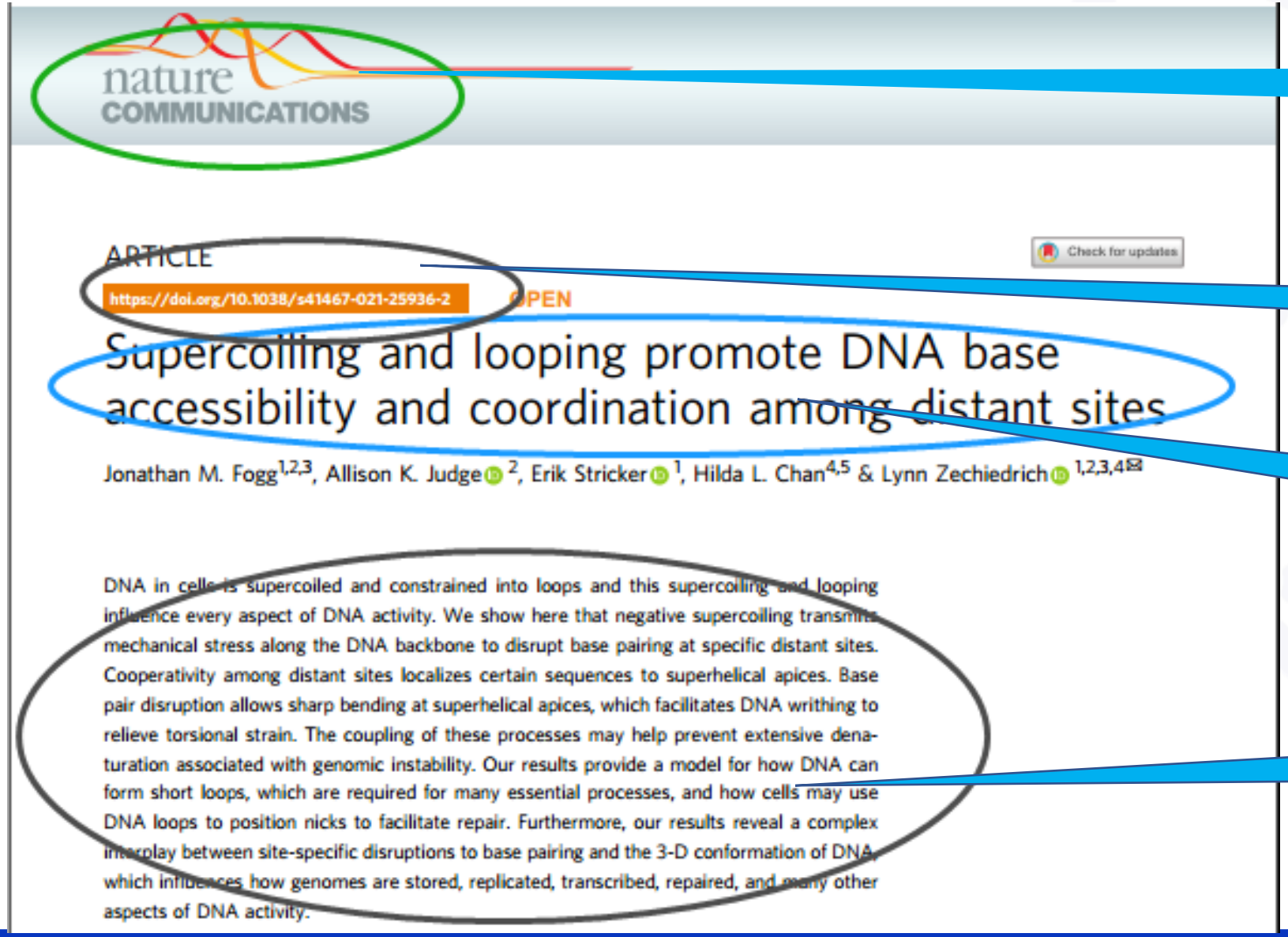

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ARTICLE

https://doi.org/10.1038/s41467-021-25936-2 OPEN

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Supercoiling and looping promote DNA base accessibility and coordination among distant sites

Jonathan M. Fogg[1,2,3], Allison K. Judge[2], Erik Stricker[1], Hilda L. Chan[4,5] & Lynn Zechiedrich[1,2,3,4]✉

DNA in cells is supercoiled and constrained into loops and this supercoiling and looping influence every aspect of DNA activity. We show here that negative supercoiling transmits mechanical stress along the DNA backbone to disrupt base pairing at specific distant sites. Cooperativity among distant sites localizes certain sequences to superhelical apices. Base pair disruption allows sharp bending at superhelical apices, which facilitates DNA writhing to relieve torsional strain. The coupling of these processes may help prevent extensive denaturation associated with genomic instability. Our results provide a model for how DNA can form short loops, which are required for many essential processes, and how cells may use DNA loops to position nicks to facilitate repair. Furthermore, our results reveal a complex interplay between site-specific disruptions to base pairing and the 3-D conformation of DNA, which influences how genomes are stored, replicated, transcribed, repaired, and many other aspects of DNA activity.

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Supercoiling and looping promote DNA base accessibility and coordination among distant sites

Jonathan M. Fogg[1,2,3], Allison K. Judge[2], Erik Stricker[1], Hilda L. Chan[4,5] & Lynn Zechiedrich[1,2,3,4]✉

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One of the properties of DNA that make it ideal as a medium for storing genetic information is its incredible stability, perhaps best illustrated by th
samples have been recovered and sequenc
300,000 years old[1–3]. Researchers have util
the rich data density of DNA for
information[4,5]. The bases that carry the ge
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two seemingly contradictory requirements: stable and pro
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some as short as 80 bp, have been detected in the cells of various organisms, including plants, humans, mice, and *C. elegans*[11–13]. Supercoiling and looping both play key roles in biology. Therefore, it is important to understand how they together modulate the properties of DNA.

施引位置

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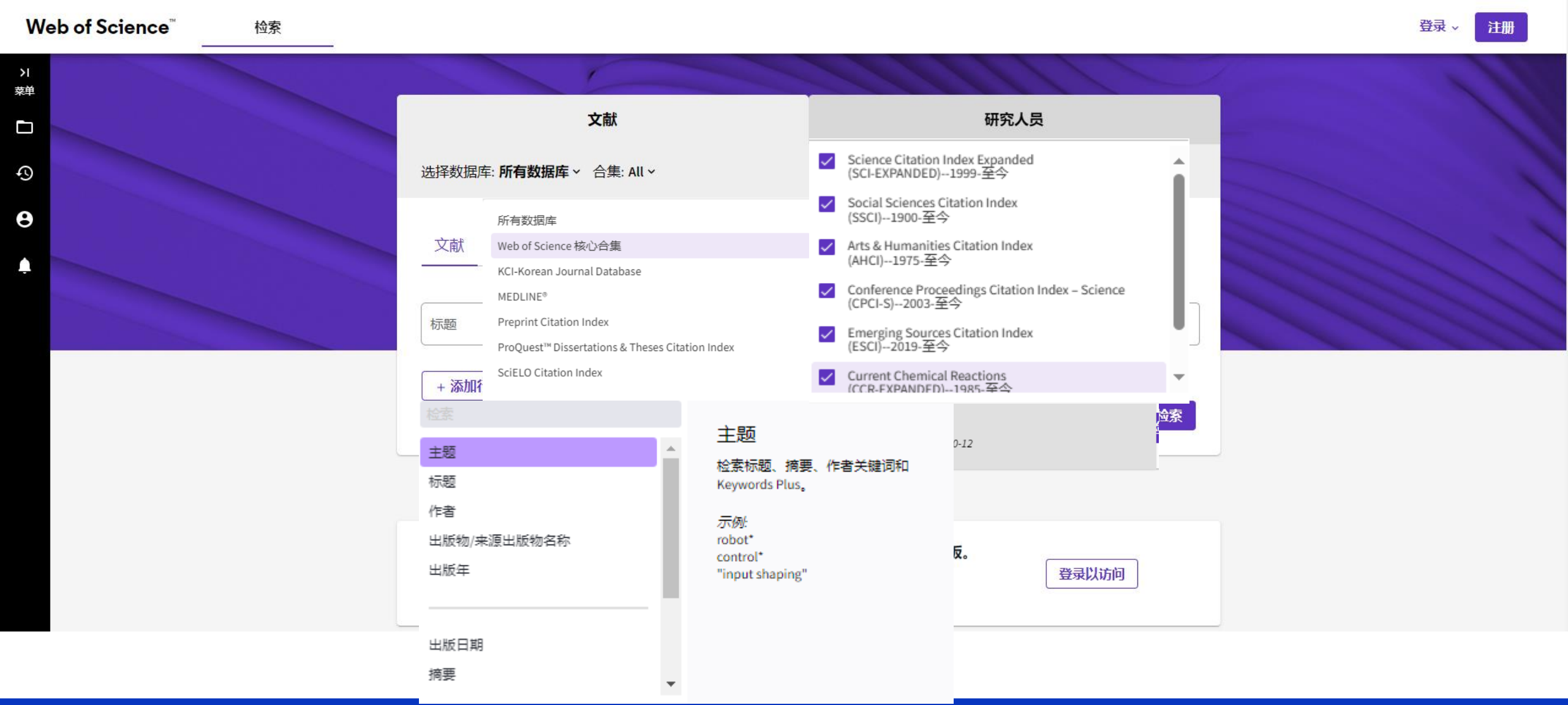
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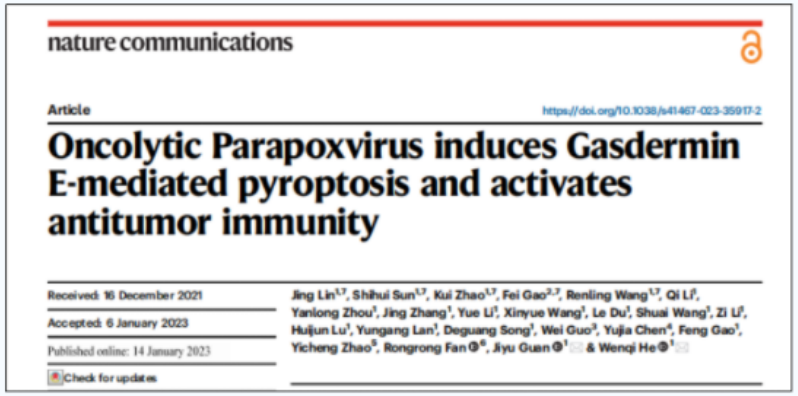
吉林大学动物医学学院动物病理学创新团队在溶瘤病毒抗肿瘤机制研究领域取得重要进展

2023年01月16日 11:33 动物医学学院

日前，吉林大学动物医学学院动物病理学研究团队在“溶瘤病毒抗肿瘤机制”研究领域取得重要进展，并于1月14日在国际知名综合期刊《Nature Communications》上发表了题为”Oncolytic Parapoxvirus induces Gasdermin E-mediated pyroptosis and activates antitumor immunity“（溶瘤性副痘病毒诱导Gasdermin E介导的焦亡并激活抗肿瘤免疫）的研究成果。论文第一完成单位为吉林大学，动物医学学院贺文琦教授、关继羽副教授为论文的共同通讯作者，动物医学学院在读博士生林静为第一作者（Nat Commun. 2023, 14: 224）。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Article

https://doi.org/10.1038/s41467-023-35917-2

Oncolytic Parapoxvirus induces Gasdermin E-mediated pyroptosis and activates antitumor immunity

Received: 16 December 2021

Accepted: 6 January 2023

Published online: 14 January 2023

Check for updates

Jing Lin[1,7], Shihui Sun[1,7], Kui Zhao[1,7], Fei Gao[2,7], Renling Wang[1,7], Qi Li[1], Yanlong Zhou[3], Jing Zhang[1], Yue Li[1], Xinyue Wang[1], Le Du[1], Shuai Wang[1], Zi Li[1], Huijun Lu[1], Yungang Lan[1], Deguang Song[1], Wei Guo[3], Yujia Chen[4], Feng Gao[1], Yicheng Zhao[5], Rongrong Fan[6], Jiyu Guan[1] & Wenqi He[1]

传统观点认为，溶瘤病毒（OV）介导的肿瘤杀伤是由于诱导肿瘤细胞发生凋亡所致，但细胞凋亡时处于免疫静息状态的理论，与OV可触发较为强烈的抗肿瘤炎症反应现象相矛盾，这是该领域尚未阐明的科学问题。

该团队的研究发现，溶瘤性副痘病毒（ORFV）可诱导肿瘤细胞及组织发生Gasdermin E（GSDME）介导的的细胞焦亡。ORFV疗法可通过抑制GSDME蛋白的泛素化降解，增强GSDME的胞内蛋白水平，进而ORFV诱导GSDME裂解活化，促进细胞焦亡发生；肿瘤细胞焦亡将CTL募集到肿瘤微环境中，同时释放炎症介质，进一步激活抗肿瘤免疫应答，重塑了免疫微环境，使“冷”肿瘤转化为“热”肿瘤，显著敏感化免疫“冷”肿瘤对免疫检查点阻断疗法的应答；利用病毒重组技术构建的毒力基因缺失重组病毒，在获得良好生物安全性的同时维持了其抗肿瘤能力（如图所示）。

吉林大学动物医学学院动物病理学研究团队在“溶瘤病毒抗肿瘤机制”研究领域取得重要进展，并于1月14日在国际知名综合期刊《Nature Communications》上发表了题为”Oncolytic Parapoxvirus induces Gasdermin E-mediated pyroptosis and activates antitumor immunity“的研究成果。

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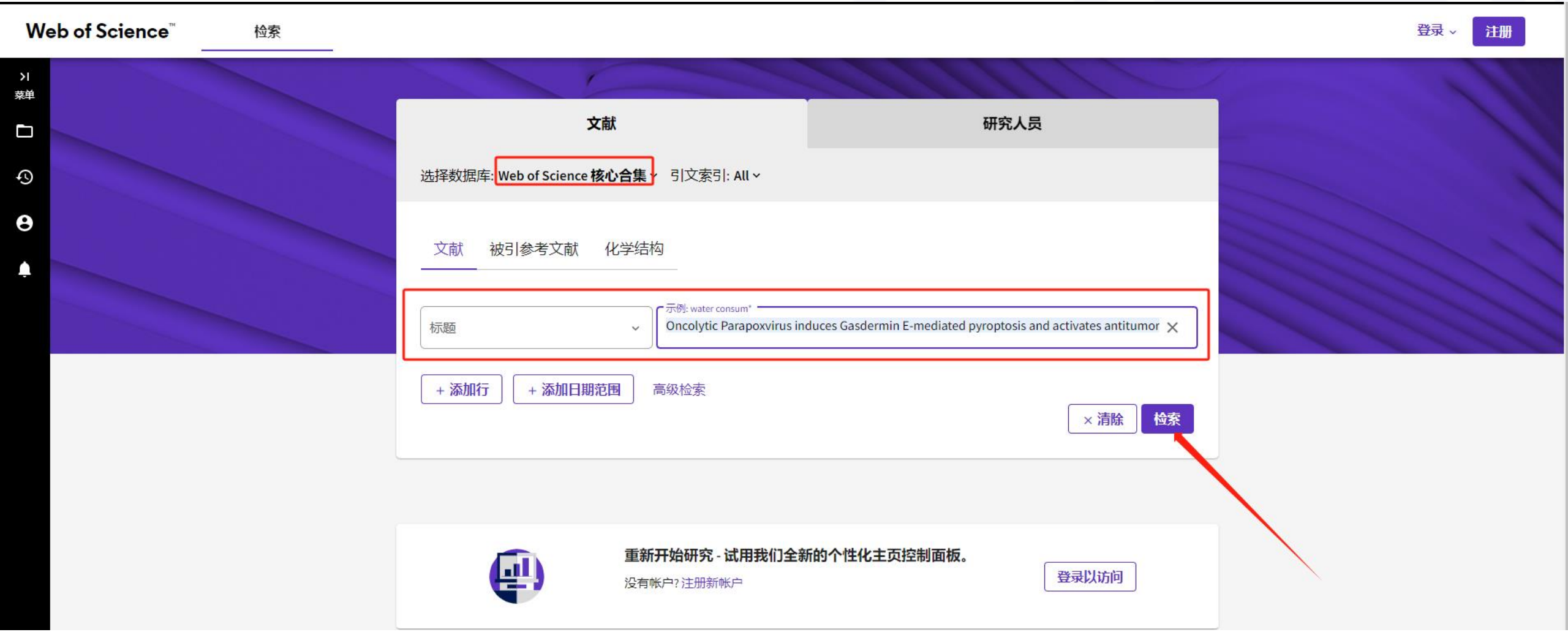

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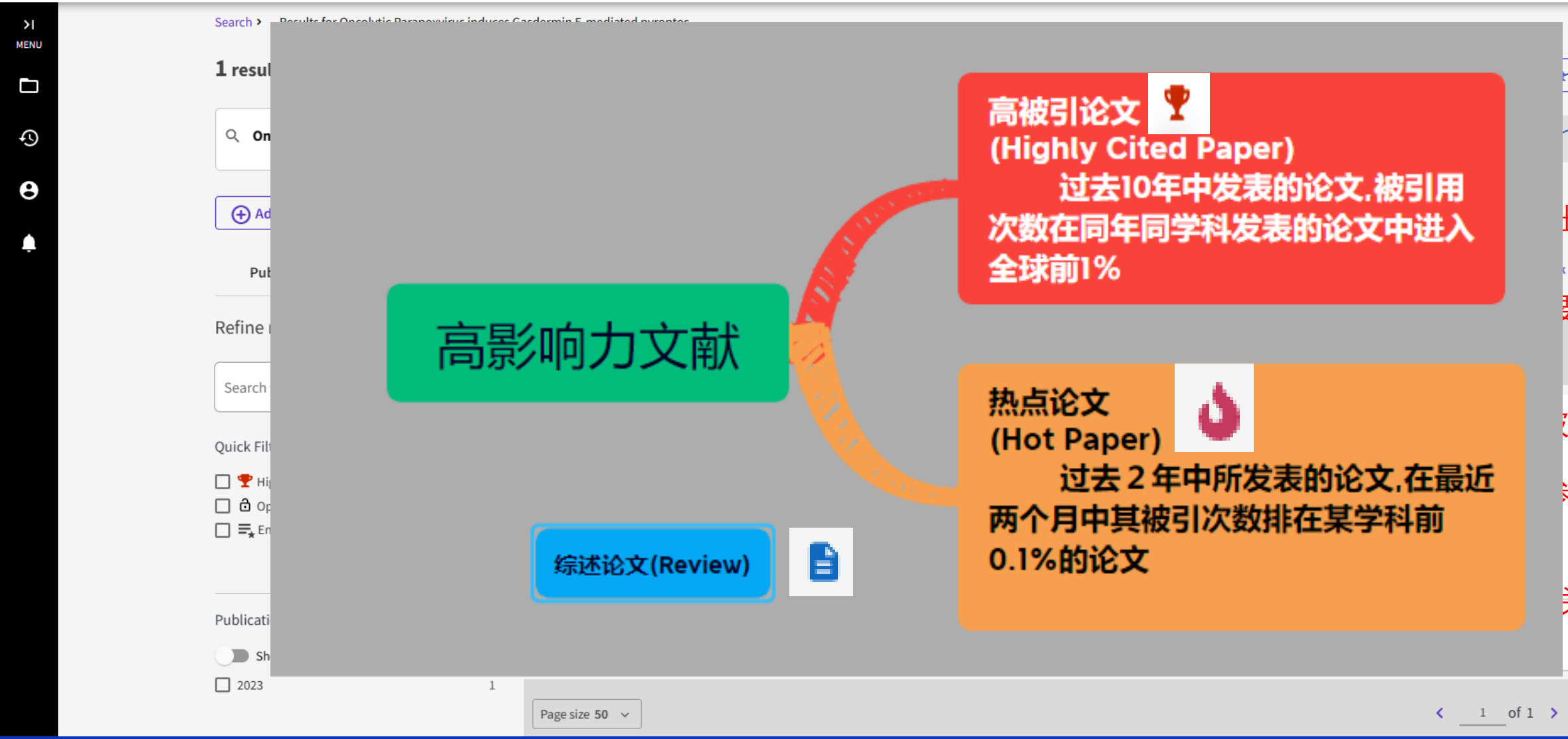

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Abstract

The advantage of oncolytic viruses (OV) in cancer therapy is their dual effect of directly killing tumours while prompting anti-tumour immune response. Oncolytic parapoxvirus ovis (ORFV) and other OVs are thought to induce apoptosis, but apoptosis, being the immunogenically inert compared to other types of cell death, does not explain the highly inflamed microenvironment in OV-challenged tumors. Here we show that ORFV and its recombinant therapeutic derivatives are able to trigger tumor cell pyroptosis via Gasdermin E (GSDME). This effect is especially prominent in GSDME-low tumor cells, in which ORFV-challenge pre-stabilizes GSDME by decreasing its ubiquitination and subsequently initiates pyroptosis. Consistently, GSDME depletion reduces the proportion of intratumoral cytotoxic T lymphocytes, pyroptotic cell death and the success of tumor ORFV virotherapy. In vivo, the OV preferentially accumulates in the tumour upon systemic delivery and elicits pyroptotic tumor killing. Consequentially, ORFV sensitizes immunologically 'cold' tumors to checkpoint blockade. This study thus highlights the critical role of GSDME-mediated pyroptosis in oncolytic ORFV-based antitumor immunity and identifies combinatorial cancer therapy strategies.

Oncolytic viruses are able to target tumours and thought to induce apoptosis while remodelling the tumour immune microenvironment. Here authors show in an oncolytic parapoxvirus ovis model that pyroptosis, a highly immunogenic Gasdermin-

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摘要

The advantage of oncolytic viruses (OV) in cancer therapy is their dual effect of directly killing tumours while prompting anti-tumour immune response. Oncolytic parapoxvirus ovis (ORFV) and other OVs are thought to induce apoptosis, but apoptosis, being the immunogenically inert compared to other types of cell death, does not explain the highly inflamed microenvironment in OV-challenged tumors. Here we show that ORFV and its recombinant therapeutic derivatives are able to trigger tumor cell pyroptosis via Gasdermin E (GSDME). This effect is especially prominent in GSDME-low tumor cells, in which ORFV-challenge pre-stabilizes GSDME by decreasing its ubiquitination and subsequently initiates pyroptosis. Consistently, GSDME depletion reduces the proportion of intratumoral cytotoxic T lymphocytes, pyroptotic cell death and the success of tumor ORFV virotherapy. In vivo, the OV preferentially accumulates in the tumour upon systemic delivery and elicits pyroptotic tumor killing. Consequentially, ORFV sensitizes immunologically 'cold' tumors to checkpoint blockade. This study thus highlights the critical role of GSDME-mediated pyroptosis in oncolytic ORFV-based antitumor immunity and identifies combinatorial cancer therapy strategies.

Oncolytic viruses are able to target tumours and thought to induce apoptosis while remodelling the tumour immune microenvironment. Here authors show in an oncolytic parapoxvirus ovis model that pyroptosis, a highly immunogenic Gasdermin-E-dependent cell death mechanism, is the dominant cell death pathway during virotherapy.

关键词

Keywords Plus: T-CELL INFILTRATION; DFNA5 GENE; VIRUS; TUMOR; IMMUNOTHERAPY; METHYLATION; CISPLATIN; BLOCKADE; CLEAVAGE; POXVIRUS

作者信息

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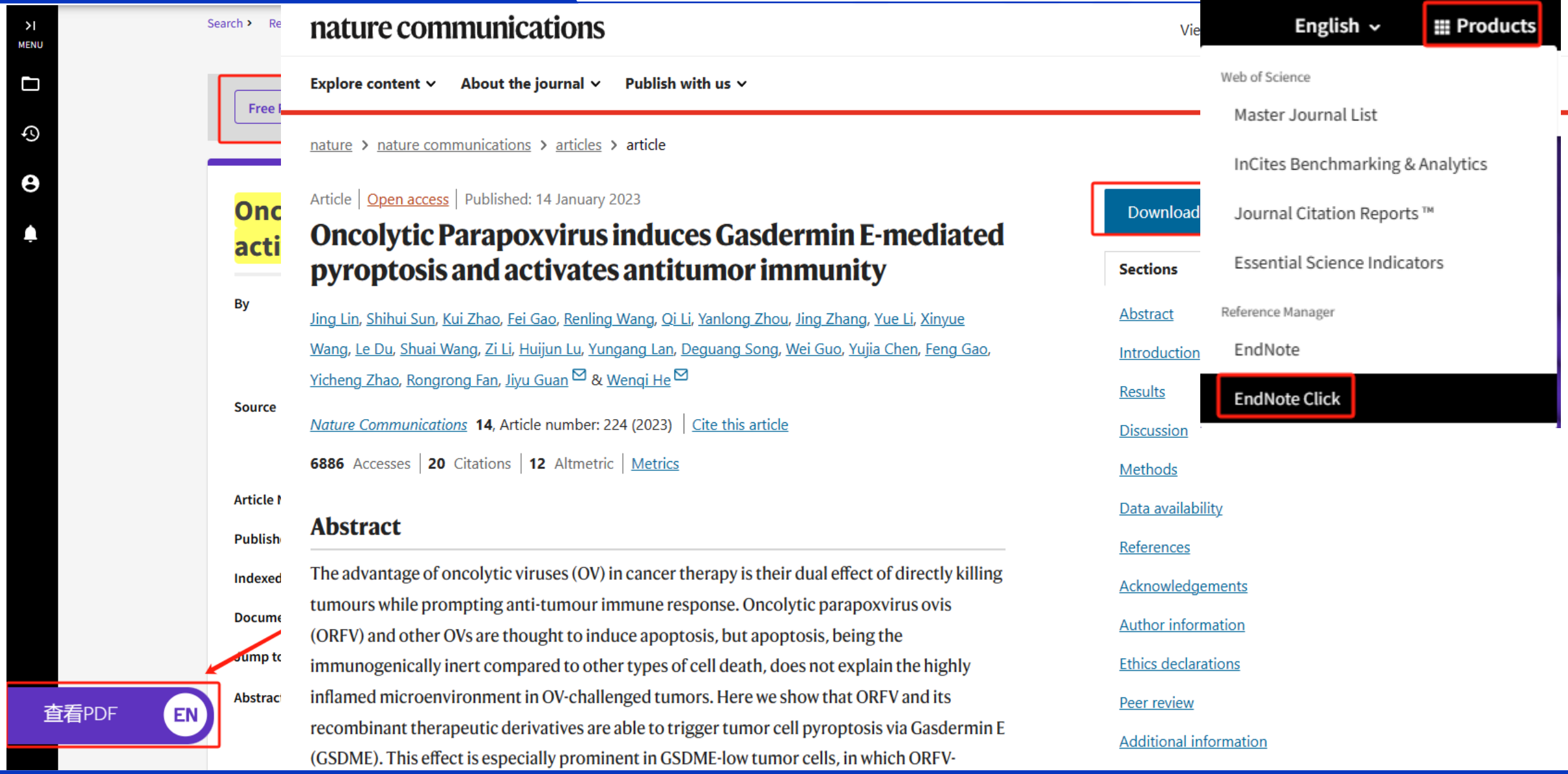
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Jing Lin, Shihui Sun, Kui Zhao, Fei Gao, Renling Wang, Qi Li, Yanlong Zhou, Jing Zhang, Yue Li, Xinyue Wang, Le Du, Shuai Wang, Zi Li, Huijun Lu, Yungang Lan, Deguang Song, Wei Guo, Yujia Chen, Feng Gao, Yicheng Zhao, Rongrong Fan, Jiyu Guan & Wenqi He
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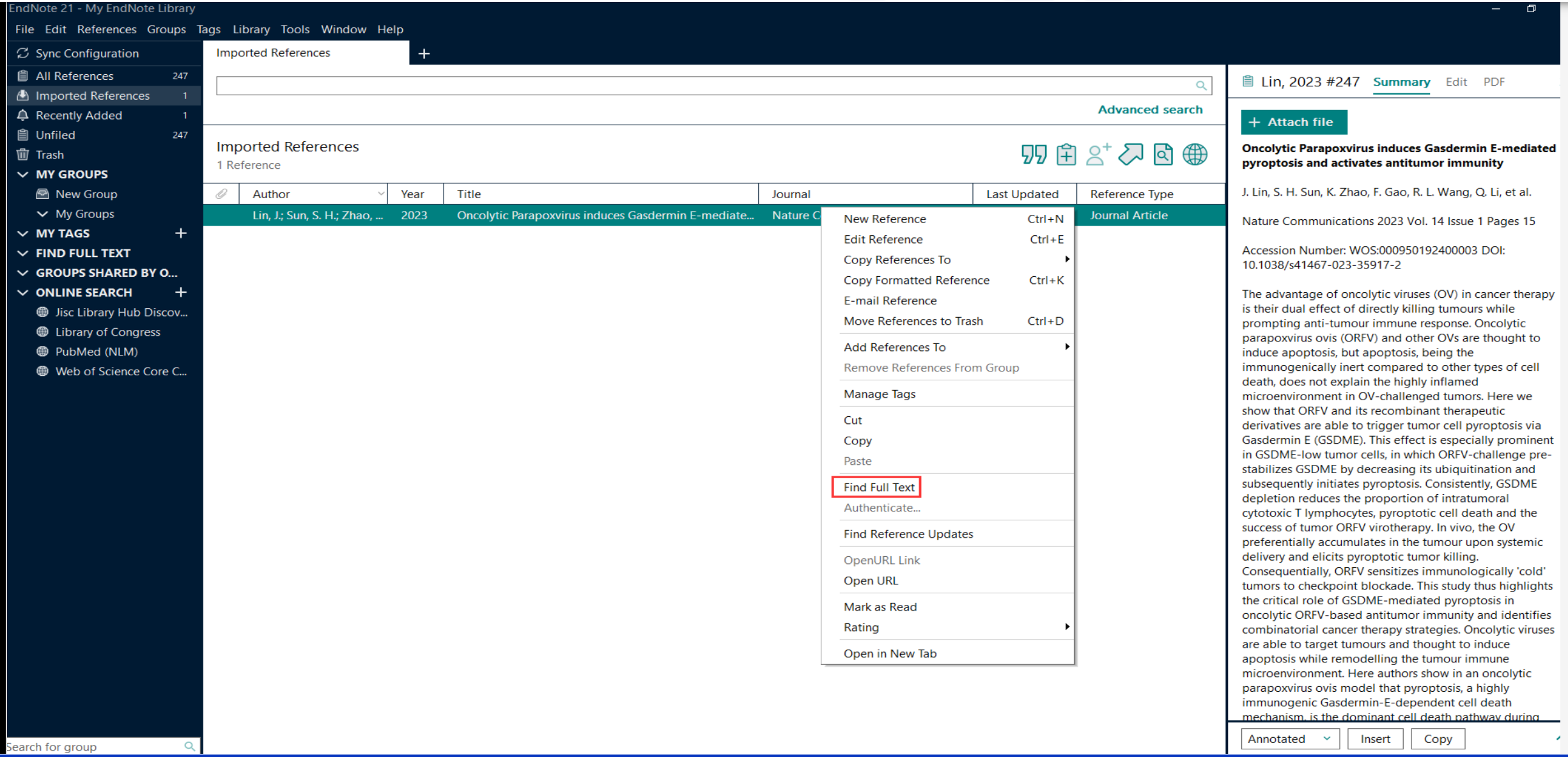
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J. Lin, S. H. Sun, K. Zhao, F. Gao, R. L. Wang, Q. Li, et al.
Nature Communications 2023 Vol. 14 Issue 1 Pages 15
Accession Number: WOS:000950192400003 DOI: 10.1038/s41467-023-35917-2
The advantage of oncolytic viruses (OV) in cancer therapy is their dual effect of directly killing tumours while prompting anti-tumour immune response. Oncolytic parapoxvirus ovis (ORFV) and other OVs are thought to induce apoptosis, but apoptosis, being the immunogenically inert compared to other types of cell death, does not explain the highly inflamed microenvironment in OV-challenged tumors. Here we show that ORFV and its recombinant therapeutic derivatives are able to trigger tumor cell pyroptosis via Gasdermin E (GSDME). This effect is especially prominent in GSDME-low tumor cells, in which ORFV-challenge pre-stabilizes GSDME by decreasing its ubiquitination and subsequently initiates pyroptosis. Consistently, GSDME depletion reduces the proportion of intratumoral cytotoxic T lymphocytes, pyroptotic cell death and the success of tumor ORFV virotherapy. In vivo, the OV preferentially accumulates in the tumour upon systemic delivery and elicits pyroptotic tumor killing. Consequentially, ORFV sensitizes immunologically 'cold' tumors to checkpoint blockade. This study thus highlights the critical role of GSDME-mediated pyroptosis in oncolytic ORFV-based antitumor immunity and identifies combinatorial cancer therapy strategies. Oncolytic viruses are able to target tumours and thought to induce apoptosis while remodelling the tumour immune microenvironment. Here authors show in an oncolytic parapoxvirus ovis model that pyroptosis, a highly immunogenic Gasdermin-E-dependent cell death
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Zhang, Hongyue ; Liu, Jiancong ; (...); Yu, Jihong

Published May 2020 | Materials Chemistry Frontiers

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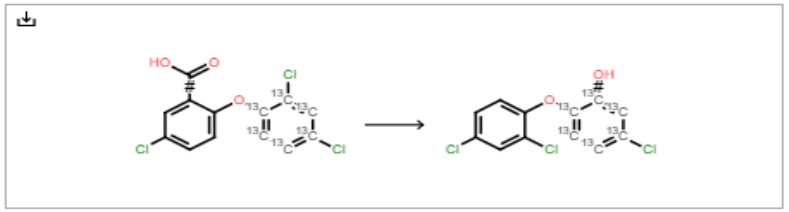

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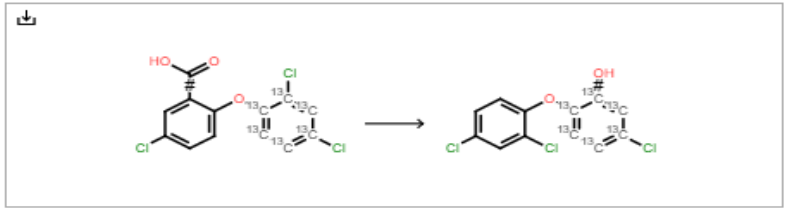

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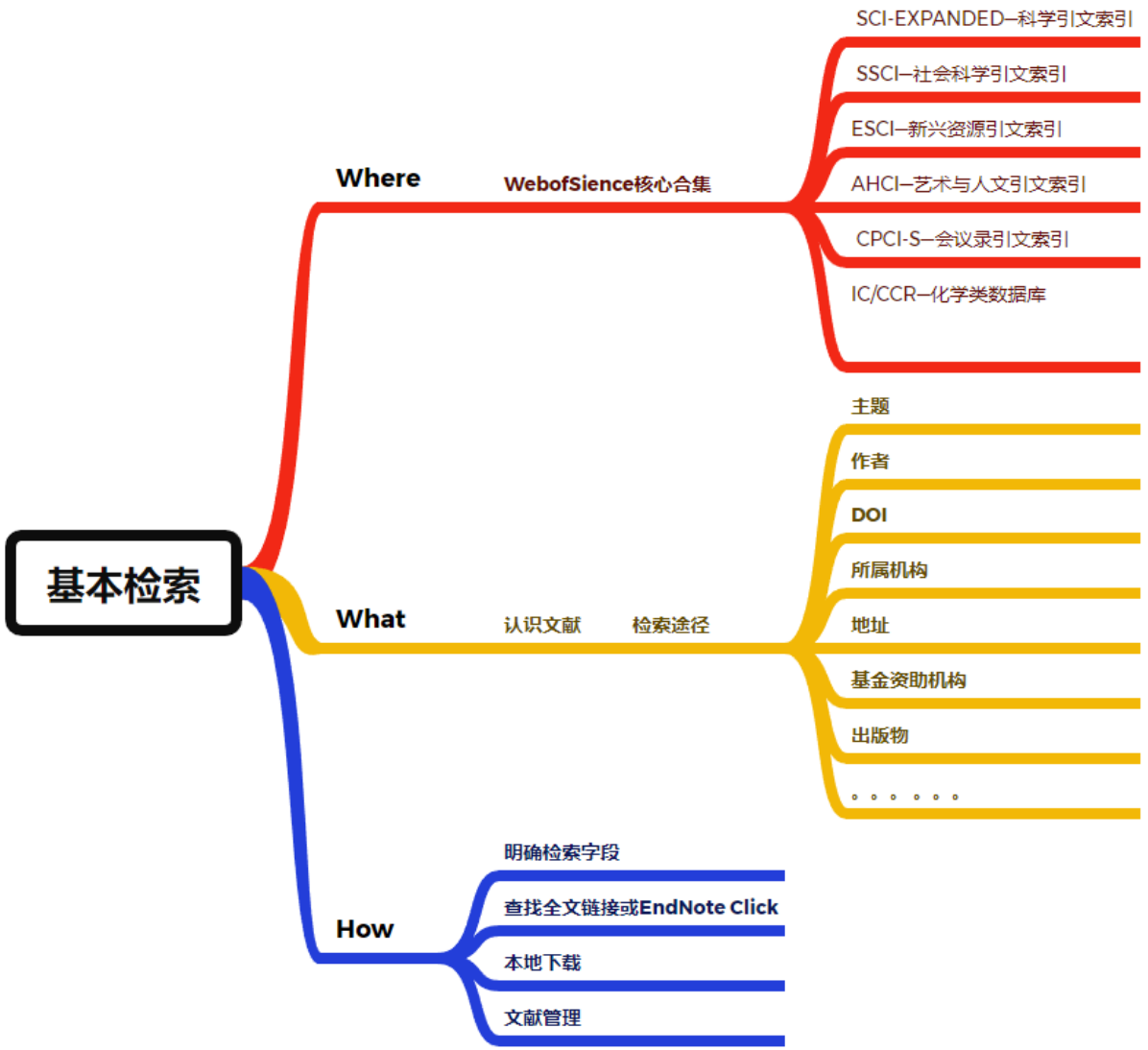
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Sun, CX; Li, BH; (...); Zhang, F

Dec 11 2019 | JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 141 (49) , pp.19221-19225

Light in the second near-infrared window, especially beyond 1500 nm, shows enhanced tissue transparency for high-resolution in vivo optical bioimaging due to decreased tissue scattering, absorption, and autofluorescence. Despite some inorganic luminescent nanoparticles have been developed to improve the bioimaging around 1500 nm, it is still a great challenge to synthesize organic molecules wit ... 显示更多

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Li, T; Zhang, FW; (...); Wu, LJ

Aug 2017 | ACS PHOTONICS 4 (8) , pp.2003-2010

The mechanism for the photoluminescence (PL) emission from gold nanoparticles has attracted considerable attention for many years. However, there is an important gap between small nanoclusters (similar to 2 nm) and larger plasmonic particles (similar to 50 nm). In this work, using defocused imaging technique, we investigate the PL properties of gold nanospheres (15-20 nm in diameter) on a singl ... 显示更多

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Apr 28 2022 | RSC ADVANCES 12 (21) , pp.13464-13471

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End-to-end gold nanorod dimers provide unique plasmonic hotspots with extremely large near-field enhancements in the gaps. Thereby they are beneficial in a wide range of applications, such as enhancing the emissions from ultra-weak emitters. For practical purposes, synthesis of gold nanorod dimers with high yield, especially on the substrates, is essential. Here, we demonstrate two controllable ... 显示更多

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Jul 7 2019 | CHEMICAL COMMUNICATIONS 55 (53) , pp.7707-7710

An effective strategy for regioselective modification and directional assembly of anisotropic nanoparticles is demonstrated to explore the electric field enhancement in assembled gold nanobipyramids compared with gold nanorods. The well-defined secondary plasmonic hot spots between the coupled gold nanobipyramids exhibit the capability for single molecule detection.

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3 Plasmonic Enhancement of Two-Photon Excited Luminescence of Gold Nanoclusters

Pniakowska, A and Olesiak-Banska, J

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1 DNA origami based assembly of gold nanoparticle dimers for surface-enhanced Raman scattering

Thacker, VV; Herrmann, LO; (...); Keyser, UF

Mar 2014 | NATURE COMMUNICATIONS 5

Plasmonic sensors are extremely promising candidates for label-free single-molecule analysis but require exquisite control over the physical arrangement of metallic nanostructures. Here we employ self-assembly based on the DNA origami technique for accurate positioning of individual gold nanoparticles. Our innovative design leads to strong plasmonic coupling between two 40 nm gold nanoparticles ... 显示更多

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Wang, YQ; Yan, B and Chen, LX

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1 Recent Progress of Magnetically Actuated DNA Micro/Nanorobots

Liu, FY; Liu, XM; (...); Arai, T

2022 | CYBORG AND BIONIC SYSTEMS 2022 , pp.1-12

In the past few decades, the field of DNA origami-based micro/nanotechnology has developed dramatically and spawned attention increasingly, as its high integrality, rigid structure, and excellent resistance ability to enzyme digestion. Many two-dimensional and three-dimensional DNA nanostructures coordinated with optical, chemical, or magnetic triggers have been designed and assembled, extensiv ... 显示更多

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2 Recent Progress in Surface-Enhanced Fluorescence Using Gold Nanorods

Catingan, SD and Moores, A

Jan 2024 (在线发表) | ACS APPLIED NANO MATERIALS

Plasmonic nanoparticles have been intensely used in research because they possess powerful optical properties. Gold nanorods (Au NRs), in particular, feature the interesting ability to absorb and scatter light in the near-infrared region through their longitudinal localized surface plasmon resonance. This property is particularly interesting in biology because these wavelengths are associated w ... 显示更多

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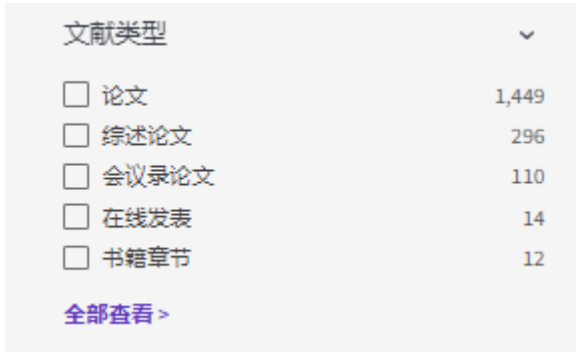
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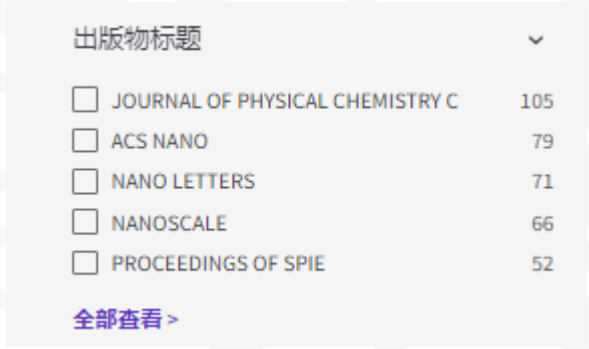
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Intrinsic and well-defined second generation hot spots in gold nanobipyramids versus gold
Pardehkhorram, R; Bonaccorsi, S; (...); Gooding, JJ
Jul 7 2019 | CHEMICAL COMMUNICATIONS 55 (53) , pp.7707-7710
An effective strategy for regioselective modification and directional assembly of anisotropic nanoparticles is demonstrated to explore the electric field enhancement in assembled gold nanobipyramids compared with gold nanorods. The well-defined secondary plasmonic hot spots between the coupled gold nanobipyramids exhibit the capability for single molecule detection.
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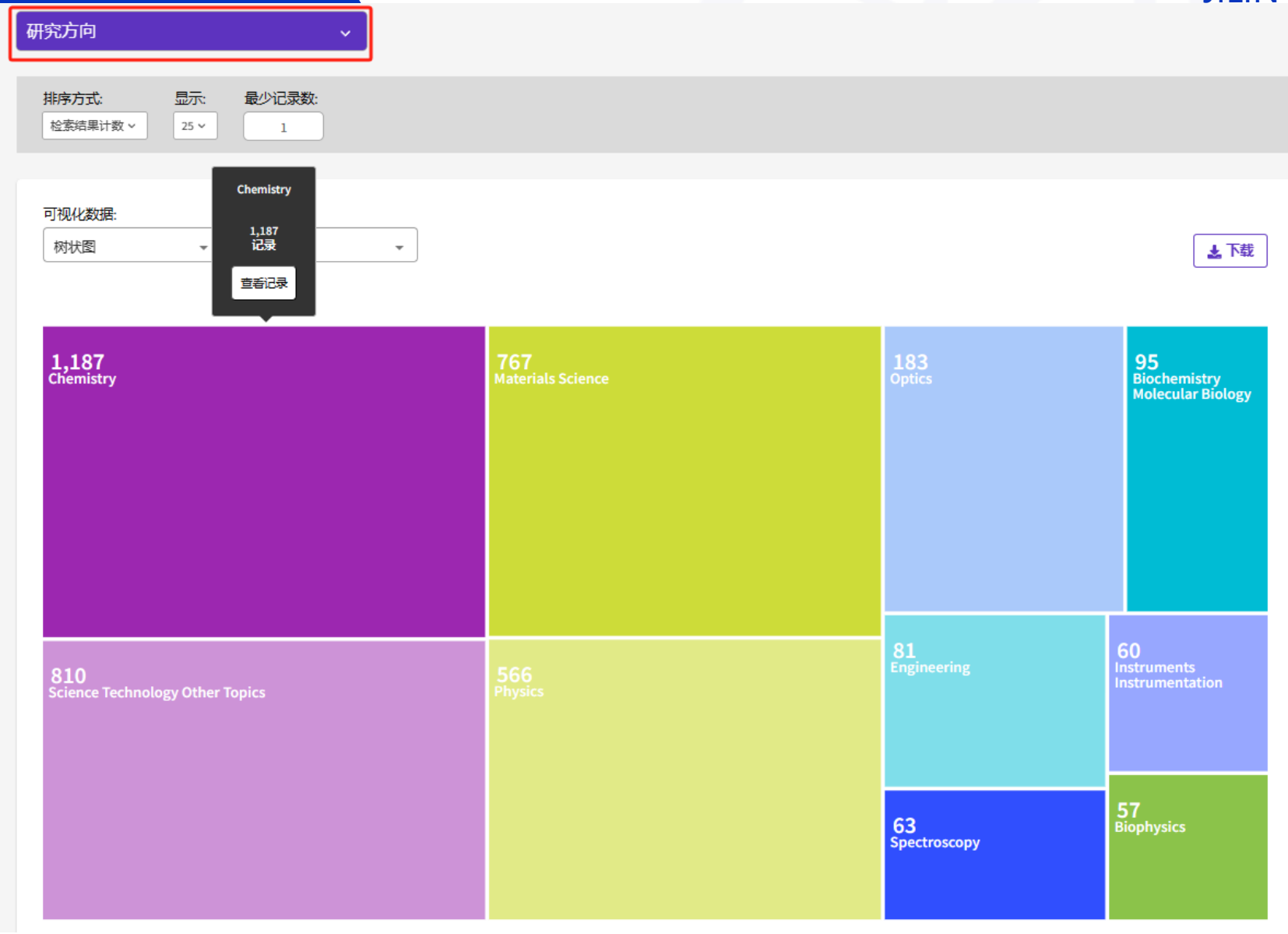
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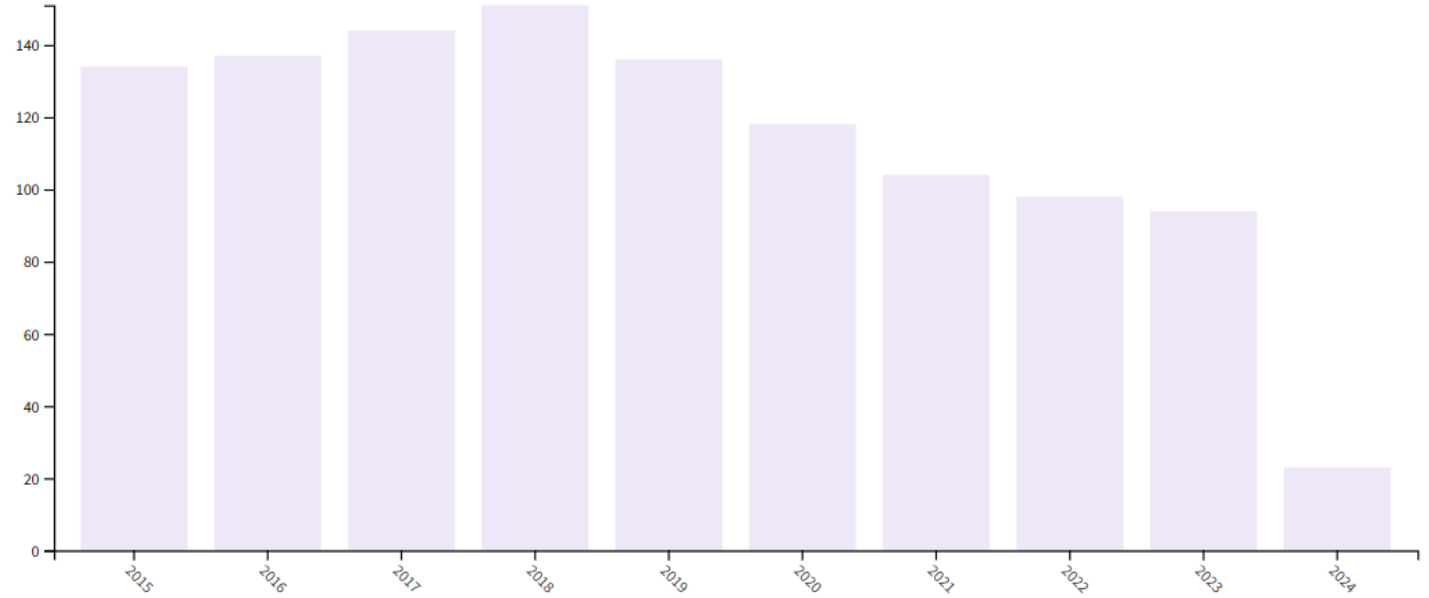

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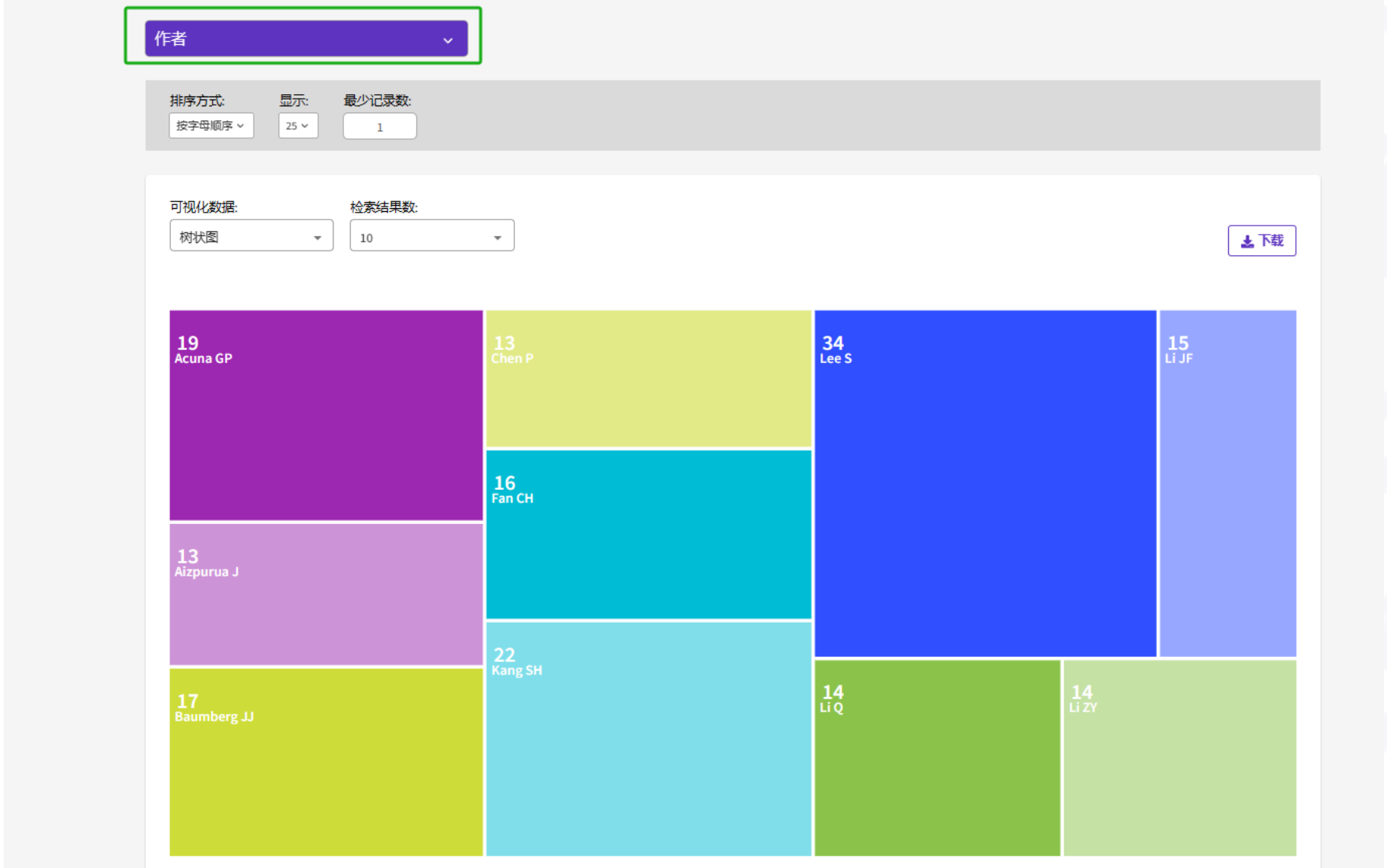
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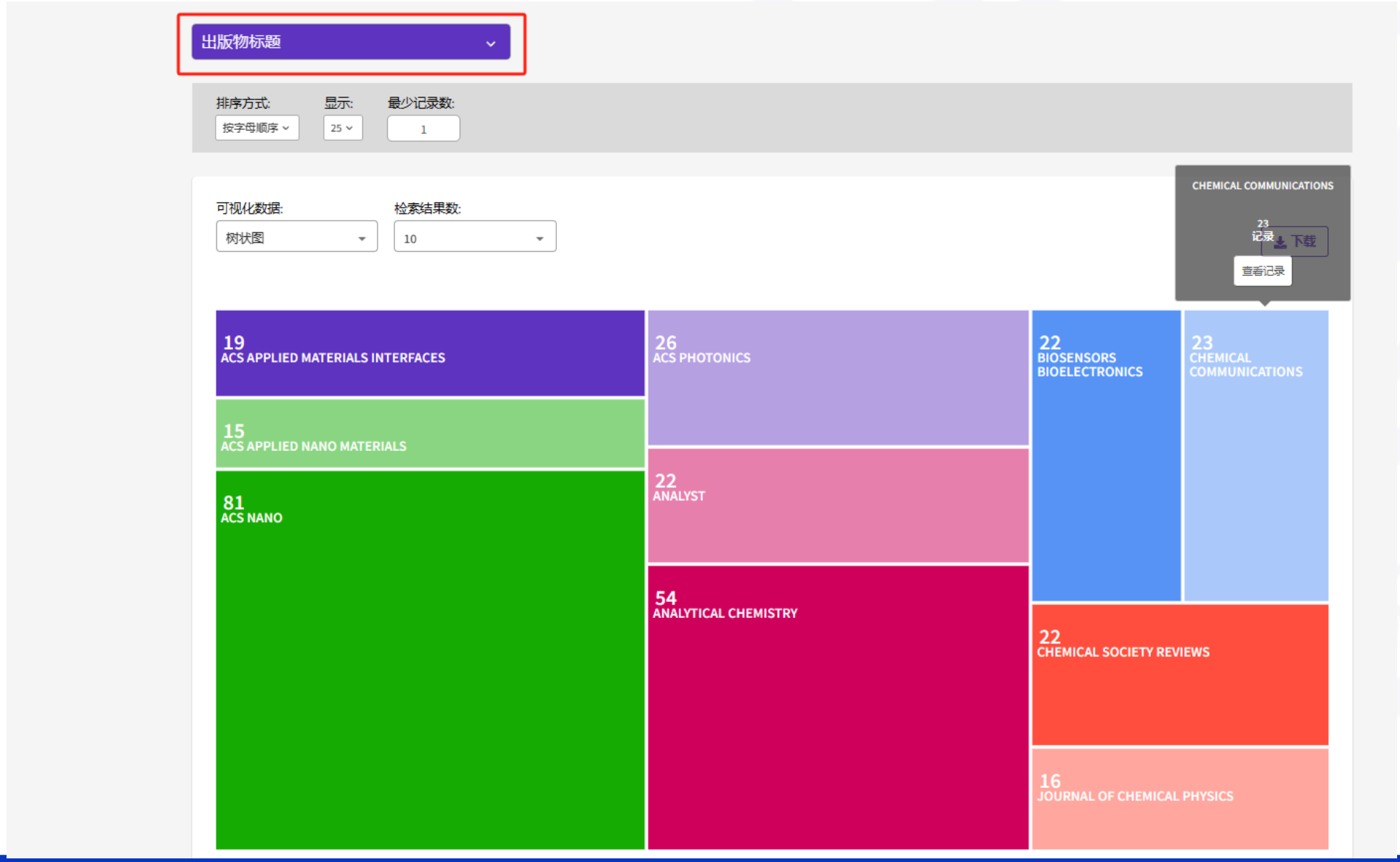
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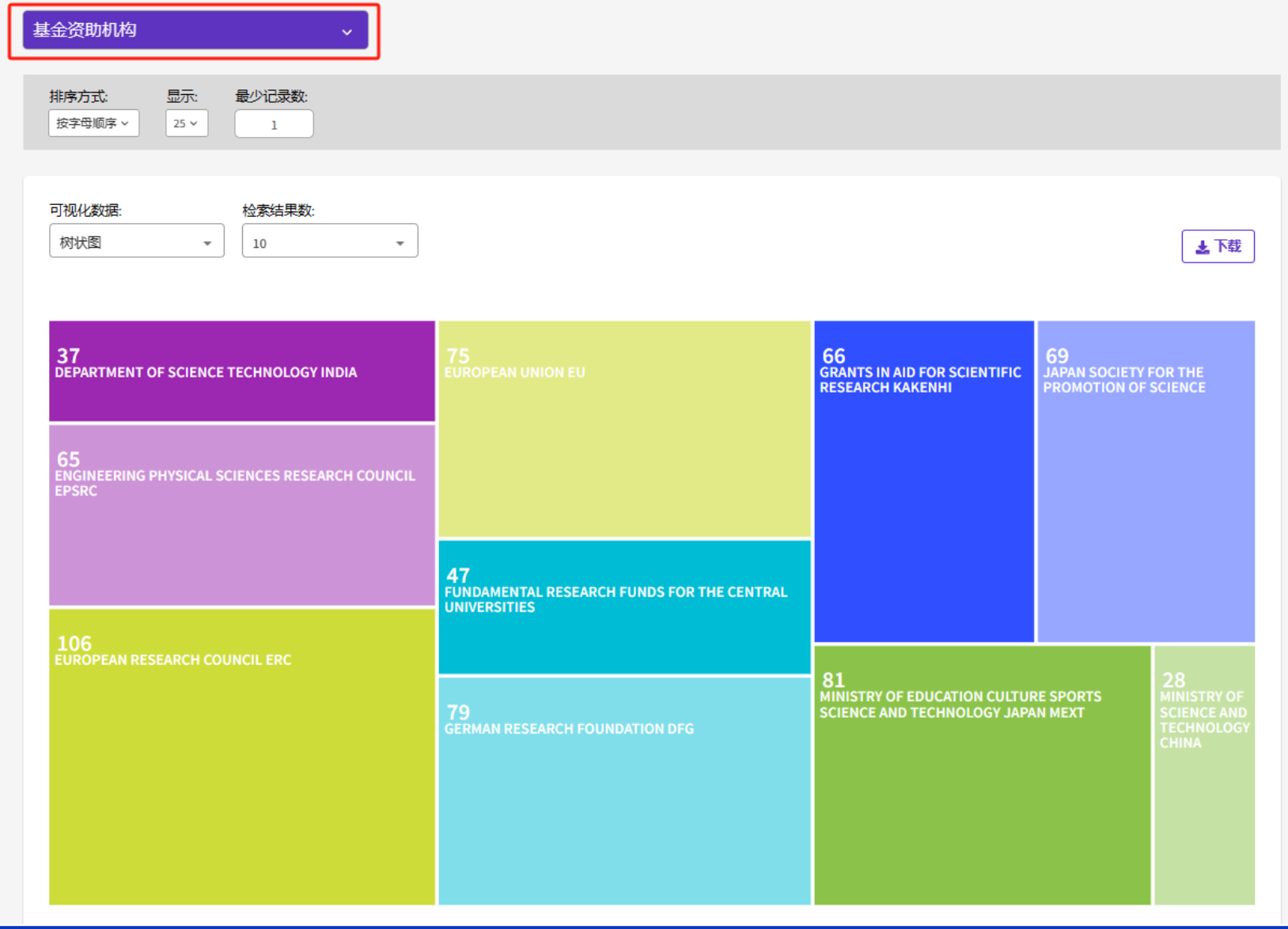
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1 One-Dimensional Metal Nanostructures: From Colloidal Syntheses to Applications

Huo, D; Kim, MJ; (...); Xia, YN

Aug 14 2019 | CHEMICAL REVIEWS 119 (15) , pp.8972-9073

This Review offers a comprehensive review of the colloidal synthesis, mechanistic understanding, physicochemical properties, and applications of one-dimensional (1D) metal nanostructures. After a brief introduction to the different types of 1D nanostructures, we discuss major concepts and methods typically involved in a. colloidal synthesis of 1D metal nanostructures, as well as the current mec ... 显示更多

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2 Gold nanorods-based hybrids with tailored structures for photoredox catalysis: fundamental science, materials design and applications

Han, C; Qi, MY; (...); Xu, YJ

Aug 2019 | NANO TODAY 27 , pp.48-72

Gold nanorods (Au NRs) have received extensive attention owing to their extremely attractive applications in photoredox catalysis, plasmon-enhanced spectroscopy, biomedical technologies and optoelectronic devices. Enabled by the unique and tunable surface plasmon resonance (SPR), anisotropic Au NRs can interact with and harvest incident light covering the much of the solar spectrum. As such, th ... 显示更多

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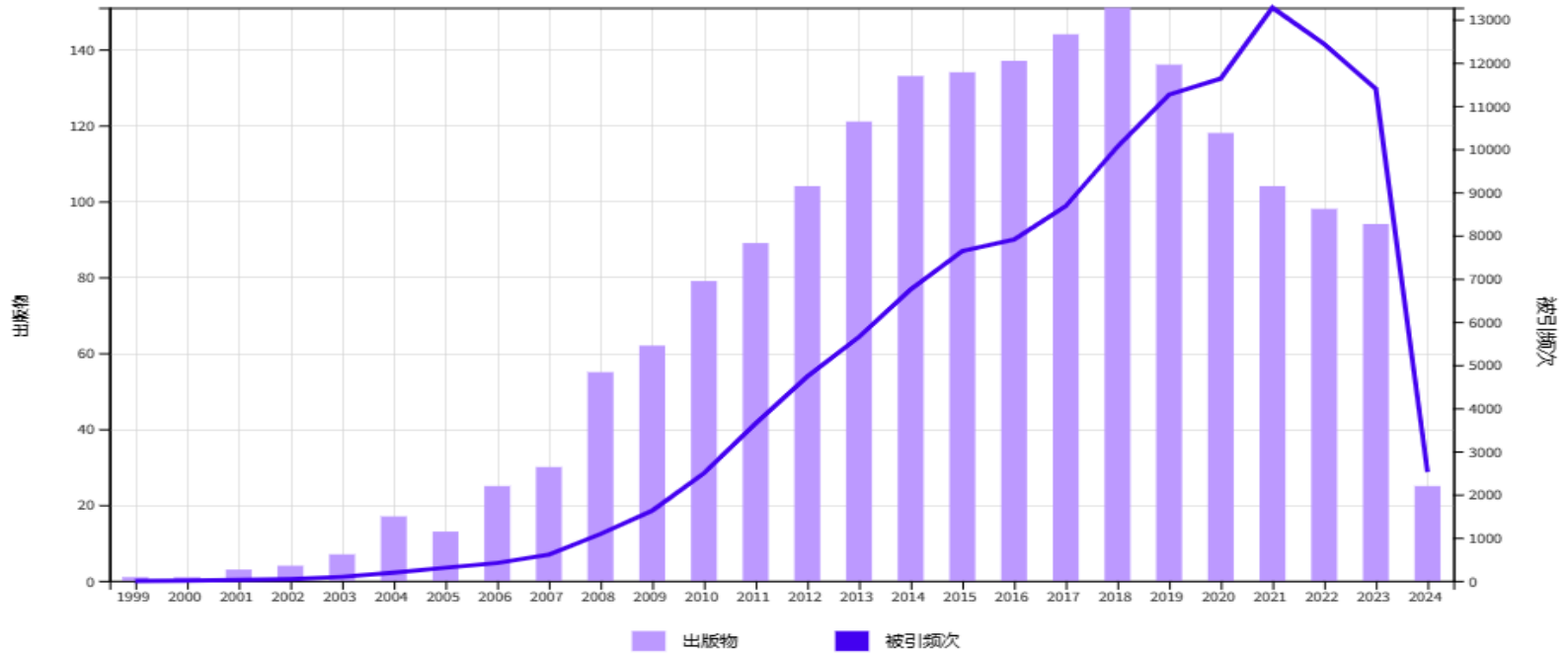

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17	Surface-Er	Schluecker				ANGEWAN	MAY 5 201	2014	53	19				4756	4795		10.1002/ar			1741	174.1
18	Electromag	Hao, E; Sch				JOURNAL (	JAN 1 2004	2004	120	1				357	366		10.1063/1.			1623	81.15
19	Gold Nanc	Huang, Xia				ADVANCEI	DEC 28 20(	2009	21	48				4880	4910		10.1002/ac			1570	104.67
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37	Surface-er	Cialla, Dana				ANALYTIC/	APR 2012	2012	403	1				27	54		10.1007/s0			646	53.83
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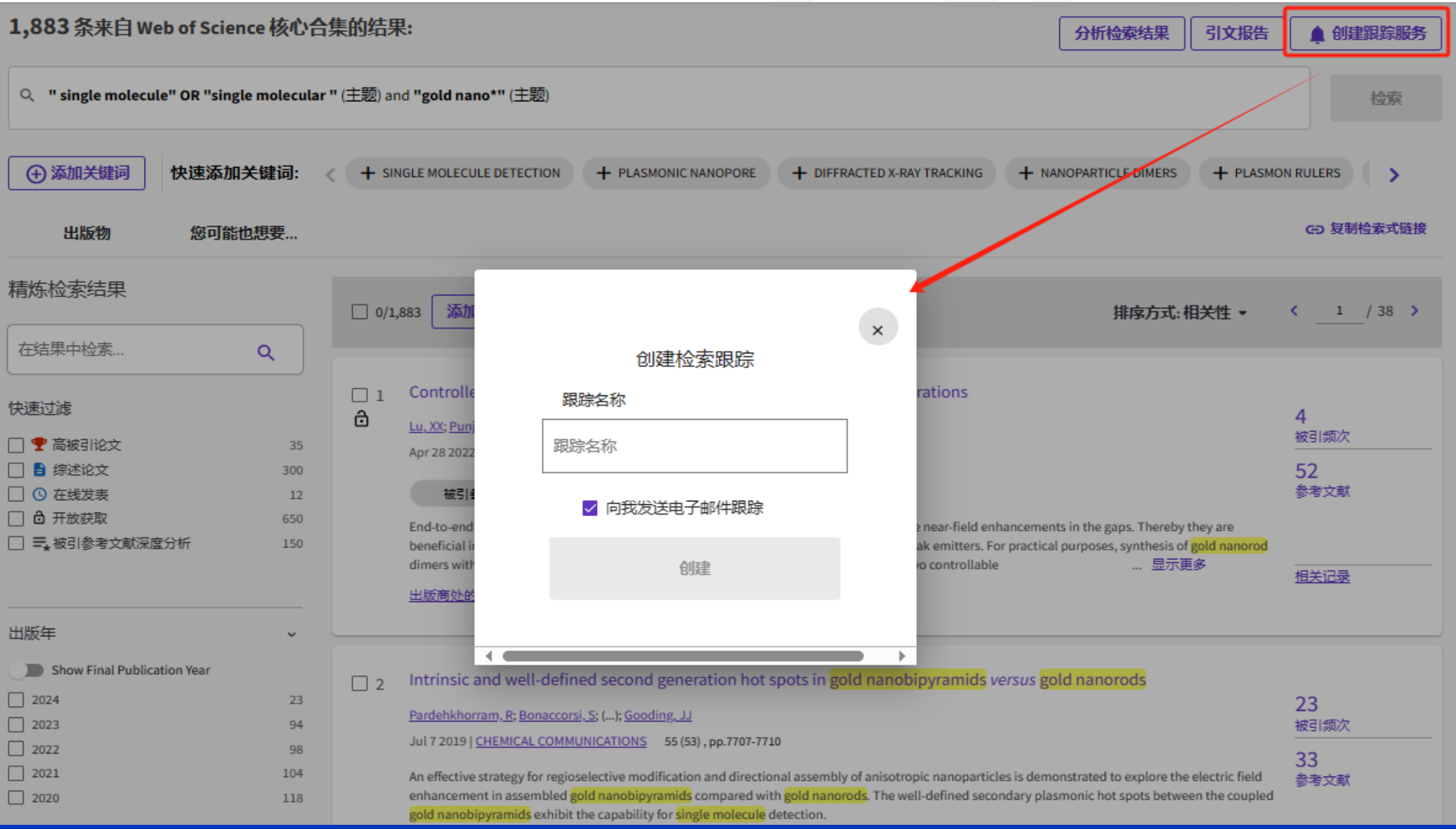
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Intrinsic and well-defined second generation hot spots in gold nanobipyramids versus gold nanorods
Pardehkhorram, R; Bonaccorsi, S; (...); Gooding, JJ
Jul 7 2019 | CHEMICAL COMMUNICATIONS 55 (53) , pp.7707-7710
An effective strategy for regioselective modification and directional assembly of anisotropic nanoparticles is demonstrated to explore the electric field enhancement in assembled gold nanobipyramids compared with gold nanorods. The well-defined secondary plasmonic hot spots between the coupled gold nanobipyramids exhibit the capability for single molecule detection.
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Controlled synthesis of gold nanorod dimers with end-to-end configurations

作者 Lu, XX (Lu, Xuxing) [1] ; Punj, D (Punj, Deep) [1] ; Orrit, M (Orrit, Michel) [1]

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来源出版物 RSC ADVANCES

卷: 12 期: 21 页: 13464-13471

DOI: 10.1039/d2ra01288j

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摘要 End-to-end gold nanorod dimers provide unique plasmonic hotspots with extremely large near-field enhancements in the gaps. Thereby they are beneficial in a wide range of applications, such as enhancing the emissions from ultra-weak emitters. For practical purposes, synthesis of gold nanorod dimers with high yield, especially on the substrates, is essential. Here, we demonstrate two controllable strategies to synthesize gold nanorod dimers based on the self-assembly of gold nanorods, either in bulk solution or on the surface of a glass substrate directly. Both methods can give a high yield of gold nanorod dimers, yet, assembling them directly on the substrate provides more flexibility in controlling the shape and size of each nanorod within the dimer. We also show that these gold nanorod dimers can be used to enhance two-photon-excited fluorescence signals at the single-molecule level.

关键词 **Keywords Plus:** PLASMONIC NANOSTRUCTURES; DNA ORIGAMI; RATIONAL DESIGN; FLUORESCENCE; NANOPARTICLES; NANODIMERS; SCATTERING; DISTANCES

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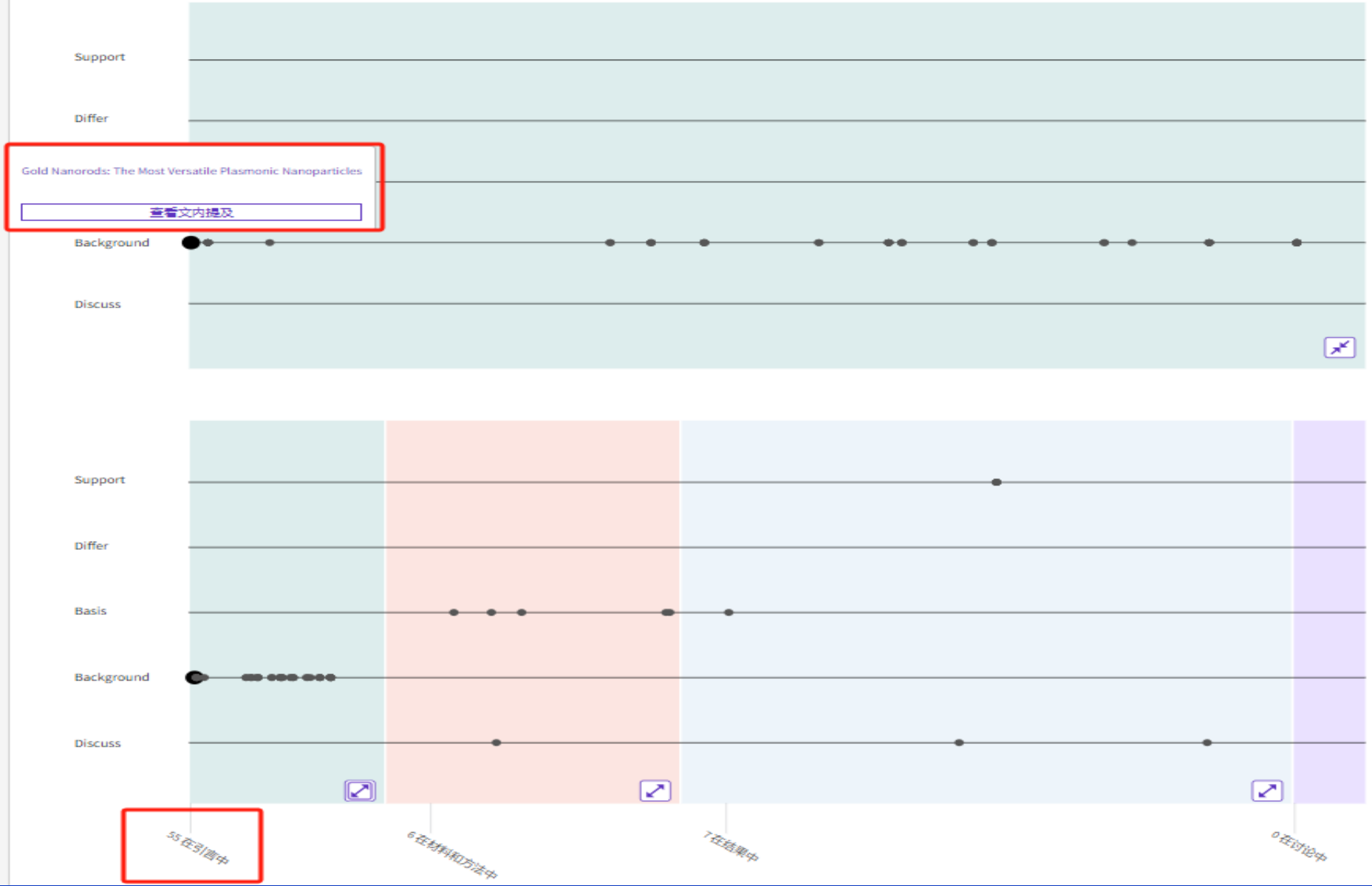

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compared to individual nanoparticles. As a cor

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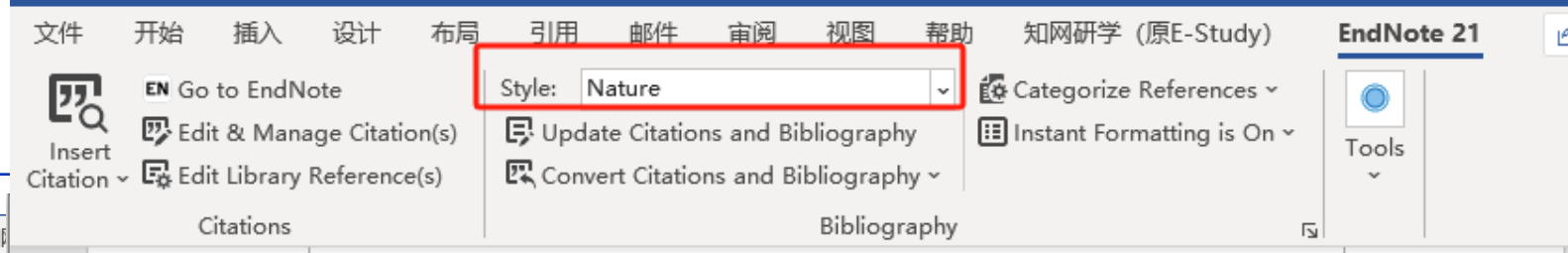

gaps, 1–10 as well as the local density of photon states, 6,11–15

compared to individual nanoparticles. As a consequence, metal

nanoparticle aggregates can be applied to enhance ultra-weak

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These TPE uorescence signals are normally [1] too weak to be

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1 Anders, K. C. Building a Multi-Format Graduate Student Information Literacy Program. *Reference & User Services Quarterly* **59**, 156-160 (2021).

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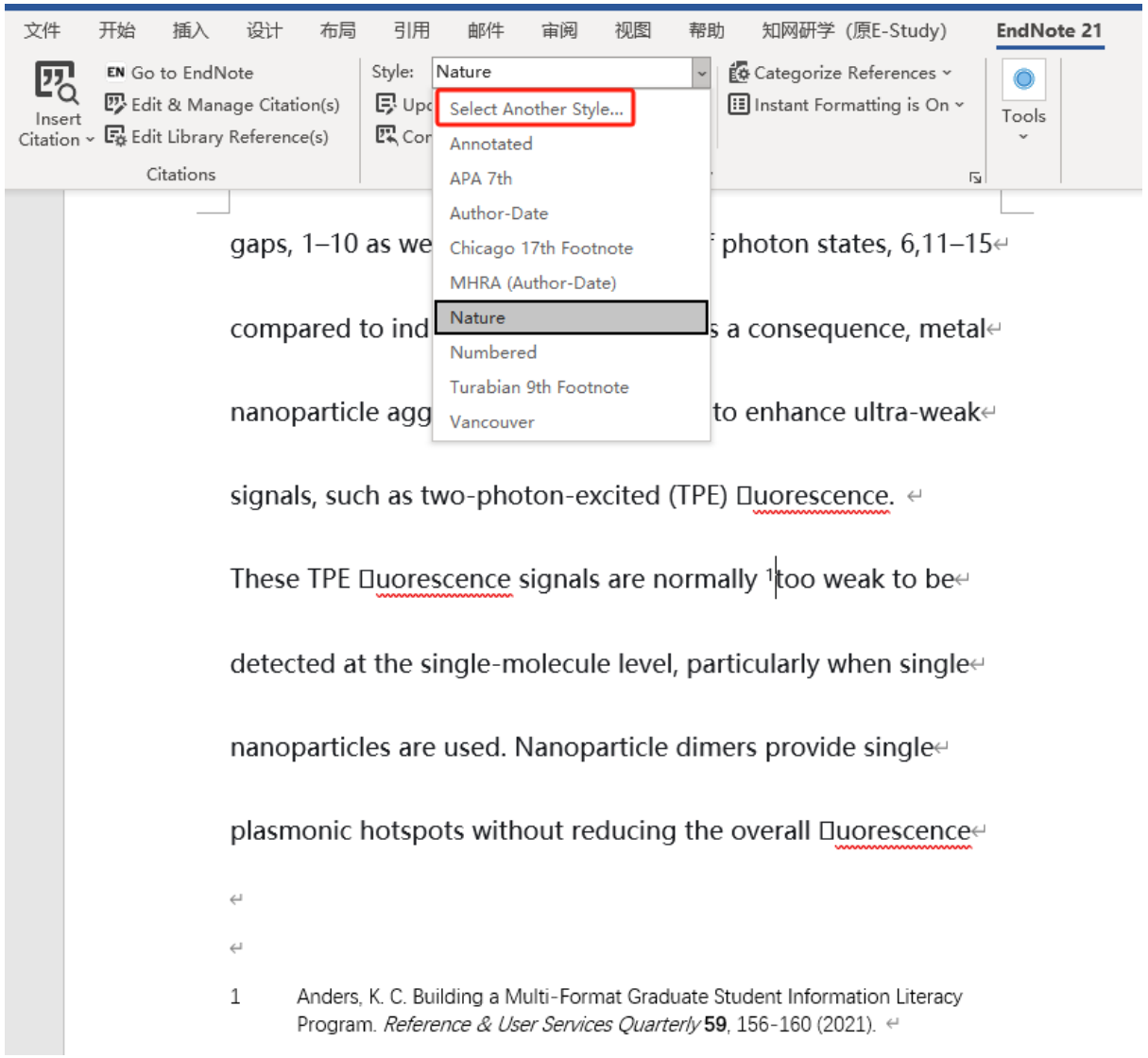

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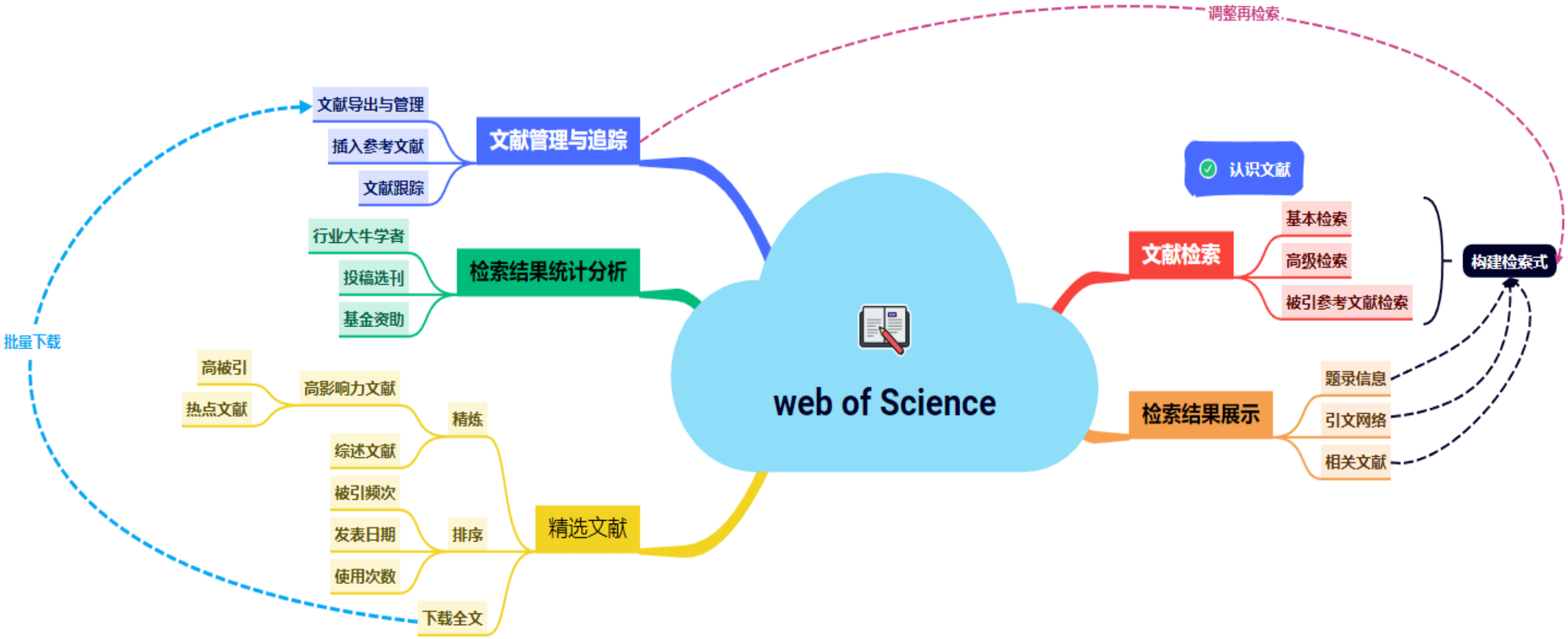
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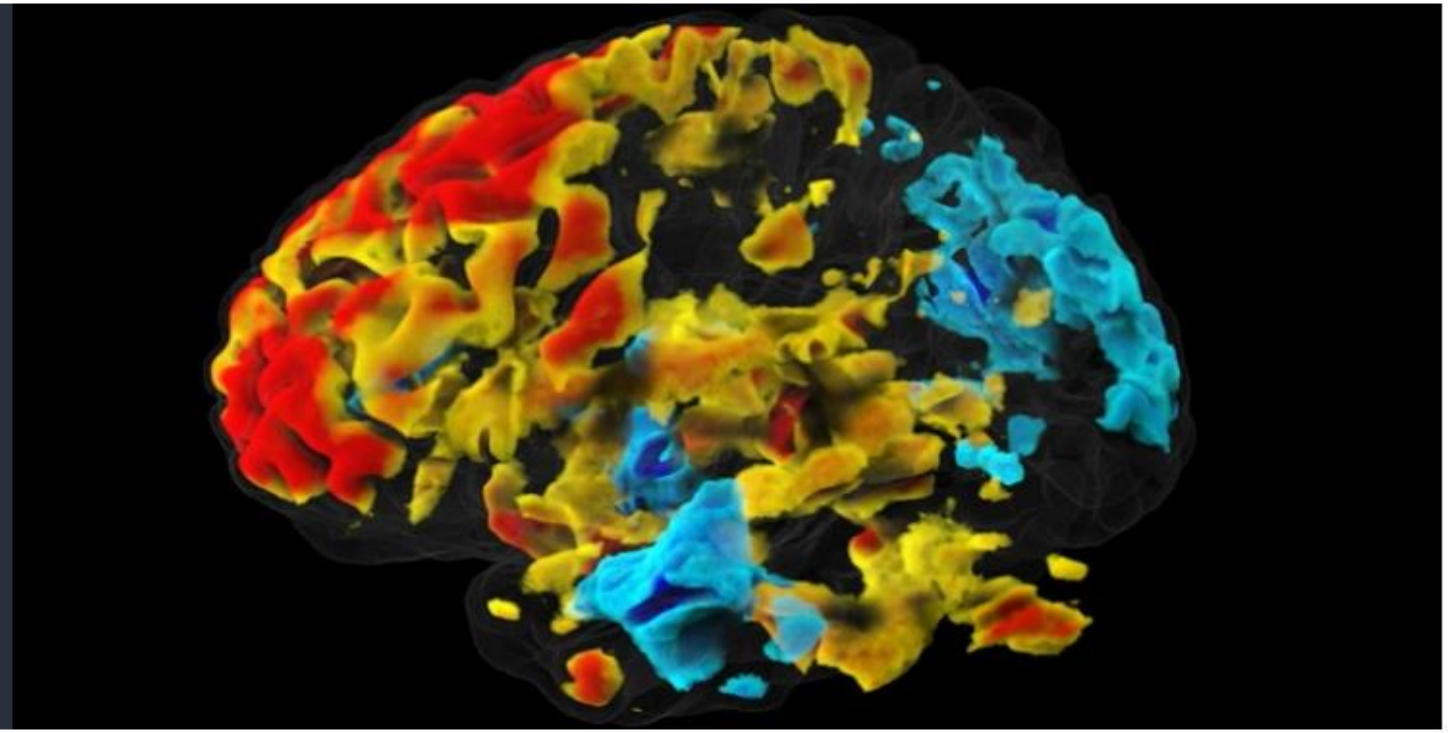

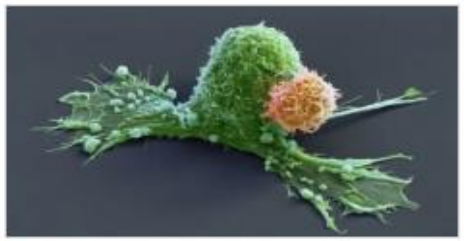

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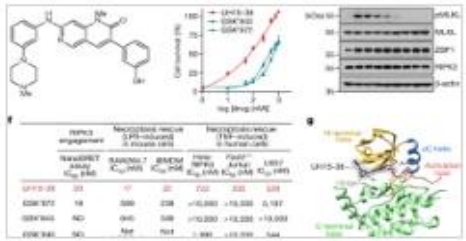

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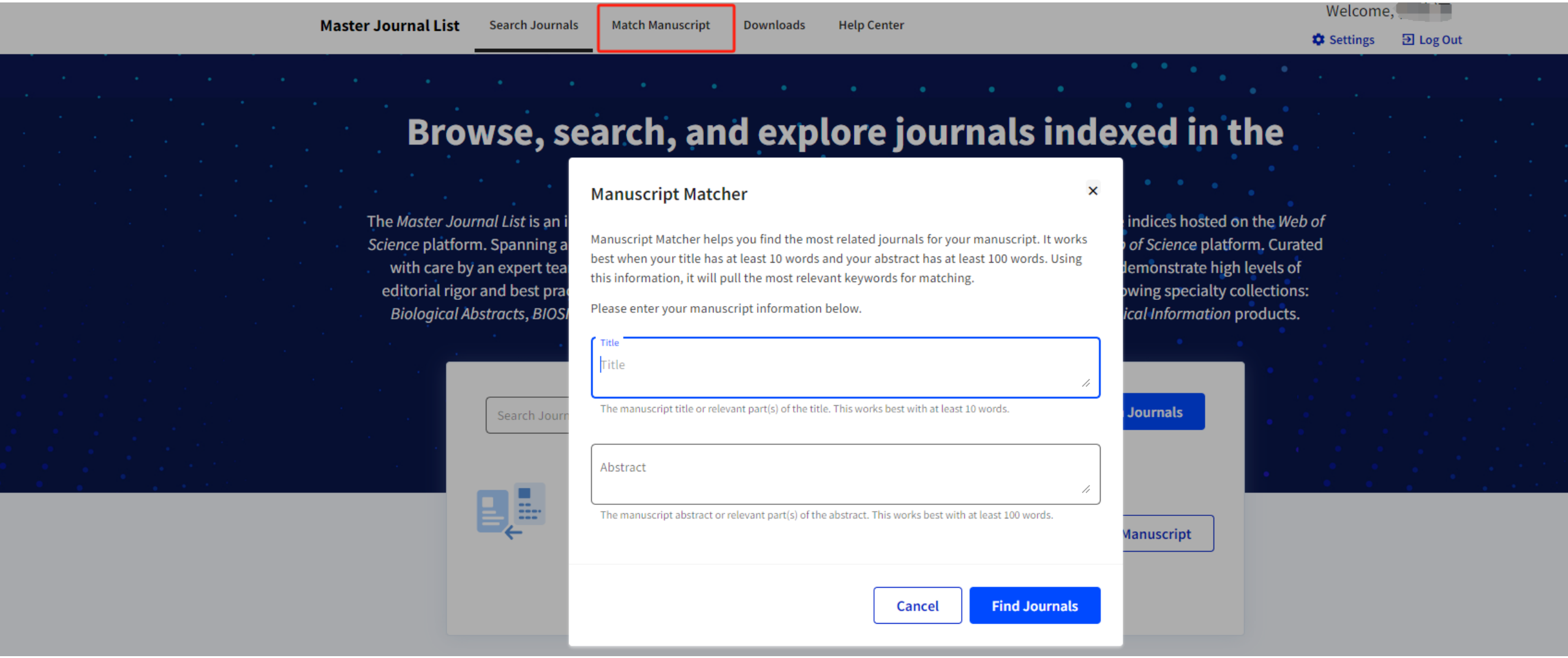
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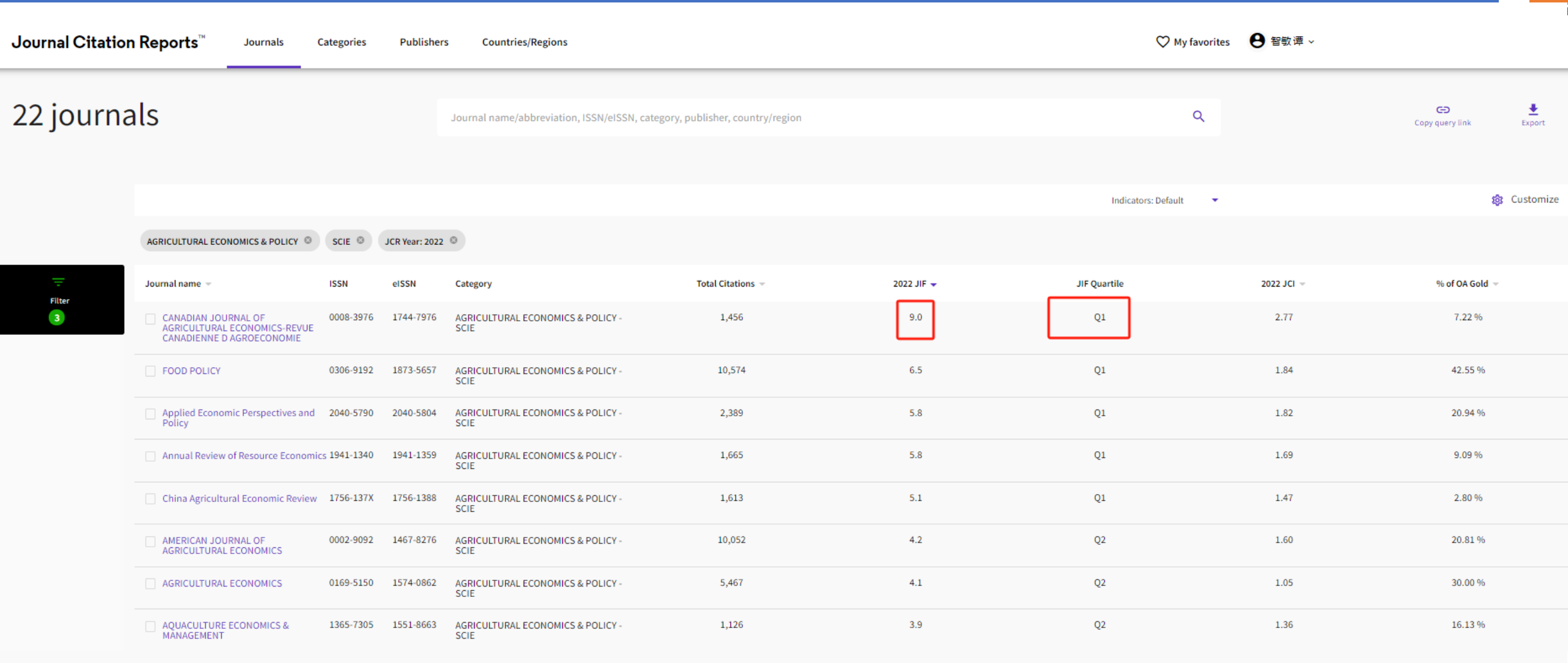

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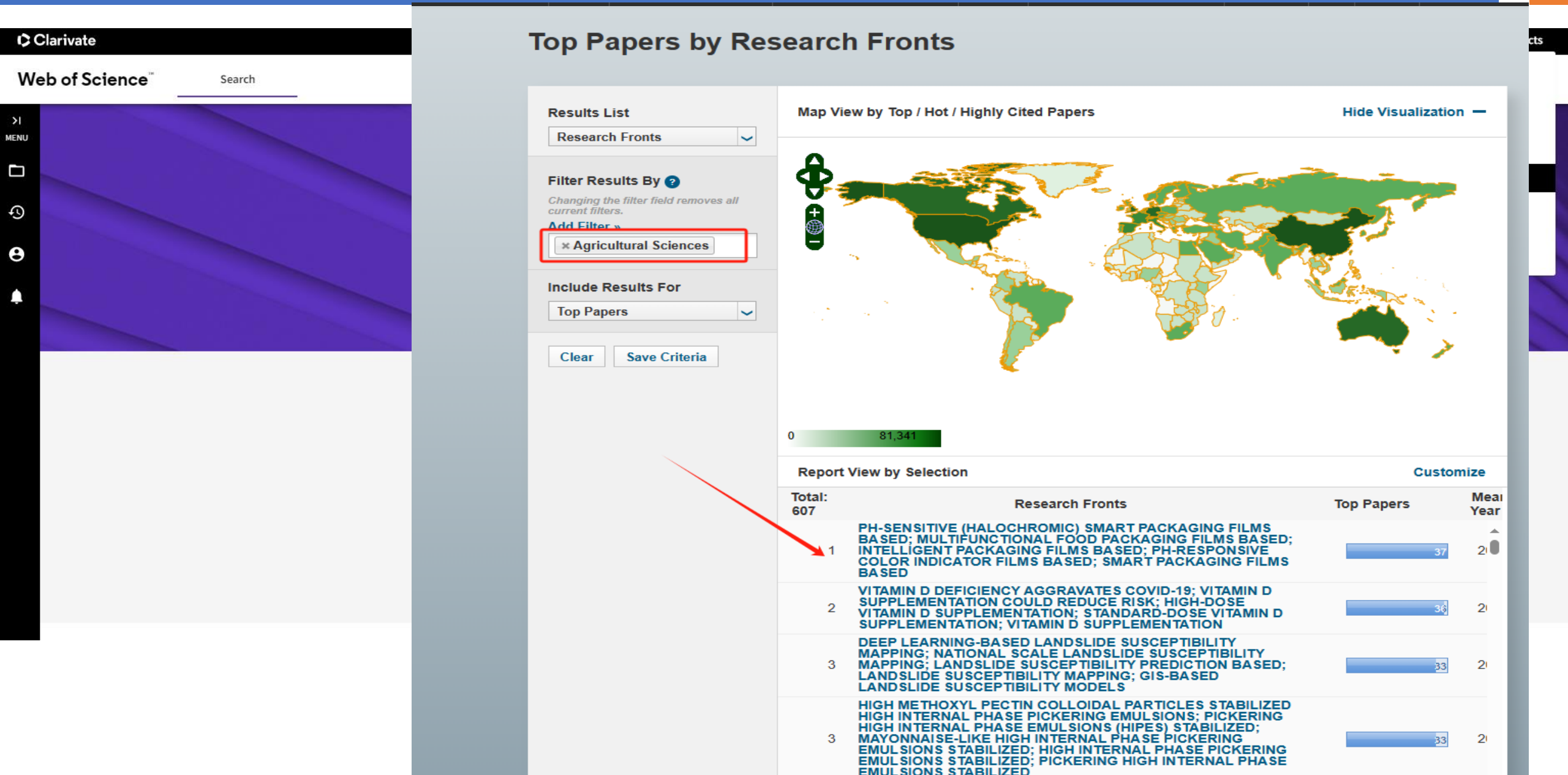
Applied Economic Perspectives and Policy	2040-5790	2040-5804	AGRICULTURAL ECONOMICS & POLICY - SCIE	2,389	5.8	Q1	1.82	20.94 %
Annual Review of Resource Economics	1941-1340	1941-1359	AGRICULTURAL ECONOMICS & POLICY - SCIE	1,665	5.8	Q1	1.69	9.09 %
China Agricultural Economic Review	1756-137X	1756-1388	AGRICULTURAL ECONOMICS & POLICY - SCIE	1,613	5.1	Q1	1.47	2.80 %
AMERICAN JOURNAL OF AGRICULTURAL ECONOMICS	0002-9092	1467-8276	AGRICULTURAL ECONOMICS & POLICY - SCIE	10,052	4.2	Q2	1.60	20.81 %
AGRICULTURAL ECONOMICS	0169-5150	1574-0862	AGRICULTURAL ECONOMICS & POLICY - SCIE	5,467	4.1	Q2	1.05	30.00 %
AQUACULTURE ECONOMICS & MANAGEMENT	1365-7305	1551-8663	AGRICULTURAL ECONOMICS & POLICY - SCIE	1,126	3.9	Q2	1.36	16.13 %

3 ESI辅助确定研究前沿



3 研究前沿报告

《2023研究前沿》报告

2024/02/02 11:12 上传

2023年11月28日 —— 科睿唯安与中国科学院今天联合发布《2023研究前沿》报告，遴选和展示自然科学和社会科学的11大学科领域中的热点前沿和新兴前沿。今年是双方连续第10年携手发布《研究前沿》系列报告。

今年的报告遴选出128个研究前沿，包括110 个热点前沿和18个新兴前沿。报告为科研管理者和政策制定者提供了全球科研的最新进展和动态，帮助他们以有限的资源来支持和推进科学进步。

《2023研究前沿热度指数》报告

2023/11/28 12:32 上传

2023年11月28日 —— 科睿唯安与中国科学院今天联合发布《2023研究前沿》报告，遴选和展示自然科学和社会科学的11大学科领域中的热点前沿和新兴前沿。今年是双方连续第10年携手发布《研究前沿》系列报告。

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调查问卷

求實創新 勵志圖強

向下生根，向上开花，
不负生活，不负自己。

tanzm@jlu.edu.cn

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感谢聆听