新型冠状病毒信息简报

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上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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内容介绍

分类	标题名称
疫情播报	1. 2020 年 11 月 12 日疫情
上海科技大学战疫科研突破	2. 从几十年前建立的人类抗体库中筛选出有效的 SARS-CoV-2 中和抗体
流行病学	3. 在貂养殖场由人传给貂的 SARS-CoV-2 会回传给人
疫苗研发	4. CEPI 扩大与三叶草生物合作，资助“S-三聚体”新冠疫苗候选物全球 II/III 期临床研究以获上市许可 5. 巴西已恢复中国新冠疫苗 III 期试验，严重不良事件为受试者自杀 6. 早期数据显示辉瑞和 Bio NTech 公司的 COVID-19 疫苗 90%有效 7. 俄罗斯称，经过中期分析，其 Sputnik V 疫苗的有效率为 92% 8. 宣布俄罗斯有争议的临床试验 Sputnik V 三期试验中期揭盲结果积极 9. 在烟草中表达可预防 Covid-19 疾病的重组病毒样候选疫苗 I 期临床试验 10. 辉瑞新冠疫苗数据显示有效，但疫苗运输存在挑战 11. hAd5 S-Fusion + N-ETSD 感染早先感染了 SARS-CoV-2 患者的自体树突状细胞诱导 Th1 主导核衣壳和刺突抗原特异性 CD4+和 CD8+记忆 T 细胞召回
药物研发	12. 新冠肺炎更新:美国食品和药物管理局授权单克隆抗体治疗新冠肺炎 13. 鼻内给药脂肽融合抑制剂有效防止雪貂传染 SARS-CoV-2 14. 高效双特异性 sybodies 中和 SARS-CoV-2
基础研究	15. 正在流行的 SARS-CoV-2 Spike 蛋白 N439K 突变体在逃避抗体介导的免疫响应同时保持了病毒的适应性 16. 人类 SARS-CoV-2 同源序列通过 NamiRNA 增强子网络上调透明质酸促进 COVID-19 的临床进展 17. 家畜和野生动物中高度分化的呼吸道上皮细胞培养株对 SARS-CoV-2 病毒的敏感性 18. 人类对 SARS-CoV-2 预先存在的和新的体液免疫 19. Baricitinib 治疗可解决 SARS-CoV-2 感染恒河猴的下呼吸道巨噬细胞炎症和中性粒细胞募集 20. SARS-CoV-2 的短程和长程 RNA-RNA 互作 21. 用相关的多模态多尺度冷冻成像揭示 SARS-CoV-2 组装和出胞的通路
疾病模型	22. K18-hACE2 小鼠中 COVID-19 的治疗和发病机制，包括嗅觉丧失
资源介绍	23. 促进关于 COVID-19 的网络药理学研究的资源整合工作流程
其他	24. 为什么 COVID 的死亡率正在下降呢？

免责申明：
本简报仅作为科研参考之用，不构成医疗建议，如您怀疑自己感染新型冠状病毒，请去正规医院或者咨询医生。

1. 2020 年 11 月 12 日疫情

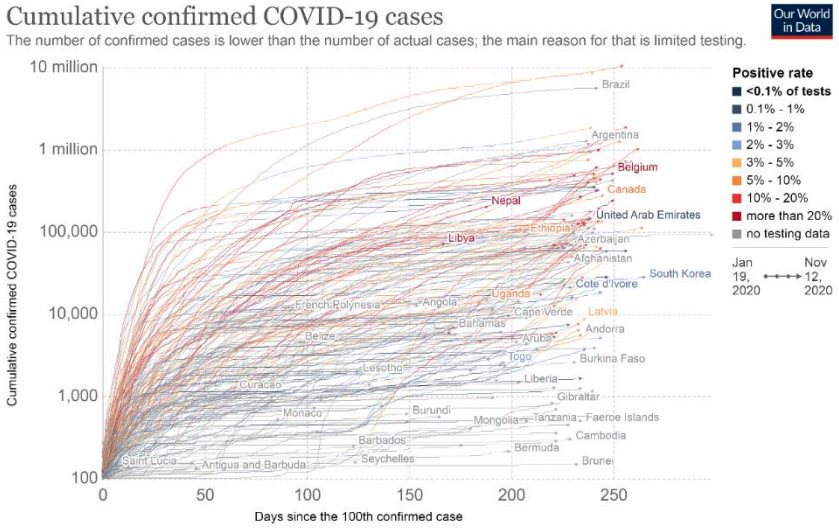
数据来源：WHO

发布时间：2020 年 11 月 12 日北京时间下午 4 点

链接：https://covid19.who.int/

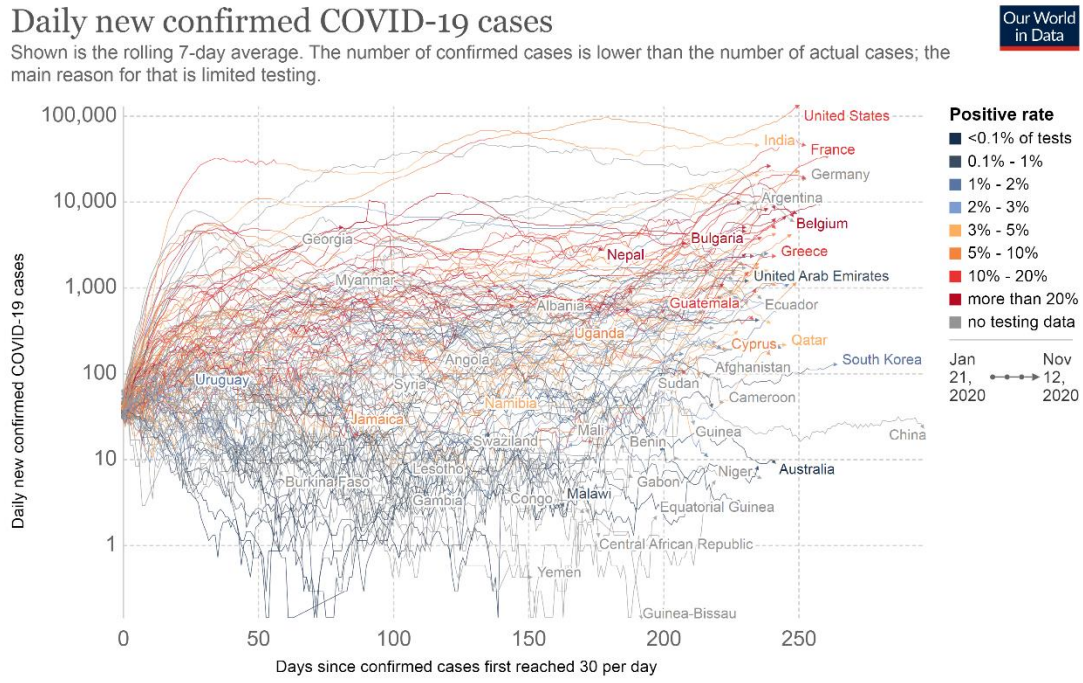
根据 WHO 提供的数据，2020 年 11 月 12 日全球累计确诊新型冠状病毒病人 **51,848,261** 例，当日新增确诊 **579,253** 例，累计死亡 **1,280,868** 例，当日新增死亡 **9,668**。

中国累计确诊 92,336 例，累计死亡 4,749 例，当日新增确诊 37 例，新增死亡 0 例。



Source: European CDC – Situation Update Worldwide – Last updated 12 November, 12:06 (London time), Official data collated by Our World in Data
CC BY

重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



Source: European CDC – Situation Update Worldwide – Last updated 12 November, 12:06 (London time), Official data collated by Our World in Data
CC BY

重点国家每日新增确诊数量曲线（https://ourworldindata.org/covid-

cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）

全国新型冠状病毒肺炎新增确诊病例分布图（11 月 12 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 从几十年前建立的人类抗体库中筛选出有效的 SARS-CoV-2 中和抗体

Potent SARS-CoV-2 neutralizing antibodies selected from a human antibody library constructed decades ago

来源：bioRxiv

发布时间：2020-11-06

链接：https://www.biorxiv.org/content/10.1101/2020.11.06.370676v1

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中文摘要：

我们使用了在 COVID-19 大流行之前 20 年构建的组合人抗体库，发现了三种高效能的抗体，可以选择性地结合 SARS-CoV-2 spike 蛋白并中和真正的 SARS-CoV-2 病毒。与来自通常具有低体细胞高突变（SHM）的 COVID-19 患者的中和抗体相比，这些抗体包含超过 13-22 个 SHM，其中许多与 SARS-CoV-2 尖峰 RBD 参与晶体结构的特异性相互作用。在大流行前文库中对这些体细胞突变抗体的鉴定引发了有关人类对 SARS-CoV-2 免疫应答的起源和进化的有趣问题。

Abstract:

Combinatorial antibody libraries not only effectively reduce antibody discovery to a numbers game, but enable documentation of the history of antibody responses in an individual. The SARS-CoV-2 pandemic has prompted a wider application of this technology to meet the public health challenge of pandemic threats in the

modern era. Herein, we used a combinatorial human antibody library constructed 20 years before the COVID-19 pandemic to discover three highly potent antibodies that selectively bind SARS-CoV-2 spike protein and neutralize authentic SARS-CoV-2 virus. Compared to neutralizing antibodies from COVID-19 patients with generally low somatic hypermutation (SHM), these antibodies contain over 13-22 SHMs, many of which are involved in specific interactions in crystal structures with SARS-CoV-2 spike RBD. The identification of these somatically mutated antibodies in a pre-pandemic library raises intriguing questions about the origin and evolution of human immune responses to SARS-CoV-2.

3. 在貂养殖场由人传给貂的 SARS-CoV-2 会回传给人

Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans

来源：science

发布时间：2020-11-10

链接：https://science.sciencemag.org/content/early/2020/11/09/science.abe5901?rss=1

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中文摘要：

动物实验表明非人灵长类、猫、仓鼠、兔子和蝙蝠可以被 SARS-CoV-2 感染。此外，在现实养殖区从猫科动物、貂的以及狗体内检测到 SARS-CoV-2 的 RNA。在这个研究中，作者们采用全基因组测序对 16 个貂养殖场的貂以及工作人员和住户进行了深度研究。研究的结论是病毒最开始被人带入并传播给貂然后开始发展进化突变，最可能的情况是，在被检测出来之前的几个星期里貂中已经存在广泛的流行。尽管加强了生物安全管理，早期预警流调以及立刻处理被感染的养殖场等多种措施，在三个主要的 3 个传播簇里面貂养殖场之间的病毒传播路径不完全清楚。在被测试的养殖场居民、工作人员以及合同工中显示有 68%的人有 SARS-CoV-2 感染。已有的全基因组测序数据显示这些人是被来自于有动物的病毒株系序列特征的病毒株感染，证明在貂养殖场中存在从貂到人的病毒传播。

Abstract:

Animal experiments have shown that non-human primates, cats, ferrets, hamsters, rabbits and bats can be infected by SARS-CoV-2.

In addition, SARS-CoV-2 RNA has been detected in felids, mink and dogs in the field. Here, we describe an in-depth investigation using whole genome sequencing of outbreaks on 16 mink farms and the humans living or working on these farms. We conclude that the virus was initially introduced from humans and has since evolved, most likely reflecting widespread circulation among mink in the beginning of the infection period several weeks prior to detection. Despite enhanced biosecurity, early warning surveillance and immediate culling of infected farms, transmission occurred between mink farms in three big transmission clusters with unknown modes of transmission. Sixty-eight percent

(68%) of the tested mink farm residents, employees and/or contacts had evidence of SARS-CoV-2 infection. Where whole genomes were available, these persons were infected with strains with an animal sequence signature, providing evidence of animal to human transmission of SARS-CoV-2 within mink farms.

4. CEPI 扩大与三叶草生物合作，资助“S-三聚体”新冠疫苗候选物全球 II/III 期临床研究以获上市许可

链接：
http://www.cloverbiopharma.com/index.php?m=content&c=index&a=show&catid=11&id=52

根据三叶草生物公司官方网站 11 月 3 日消息，CEPI 扩大与三叶草生物合作，资助“S-三聚体”新冠疫苗候选物全球 II/III 期临床研究以获上市许可。

摘要如下：

CEPI 将继续资助支持三叶草生物“S-三聚体”重组亚单位新冠疫苗候选物的开发直至其获得上市许可，这包括预计在 2020 年底前启动的全球范围关键性 II/III 期临床有效性研究。CEPI 与三叶草生物之间的协议旨在支持其研发的疫苗，在被证明安全有效的前提下，可以通过新冠肺炎疫苗实施计划（“COVAX 机制”）进行采购和分配，提供给全球最需要的人群。CEPI 对“S-三聚体”新冠疫苗的总资助将高达 3.28 亿美元，其中包括此前宣布的 6,950 万美元。

5. 巴西已恢复中国新冠疫苗 III 期试验，严重不良事件为受试者自杀

来源：丁香园

链接：https://mp.weixin.qq.com/s/MS-nFcso3peXY5KeioDFqw

编译：张丽双

当地时间 11 月 9 日晚，巴西国家卫生监督局在其网站上发布声明：因为发生“严重不良事件”——死亡，已经暂停中国科兴在当地进行的 CoronaVac 疫苗 III 期临床试验。

当地时间 11 月 10 日，巴西警方称，参加 CoronaVac 疫苗测试志愿者的死因是自杀。死者在浴室被发现，身边有注射器和安瓿瓶。巴西卫生部下属的国家研究和伦理委员会 10 日表示，该机构分析了志愿者死亡的初步数据，认为死因与疫苗无关，建议无需暂停该疫苗在巴西的测试。一个国际独立调查委员会向巴西国家卫生监督局发送了有关科兴疫苗的数据，并建议巴西恢复该疫苗的测试。

巴西国家卫生监督局 11 月 11 日宣布，由科兴开发的新冠疫苗 CoronaVac 临床试验将在巴西恢复。

6. 早期数据显示辉瑞和 Bio NTech 公司的 COVID-19 疫苗 90%有效

Early Data Shows Pfizer and BioNTech's COVID-19 Vaccine is 90% Effective

链接：https://www.biospace.com/article/pfizer-and-biontech-s-preliminary-covid-19-vaccine-data-dazzles/

编译者：雷颖

11 月 9 日，美国辉瑞公司宣布，其与德国生物技术公司 BioNTech 合作研发的 mRNA 新冠候选疫苗 BNT162b2 三期临床试验有效性超过 90%。这一数据远高于此前许多业内专家对新冠疫苗有效性的预测：在 50%到 60%之间。根据辉瑞官网消息，这一结果，是基于外部独立数据监测委员会（DMC）在 11 月 8 日对疫苗进行第一次中期效果分析后发布的，分析时临床试验中确诊感染新冠病例为 94 例，招募的 43538 名受试者中，在 11 月 8 日时已有 38955 位

接种了第二剂疫苗。辉瑞公司表示，预计将在确诊人数达到 164 名对该候选疫苗进行终期分析。辉瑞和 BioNTech 计划将于本月第三周向 FDA 申请紧急授权，预计在 2020 年底为全球提供 5000 万剂疫苗，2021 年将生产 13 亿剂疫苗。此前，美国 FDA 对于紧急使用新冠疫苗的有效性要求为 50%以上。与传统疫苗相比，mRNA 疫苗合成和生产工艺相对便捷，不需要传统疫苗必需的附加佐剂。目前，全球范围内目前尚无基于 mRNA 技术平台研发的治疗或预防性药物/疫苗获批上市。

7. 俄罗斯称，经过中期分析，其 Sputnik V 疫苗的有效率为 92%

Russia Claims its Sputnik V Vaccine is 92% Effective Following Interim Analysis

来源：BioSpace

发布时间：2020-11-11

链接：https://www.biospace.com/article/russia-claims-its-sputnik-v-vaccine-is-92-percent-effective-following-interim-analysis/

第一作者：Alex Keown

通讯作者：Alex Keown

通讯作者单位： BioSpace

DOI 或 PUBMED ID：

编译者：张鹏伟

中文摘要：

俄罗斯卫生署在公告中称，在进行中的第三阶段研究中，首次注射后 21 天获得的第一次中期分析结果证明了疗效。卫生机构说，根据对 20 例确诊冠状病毒病例的统计分析，接种疫苗的人和服用安慰剂的人之间的病例分为两组，表明第二次注射后，Sputnik V 疫苗的有效率为 92%。

俄罗斯表示，截至 11 月 11 日，已有超过 2 万名志愿者接种了第一剂疫苗，超过 1.6 万名志愿者接种了第二剂疫苗。卫生署说，除了流感样症状外，没有严重的不良反应，包括疲劳、头痛和发烧。

Sputnik V III 期临床试验正在俄罗斯，白俄罗斯，阿拉伯联合酋长国，委内瑞拉和其他国家进行。印度正在进行 II / III 期研究。

Abstract:

Efficacy was demonstrated on the basis of a first interim analysis obtained 21 days after the first injection during the ongoing Phase III study, the Russian health agency said in its announcement. As a result of a statistical analysis of 20 confirmed cases of coronavirus, the case split between vaccinated individuals and those who received the placebo indicates that the Sputnik V vaccine had an efficacy rate of 92% after the second dose, the health agency said.

As of Nov. 11, Russia said more than 20,000 volunteers have been vaccinated with the first dose of the vaccine and more than 16,000 volunteers received the second dose of the vaccine. No severe adverse events have been reported beyond flu-like symptoms, including fatigue, headache and fever, the health agency said.

Sputnik V Phase III clinical trials are ongoing in Russia, Belarus, the United Arab Emirates, Venezuela and other countries. A Phase II/III study is being conducted in India.

8. 宣布俄罗斯有争议的临床试验 Sputnik V 三期试验中期揭盲结果积极

Russia announces positive COVID-vaccine results from controversial trial

来源：Nature
发布时间：2020-11-11
链接：https://www.nature.com/articles/d41586-020-03209-0
第一作者：Ewen Callaway
通讯作者：Ewen Callaway
通讯作者单位：Nature
DOI 或 PUBMED ID：https://doi.org/10.1038/d41586-020-03209-0
编译者：张丽双
中文摘要：
对俄罗斯腺病毒载体疫苗临床试验 Sputnik V 参与者中 20 例 COVID-19 病例的 III 期临床试验中期分析发现，该疫苗的有效率为 92%。这项分析调查了超过 16000 名志愿者，他们在初次免疫疫苗或安慰剂 3 周后再次免疫疫苗或安慰剂。公告称，该试验共招收了 4 万名参与者。相比之下，辉瑞研究小组的早期分析是基于 94 例 COVID-19 例，并且在参与者服用第二剂一周后进行测量，报告了超过 90%的有效性。辉瑞公司的试验于 7 月 27 日开始，共招募了 43000 多名参与者，其中 38000 多人在分析时接受了 2 剂。批评者认为：“我担心这些数据是在辉瑞公司/生物技术公司的声明背后被匆忙发布的。”。“这不是竞争。我们需要所有的试验都按照最高标准进行，尤其重要的是要遵守预先设定的试验数据揭盲标准，以避免挑拣数据。”
Abstract:
The Gamaleya National Center of Epidemiology and Microbiology in Moscow and the Russian Direct Investment Fund said that an interim analysis of 20 COVID-19 cases identified among trial participants has found that the vaccine was 92% effective. The analysis looked at more than 16,000 volunteers — who received either the vaccine or a placebo — 3 weeks after they had taken the first dose. The trial has enrolled a total of 40,000 participants, the release said.
By contrast, the Pfizer team’s early analysis was based on 94 COVID-19 cases — and reported greater than 90% effectiveness, when measured a week after participants got their second dose. The Pfizer trial, which started on 27 July, has enrolled more than 43,000 participants, more than 38,000 of whom had received 2 doses when the analysis was carried out.
Russia’s fast-track coronavirus vaccine draws outrage over safety
“I worry that these data have been rushed out on the back of the Pfizer/BioNTech announcement,” Eleanor Riley, an immunologist at the University of Edinburgh, UK, told the SMC. “This is not a competition. We need all trials to be a carried out to the highest possible standards and it is particularly important that the pre-set criteria for unblinding the trial data are adhered to avoid cherry picking the data.”

9. 在烟草中表达可预防 Covid-19 疾病的重组病毒样候选疫苗Ⅰ期临床试验

Phase 1 trial of a Candidate Recombinant Virus-Like Particle Vaccine for Covid-19 Disease Produced in Plants
来源：medRxiv
发布时间：2020-11-6
链接：https://www.medrxiv.org/content/10.1101/2020.11.04.20226282v

第一作者：Brian J Ward
通讯作者：Nathalie Landry
通讯作者单位：Medicago Inc
DOI 或 PUBMED ID：https://doi.org/10.1101/2020.11.04.20226282
编译者：姜连连
中文摘要：
背景：在本氏烟草中瞬时表达急性呼吸综合征冠状 2 型病毒(SARS-CoV-2)Spike 重组三聚体的病毒样颗粒（CoVLP），将 CoVLP 单独或于佐剂 AS03 或 CpG1018 乳化后制备成候选疫苗在 18-55 岁健康人群中进行免疫保护效果评估 (NCT04450004)。
方法：选择 18-55 岁新冠病毒血清检测阴性的健康人群进行随机、部分盲法分组，将在烟草中表达的 CoVLP 单独或与佐剂 AS03 或 CpG1018 乳化后肌肉注射免疫分组人群，免疫程序为双剂量，且剂量递增式 (3.75, 7.5 or 15 μg/dose)免疫。免疫后 42 天内收集数据进行安全性和免疫原性评估，利用假病毒中和实验检测受试者体内病毒抗体效价和利用酶联免疫斑点实验检测其体内的细胞免疫应答（IFNγ 和 IL-4）。
结果：180 名受试者（平均年龄 34.3 岁）均可耐受其接种剂量，且佐剂会增强疫苗的免疫原性。CoVLP+AS03 免疫组出现最多例疫苗的不良反应且二次免疫后不良反应的频率和严重程度提高。而未使用佐剂的 CoVLP 免疫组在二免疫之后激发机体产生较弱的体液免疫和适中的细胞应答。两种佐剂 AS03 和 CpG1018 在二免之后均可显著提高疫苗的免疫原性。但仅 CoVLP+AS03 受试组在一免之后即可检测到显著的病毒中和抗体效价，且疫苗接种剂量对机体中和性抗体产生强弱影响较小。两种佐剂同样也可以提高 IFNγ 和 IL-4 的细胞免疫应答，且 AS03 佐剂组呈现出高水平的细胞免疫应答。
结论：受试者对有无佐剂的重组 CoVLP 疫苗均有很好的耐受性。而一些佐剂苗在二免后可激发机体产生强体液和细胞免疫应答。其中低剂量 CoVLP+AS03 组可检测到高于康复人群约 10 倍的病毒中和抗体水平，同时还检测到与之匹配的细胞免疫应答。这些实验结果表明 3.75ug+AS03 佐剂型疫苗可进一步进行临床性评估。
Abstract:
Background: Virus-like particles (VLP) displaying recombinant SARS-CoV-2 spike protein trimers were produced by transient expression in Nicotiana benthamiana. This candidate vaccine (CoVLP) was evaluated in healthy adults 18-55 years of age alone or with AS03 or CpG1018 (NCT04450004).
Methods: This randomized, partially-blinded, two-dose, dose-escalation study assessed CoVLP (3.75, 7.5 or 15 μg/dose) administered intramuscularly alone or with CpG1018 or AS03 in SARS-CoV-2 seronegative adults (18-55 years). Primary endpoints of safety and immunogenicity are reported to day 42. Neutralizing antibodies (NtAb) were assessed using a VSV pseudovirus assay and cellular responses by ELISpot (IFNγ, IL-4).
Results: 180 subjects (avg.34.3yrs) were recruited. All formulations were well-tolerated but adjuvants increased reactogenicity. Adverse events were highest in the CoVLP+AS03 groups and increased in frequency/severity after dose two. CoVLP alone elicited weak humoral responses but modest cellular responses were detectable after dose two. Both adjuvants increased immunogenicity significantly, particularly after dose two. A significant NtAb response after dose one was only seen in CoVLP+AS03 groups. The vaccine dose had little impact on levels of NtAb responses achieved in the CoVLP+AS03 groups. Both adjuvants also increased IFNγ

and IL-4 responses but these cellular responses also tended to be highest in the AS03-adjuvanted groups.
Conclusion: CoVLP ± adjuvants was well-tolerated. Several adjuvanted formulations elicited strong humoral and T cell responses after dose 2. Even at the lowest CoVLP+AS0+3 dose, NtAb titers were ~10-times higher than in convalescent serum with a balanced IFNγ and IL-4 response. These findings support the transition of CoVLP (3.75μg+AS03) to further clinical evaluation.

10. 辉瑞新冠疫苗数据显示有效，但疫苗运输存在挑战

Pfizer's Positive Vaccine Data is a Relief for Many, but Logistical Hurdles Remain
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链 接 ： https://www.biospace.com/article/pfizer-and-biontech-s-covid-19-vaccine-faces-hurdles-even-if-approved/
作者：Alex Keown
编译者：姜连连
中文摘要：
BioNTech 创始人兼首席执行官乌古尔•萨欣（Ugur Sahin）表示其公司与辉瑞合作研发的 mRNA 疫苗 BNT162b2 存在巨大保护潜力，有希望成为新冠流行的终结者。疫苗III期临床试验结果显示对受试者可达到 90%的保护性。该公司于年初中国新冠病毒流行时即开始疫苗的研发，之后与辉瑞和复兴医药合作，进入疫苗临床试验。期望 11 月底能拿到美国 FDA 紧急授权疫苗许可，并陆续申请其他国家的疫苗准入许可。
审批机构即使对该疫苗开放绿色通道，若普及至全球仍需时日。限制因素之一即是超低温运输，该 mRNA 疫苗需在-73℃ 以下保存，解冻后立即使用，否则将会失去免疫效果。疫苗运输体系建立将花费大量的财力物力，对一些发展中国家是巨大的挑战。另外，该疫苗需在免疫后 28 天内二次免疫方能确保对 COVID-19 产生有效保护效价。Moderna 公司的候选疫苗虽然需要相同免疫程序，但-29oC 运输储存条件是其优势。
中国复星医药将联合国药集团，批量进口 BNT162b2 核酸疫苗，在中国分装后推广使用。辉瑞和 BioNTech 已着手投资产能建设以满足全球疫苗供给需求。9 月份新收购的诺华工厂预计每年生产 7.5 亿份 COVID-19 核酸疫苗。公司还与全各国政府达成协议，在药物批准后将提供疫苗供给。如 7 月份与美国政府达成了一项价值 19.5 亿美元的 1 亿剂疫苗供给协议，公司刚与欧盟委员会达成 2 亿剂疫苗供给协议。这些疫苗将在 BioNTech 公司德国工厂和辉瑞公司比利时工厂生产。公司计划到 2021 年，疫苗产能增加到 13 亿剂，可满足 6.5 亿人的接种需求。
目前，这些协议签订意味着全球发达国家将数百万人将接种此 mRNA 疫苗。对于发展中国家，COVAX 基金将筹集约 20 亿美元帮助购买疫苗。目标是按国家人口的 20%提供疫苗份数，优先接种高风险人群。若疫苗供应短缺，将按 3%份额优先提供给一线医护人员。
Abstract:
Ugur Sahin, founder and chief executive officer of Germany-based BioNTech, sees the potent efficacy of BNT162b2, the vaccine developed by his company and partner Pfizer, as the possible "beginning of the end" of the coronavirus pandemic.
BioNTech initiated Project when coronavirus outbreak in China, Vaccines like BNT162b2, which requires storage at extremely cold temperatures of -100 degrees

Fahrenheit.Once the doses of the vaccine are thawed, they must be used within a short window of time or else they will become worthless.
That's an important point to note for the Pfizer/BioNTech vaccine, which is a two shot regimen - meaning patients will have to receive two doses of the medication within 28 days to ensure protection against COVID-19.
Fosun will partner with the state-owned Sinopharm Group to deliver vaccine doses in China. Pfizer and BioNTech have invested in manufacturing capabilities in order to meet demand across the globe. The companies have also been striking deals with various global governments to supply the medication if it's approved.
The COVAX Facility was established to provide governments, including those in the emerging markets, with early access to a large portfolio of COVID-19 candidate vaccines produced by multiple manufacturers across the globe.

11. hAd5 S-Fusion + N-ETSD 感染早先感染了 SARS-CoV-2 患者的自体树突状细胞诱导 Th1 主导核衣壳和刺突抗原特异性 CD4+和 CD8+记忆 T 细胞召回

Th1 Dominant Nucleocapsid and Spike Antigen-Specific CD4+ and CD8+ Memory T Cell Recall Induced by hAd5 S-Fusion + N-ETSD Infection of Autologous Dendritic Cells from Patients Previously Infected with SARS-CoV-2

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编译者：张怡
中文摘要：

一个安全、有效的 SARS-CoV-2 疫苗，关键是阻止病毒进入细胞和清除已经感染的细胞中的病毒,研究者们已经开发出一种二价,人类腺病毒血清型 5 (hAd5) SARS-CoV- 2 S-fusion + N-ETSD 疫苗,目前在临床测试。这种疫苗使用下一代 hAd5 (E1-,E2b-,E3-)平台之前成功地用于预先存在的腺病毒免疫力的癌症患者,同时表达 SARS-CoV-2 的刺突蛋白(S),以提高中和抗体阻断病毒，核衣壳蛋白(N)，增强 T 细胞刺激域(ETSD)激活 CD4 +和 CD8 + T 细胞以清除病毒和通过杀死感染细胞来阻断复制。N 蛋白靶向核内体和溶酶体来增强 CD4+和 CD8+T 细胞应答,这使他们的疫苗与众不同。在之前报道的临床前研究中,研究者发现,在小鼠中,hAd5 S-Fusion + N-ETSD 疫苗可诱导体液和 T 细胞反应，且 T 辅助细胞 1 (Th1)占主导。在这里，他们报道了 hAd5 S-Fusion + N-ETSD 疫苗可以被之前感染了 SARS-CoV-2 患者的抗血清和 T 细胞识别，而 N 蛋白的存在对 T 细胞的召回是至关重要的。

研究的结果显示:(i)先前 SARS-CoV-2 感染患者的血浆抗体对 hAd5 S-Fusion + N-ETSD 感染细胞有特异性识别，但病毒未感染患者的抗体不能识别;(ii)与单纯的 hAd5 S-Fusion 相比，先前感染患者的血浆 SARS-CoV-2 抗体与表达 hAd5 S-Fusion + N-ETSD 疫苗的单核细胞来源树突状细胞(MoDCs)的结合增强; (iii)显示 N-ETSD 定位于与 MHC II 类抗原呈递相关的囊泡，包括 MoDCs 中的核内体、溶酶体和自噬小体;(iv)证明核内体/溶酶体靶向的 N-ETSD 比胞浆定位的 N 更能引起γ干扰素的 T 细胞应答;N-ETSD 单独或在 hAd5 S-Fusion + N-ETSD 结构中均可诱导 CD4+和 CD8+ T 细胞记忆的回忆。之前 SARS-CoV-2 感染患者的 T 细

胞识别 hAd5 fusion + N-ETSD 疫苗抗原,这种候选疫苗还能引起小鼠全新的免疫反应,它概述了 SARS-CoV-2 自然免疫反应激活 B 细胞和 T 细胞对病毒中和以及对感染细胞的识别,是 COVID-19 疾病预防的关键。hAd5 fusion + N-ETSD T 细胞疫苗有潜力不仅为未受感染的人提供保护,但也被用作治疗已感染病人，通过激活 T 细胞杀死感染病毒的细胞，快速清除病毒从而降低病毒复制和横向传播。

Abstract

To address the need for a safe, efficacious vaccine against SARS-CoV-2 infection with the critical properties of enabling both blocking viral entry into cells and clearing virus from cells already infected, we have developed a bivalent, human adenovirus serotype 5 (hAd5) SARS-CoV- 2 S-Fusion + N-ETSD vaccine that is currently in clinical testing. This vaccine uses the next-generation hAd5 [E1-, E2b-, E3-] platform previously used successfully in cancer patients with pre-existing adenovirus immunity, engineered to express both SARS-CoV-2 spike (S) protein modified to improve the generation of neutralizing antibodies to block entry ; of the virus, and nucleocapsid (N) protein with an Enhanced T cell Stimulation Domain (ETSD) to activate CD4+ and CD8+ T cells to clear the virus and block replication by killing infected cells. The targeting of N to endosomes and lysosomes to enhance CD4+ and CD8+ T-cell responses distinguishes our vaccine. In our previously reported pre-clinical studies we showed that in mice, the hAd5 S-Fusion + N-ETSD vaccine elicits both humoral and T-cell responses that are robust and T helper cell 1 (Th1) dominant. Here we report that the hAd5 S-Fusion + N-ETSD vaccine is recognized by anti-sera and T cells from previously infected patients, and that the presence of N is vital for T-cell recall.

The findings presented herein: (i) demonstrate specific recognition of hAd5 S-Fusion + N-ETSD infected cells by plasma antibodies from previously SARS-CoV-2 infected patients, but not antibodies from virus-naïve subjects; (ii) show enhanced binding of plasma SARS-CoV-2 antibodies from previously infected patients to monocyte-derived dendritic cells (MoDCs) expressing the hAd5 S-Fusion + N-ETSD vaccine as compared to hAd5 S-Fusion alone;(iii) reveal N-ETSD localizes to vesicles associated with MHC class II antigen presentation, including endosomes, lysosomes and autophagosomes in MoDCs; (iv) demonstrate endosome/lysosome-targeted N-ETSD elicits higher interferon-γ T-cell responses than cytoplasm-localized N; and (v) N-ETSD alone or in the hAd5 S-Fusion + N-ETSD construct induces both CD4+ and CD8+ T cell memory recall. This recognition of hAd5 S-Fusion + N-ETSD vaccine antigens by T cells from previously SARS-CoV-2 infected patients, together with the ability of this vaccine candidate to elicit de novo immune responses in naïve mice suggests that it re-capitulates the natural immune response to SARS-CoV-2 to activate both B and T cells towards viral neutralization and recognition of infected cells, critical for prevention of COVID-19 disease. Intriguingly, our hAd5 S-Fusion + N-ETSD T-cell biased vaccine has the potential to not only provide protection for uninfected individuals, but also to be utilized as a therapeutic for already infected patients to induce rapid clearance of the virus by activating T cells to kill the virus-infected cells, thereby reducing viral replication and lateral

transmission.

12. 新冠肺炎更新:美国食品和药物管理局授权单克隆抗体治疗新冠肺炎

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19

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链 接 ： https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibody-treatment-covid-19

编译者：孔娟

礼来的新冠病毒抗体 bamlanivimab（LY-CoV555）被 FDA 授予紧急使用授权治疗成人及儿童轻至中度新冠病毒感染患者。与安慰剂相比，在治疗后 28 天内，bamlanivimab 在临床试验中显示可减少新冠肺炎相关的住院或急诊室就诊。

13. 鼻内给药脂肽融合抑制剂有效防止雪貂传染 SARS-CoV-2

Intranasal fusion inhibitory lipopeptide prevents direct contact SARS-CoV-2 transmission in ferrets

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中文摘要：

遏制新冠肺炎大流行需要减少病毒传播。SARS-CoV-2 感染是由病毒和宿主细胞膜之间的膜融合引起的，由病毒 S 蛋白介导。文中研究者设计了一种二聚脂肽融合抑制剂，可以阻断 SARS-CoV-2 感染第一步，并证明它可以完全防止雪貂感染 SARS-CoV-2。研究者每天对未感染的雪貂进行鼻内给药，将其与已感染的雪貂直接接触 24h，未给药的雪貂 100%感染，而给药的雪貂则被完全保护。这些脂肽高度稳定且无毒，因此易于转化为安全有效的鼻内预防方法，可以有效阻止 SARS-CoV-2 的感染。

Abstract

Containment of the COVID-19 pandemic requires reducing viral transmission. SARS-CoV-2 infection is initiated by membrane fusion between the viral and host cell membranes, mediated by the viral spike protein. We have designed a dimeric lipopeptide fusion inhibitor that blocks this critical first step of infection for emerging coronaviruses and document that it completely prevents SARS-CoV-2 infectionin ferrets. Daily intranasal administration to ferrets completely prevented SARS-CoV-2 direct-contact transmission during 24-hour co-housing with infected animals, under stringent conditions that resulted in infection of 100% of untreated animals. These lipopeptides are highly stable and non-toxic and thus readily translate into a safe and effective intranasal prophylactic approach

to reduce transmission of SARS-CoV-2.

14. 高效双特异性 sybodies 中和 SARS-CoV-2

Highly potent bispecific sybodies neutralize SARS-CoV-2

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编译者：张怡

中文摘要：

新冠肺炎大流行已导致全球危机。研究者报道了合成的纳米体，称为 sybodies，针对 SARS-CoV-2 刺突蛋白的受体结合域(RBD)。他们鉴定了一个 sybody 对(sb# 15 和 sb# 68)，它可以同时与 RBD 结合，并阻断 ACE2 结合，从而中和假病毒和活 SARS-CoV-2 病毒。Cryo-EM 分析表明，刺突蛋白在两个系统的 sybodies 呈现对称和非对称的构象状态。在对称复合物中，三个 RBD 均由两个 sybodies 结合，并采用上构象。不对称构象具有 3 个 sb# 15 和 2 个 sb# 68，包括一个向下 RBD、一个 up-out RBD 和一个向上 RBD。与单一结合剂相比，sybodies 的双特异性融合使中和能力提高了 100 倍。研究表明，将两个识别空间离散结合位点的结合剂连接在一起，可产生有潜在治疗应用的高效 SARS-CoV-2 抑制剂。

Abstract

The COVID-19 pandemic has resulted in a global crisis. Here, we report the generation of synthetic nanobodies, known as sybodies, against the receptor-binding domain (RBD) of SARS-CoV-2 spike protein. We identified a sybody pair (Sb#15 and Sb#68) that can bind simultaneously to the RBD, and block ACE2 binding, thereby neutralizing pseudotyped and live SARS-CoV-2 viruses. Cryo-EM analyses of the spike protein in complex with both sybodies revealed symmetrical and asymmetrical conformational states. In the symmetric complex each of the three RBDs were bound by both sybodies, and adopted the up conformation. The asymmetric conformation, with three Sb#15 and two Sb#68 bound, contained one down RBD, one up-out RBD and one up RBD. Bispecific fusions of the sybodies increased the neutralization potency 100-fold, as compared to the single binders. Our work demonstrates that linking two binders that recognize spatially-discrete binding sites result in highly potent SARS-CoV-2 inhibitors for potential therapeutic applications.

15. 正在流行的 SARS-CoV-2 Spike 蛋白 N439K 突变体在逃避抗体介导的免疫响应同时保持了病毒的适应性

The circulating SARS-CoV-2 spike variant N439K maintains fitness while evading antibody-mediated immunity

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DOI 或 PUBMED ID：
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中文摘要：

SARS-CoV-2 病毒可以通过突变逃避人体的免疫响应，从而影响新开发的疫苗和抗体药物的功效。本文中，作者证明了 SARS-CoV-2 病毒中免疫显性的 Spike（S）蛋白受体结合基序（RBM）是 S 蛋白中差异最大的区域，并对一种正在流行的 N439K RBM 突变体提供了流行病学，临床和分子表征的数据。作者证明，携带 N439K 突变的 S 蛋白与 hACE2 受体的结合亲和力更强。同时，与野生型相比，N439K 突变病毒具有相似的临床结果和体外复制适应性。作者还发现，N439K 突变导致了病毒对一组中和性单克隆抗体，包括一项正在临床试验中的抗体，的免疫逃逸；以及对从相当一部分恢复后的被感染患者中分离出来的多克隆血清的免疫逃逸。在 SARS-CoV-2 病毒的 S 蛋白上可能会发生诸如 N439K 之类的免疫逃逸突变，使病毒维持感染能力和适应性。这表明人们需要进行持续的分子级别监测，以指导疫苗和治疗药物的开发和使用。

Abstract:
SARS-CoV-2 can mutate to evade immunity, with consequences for the efficacy of emerging vaccines and antibody therapeutics. Herein we demonstrate that the immunodominant SARS-CoV-2 spike (S) receptor binding motif (RBM) is the most divergent region of S, and provide epidemiological, clinical, and molecular characterization of a prevalent RBM variant, N439K. We demonstrate that N439K S protein has enhanced binding affinity to the hACE2 receptor, and that N439K virus has similar clinical outcomes and in vitro replication fitness as compared to wild- type. We observed that the N439K mutation resulted in immune escape from a panel of neutralizing monoclonal antibodies, including one in clinical trials, as well as from polyclonal sera from a sizeable fraction of persons recovered from infection. Immune evasion mutations that maintain virulence and fitness such as N439K can emerge within SARS-CoV-2 S, highlighting the need for ongoing molecular surveillance to guide development and usage of vaccines and therapeutics.

16. 人类 SARS-CoV-2 同源序列通过 NamiRNA 增强子网络上调透明质酸促进 COVID-19 的临床进展

Human Identical Sequences of SARS-CoV-2 Promote Clinical Progression of COVID-19 by Upregulating Hyaluronan via NamiRNA-Enhancer Network

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DOI 或 PUBMED ID：
编译者：王玮
中文摘要：
COVID-19 大流行是一种广泛而致命的公共卫生危机。病原体 SARS-CoV-2 在下呼吸道复制，导致致命的肺炎。尽管人们对 SARS-CoV-2 的致病机理进行了大量的研究，但 SARS-CoV-2 如何与宿主相互作用的潜在机制仍有待深入研究。该研究通过对 SARS-CoV-2 与人类基因组序列的比较，确定了 SARS-CoV-2 基因组中 5 个完全保守的元件，称为人类同源序列（human identical sequences, HIS）。HIS 在 SARS-CoV 和 MERS-CoV 的基因组中均存在。同时，HIS-SARS-CoV-2 在灵长类动物中高度保守。理论上讲，HIS-SARS-CoV-2 会表现为病毒源性 miRNAs，直接靶向人类基因组，并进一步与宿主增强子相互作用，激活邻近和远处基因的表达，包括细胞因子基因和血管紧张素转换酶 II（ACE2），即 SARS-CoV-2 细胞进入的受体，以及透明质酸合成酶 2（HAS2），进一步增加透明质酸的形成。值得注意的是，COVID-19 患者血浆中透明质酸水平与急性呼吸窘迫综合征（ARDS）的严重程度和高风险密切相关，并可作为 COVID-19 进展的预测因子。HIS 的拮抗剂能有效地下调透明质酸水平，4-Methylumbelliferone（MU）是透明质酸合成的抑制剂，是缓解 COVID-19 治疗肺部 ARDS 的潜在药物。该研究结果显示，SARS-CoV-2 中的 HIS 元素参与了 COVID-19 患者的细胞因子风暴和 ARDS。因此，通过 4-MU 直接阻断 HIS 参与的激活过程或透明质酸的合成可能是缓解 COVID-19 进展的有效策略。
Abstract:
The COVID-19 pandemic is a widespread and deadly public health crisis. The pathogen SARS-CoV-2 replicates in the lower respiratory tract and causes fatal pneumonia. Although tremendous efforts have been put into investigating the pathogeny of SARS-CoV-2, the underlying mechanism of how SARS-CoV-2 interacts with its host is largely unexplored. Here, by comparing the genomic sequences of SARS-CoV-2 and human, we identified five fully conserved elements in SARS-CoV-2 genome, which were termed as “human identical sequences (HIS)”. HIS are also recognized in both SARS-CoV and MERS-CoV genome. Meanwhile, HIS-SARS-CoV-2 are highly conserved in the primate. Mechanically, HIS-SARS-CoV-2, behaving as virus-derived miRNAs, directly target to the human genomic loci and further interact with host enhancers to activate the expression of adjacent and distant genes, including cytokines gene and angiotensin converting enzyme II (ACE2), a well-known cell entry receptor of SARS-CoV-2, and hyaluronan synthase 2 (HAS2), which further increases hyaluronan formation. Noteworthily, hyaluronan level in plasma

of COVID-19 patients is tightly correlated with severity and high risk for acute respiratory distress syndrome (ARDS) and may act as a predictor for the progression of COVID-19. HIS antagomirs, which downregulate hyaluronan level effectively, and 4-Methylumbelliferone (MU), an inhibitor of hyaluronan synthesis, are potential drugs to relieve the ARDS related ground-glass pattern in lung for COVID-19 treatment. Our results revealed that unprecedented HIS elements of SARS-CoV-2 contribute to the cytokine storm and ARDS in COVID-19 patients. Thus, blocking HIS-involved activating processes or hyaluronan synthesis directly by 4-MU may be effective strategies to alleviate COVID-19 progression.

17. 家畜和野生动物中高度分化的呼吸道上皮细胞培养株对 SARS-CoV-2 病毒的敏感性

Susceptibility of well-differentiated airway epithelial cell cultures from domestic and wildlife animals to SARS-CoV-2

来源：bioRxiv

发布时间：2020-11-10

链接：https://www.biorxiv.org/content/10.1101/2020.11.10.374587v1

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中文摘要：

SARS-CoV-2 病毒已在全球蔓延，世界各地的确诊病例数在持续增加。除人以外，SARS-CoV-2 病毒的动物源头，以及中间宿主和潜在的反向传播的寄主、宿主，目前还都不明确。为了规避伦理和实验方面的限制，更重要的是，为了减少和完善动物实验，作者采用了由多种家畜和野生动物的呼吸道上皮细胞（AEC）构成的细胞培养株库，评估这些细胞对 SARS-CoV-2 病毒的易感性。在这项研究中，作者将分化良好的猴，猫，雪貂，狗，兔，猪，牛，山羊，美洲驼，骆驼和两种新热带蝙蝠物种的 AEC 培养株接种了 SARS-CoV-2 病毒。作者发现，SARS-CoV-2 病毒仅在猴和猫的 AEC 培养株模型中发生了有效的复制。子代病毒的全基因组测序结果显示，没有明显的迹象表明，SARS-CoV-2 有效感染猴和猫的呼吸道上皮细胞需要核酸变化。本文的发现和先前报道的人传染动物的案例都值得密切的关注，以了解猫，猴，及其他密切相关的物种作为 SARS-CoV-2 病毒的反向传播的寄主、宿主的潜在作用。

Abstract:

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has spread globally, and the number of cases continues to rise all over the world. Besides humans, the zoonotic origin, as well as intermediate and potential spillback host reservoirs of SARS-CoV-2 are unknown. To circumvent ethical and experimental constraints, and more importantly, to reduce and refine animal experimentation, we employed our airway epithelial cell (AEC) culture repository composed of various domesticated and wildlife animal species to assess their susceptibility to SARS-CoV-2. In this study, we inoculated well-differentiated animal AEC

cultures of monkey, cat, ferret, dog, rabbit, pig, cattle, goat, llama, camel, and two neotropical bat species with SARS-CoV-2. We observed that SARS-CoV-2 only replicated efficiently in monkey and cat AEC culture models. Whole-genome sequencing of progeny virus revealed no obvious signs of nucleotide transitions required for SARS-CoV-2 to productively infect monkey and cat epithelial airway cells. Our findings, together with the previously reported human-to-animal spillover events warrants close surveillance to understand the potential role of cats, monkeys, and closely related species as spillback reservoirs for SARS-CoV-2.

18. 人类对 SARS-CoV-2 预先存在的和新的体液免疫

Preexisting and de novo humoral immunity to SARS-CoV-2 in humans

来源：Science

发布时间：2020-11-06

链接：https://science.sciencemag.org/content/early/2020/11/05/science.abe1107

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DOI 或 PUBMED ID：10.1126/science.abe1107

编译者：刘焕珍

中文摘要：

使用识别 SARS-CoV-2 蛋白的抗体的多种检测方法，我们可以检测到先前存在的体液免疫。可以通过以流式细胞术为基础的方法在未感染 SARS-CoV-2 的个体中检测到 SARS-CoV-2 刺突蛋白（S）的反应性抗体，并且在儿童和青少年中特别普遍。它们主要是 IgG 类，并靶向 S2 亚基。相比之下，SARS-CoV-2 感染可诱导更高滴度的 SARS-CoV-2 S 反应性 IgG 抗体，既靶向 S1 和 S2 亚基，也伴随 IgM 和 IgA 抗体，持续整个观察期。值得注意的是，未感染 SARS-CoV-2 的供体血清对 SARS-CoV-2 和 SARS-CoV-2 S 假型表现出特定的中和活性。区分原有免疫和新生免疫对于我们了解 SARS-CoV-2 感染的易感性和自然病程至关重要。

Abstract:

Zoonotic introduction of novel coronaviruses may encounter preexisting immunity in humans. Using diverse assays for antibodies recognizing SARS-CoV-2 proteins, we detect preexisting humoral immunity. SARS-CoV-2 spike glycoprotein (S)-reactive antibodies were detectable by a flow cytometry-based method in SARS-CoV-2-uninfected individuals and were particularly prevalent in children and adolescents. They were predominantly of the IgG class and targeted the S2 subunit. By contrast, SARS-CoV-2 infection induced higher titers of SARS-CoV-2 S-reactive IgG antibodies, targeting both the S1 and S2 subunits, and concomitant IgM and IgA antibodies, lasting throughout the observation period. Notably, SARS-CoV-2-uninfected donor sera exhibited specific neutralizing activity against SARS-CoV-2 and SARS-CoV-2 S pseudotypes. Distinguishing preexisting and de novo immunity will be critical for our understanding of susceptibility to and the natural course of SARS-CoV-2 infection.

19. Baricitinib 治疗可解决 SARS-CoV-2 感染恒河猴的下呼吸道巨噬细胞炎症和中性粒细胞募集

Baricitinib treatment resolves lower airway macrophage inflammation and neutrophil recruitment in SARS-CoV-2-infected rhesus macaques

来源：cell

发布时间：2020-11-09

链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31466-5

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DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2020.11.007

编译者：刘焕珍

中文摘要：

SARS-CoV-2 诱导的高细胞血症和炎症与 COVID-19 疾病的严重程度严重相关。Baricitinib 是一种临床批准的 JAK1/2 抑制剂，目前正在 COVID-19 临床试验中进行研究。在这里，我们研究了 baricitinib 在恒河猴感染 SARS-CoV-2 的模型中的免疫学和病毒学功效。使用 Baricitinib 不会减少从鼻和咽拭子、支气管肺泡灌洗液和组织中脱落的病毒。两组之间的 I 型 IFN 抗病毒反应和 SARS-CoV-2 特异性 T 细胞反应仍然相似。用 Baricitinib 治疗的动物显示出炎症减轻，炎症细胞肺部浸润减少，网状组织活动减少以及肺部病理更加有限。重要的是，用 baricitinib 治疗的动物对引起炎症和嗜中性粒细胞募集的细胞巨噬细胞和趋化因子的肺巨噬细胞产生具有迅速而显着的抑制作用。这些数据支持使用 Baricitinib 作为由 SARS-CoV-2 感染引起的炎症的一线治疗的有益作用，并阐明了其潜在的免疫学机制。

Abstract:

SARS-CoV-2 induced hypercytokinemia and inflammation are critically associated with COVID-19 disease severity. Baricitinib, a clinically approved JAK1/2 inhibitor, is currently being investigated in COVID-19 clinical trials. Here, we investigated the immunologic and virologic efficacy of baricitinib in a rhesus macaque model of SARS-CoV-2 infection. Viral shedding measured from nasal and throat swabs, bronchoalveolar lavages and tissues was not reduced with baricitinib. Type-I IFN antiviral responses and SARS-CoV-2-specific T-cell responses remained similar between the two groups. Animals treated with baricitinib showed reduced inflammation, decreased lung infiltration of inflammatory cells, reduced NETosis activity, and more limited lung pathology. Importantly, baricitinib treated animals had a rapid and remarkably potent suppression of lung macrophages production of cytokines and chemokines responsible for inflammation and neutrophil recruitment. These data support a beneficial role for, and elucidate the immunological mechanisms underlying, the use of baricitinib as a frontline treatment for inflammation induced by SARS-CoV-2 infection.

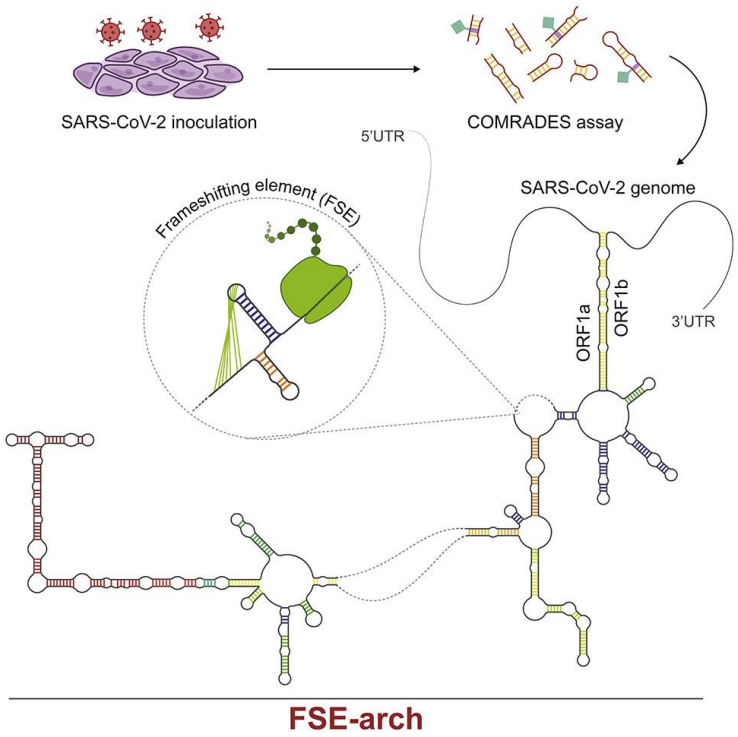
20. SARS-CoV-2 的短程和长程 RNA-RNA 互作

The short- and long-range RNA-RNA Interactome of SARS-CoV-2

来源：Molecular Cell (pre-proof)

发布时间：2020-11-05

链接：https://www.cell.com/molecular-cell/fulltext/S1097-2765(20)30782-6
第一作者：Omer Ziv
通讯作者：Eric A. Miska
通讯作者单位：University of Cambridge et al.
DOI 或 PUBMED ID：
编译者：蒋立春
重点：
在细胞中 SARS-CoV-2 的基因组和亚基因组存在非常丰富的 RNA-RNA 互作网络。这些相互作用对于调控病毒的转录和复制通路起到重要作用。
跨越上千碱基的长程结构导致的动态的拓扑结构。
在宿主和病毒 RNA 之间存在多个位点特异性的结合。
一个位于核糖体读码框移动码原件附件的一个结合弓在进化上受到负选择。可能用于指导开发新的抗病毒策略。
Highlights
Comprehensive RNA-RNA networks of the SARS-CoV-2 genome and subgenomes inside cells
Long-range structures spanning thousands of bases resulting in dynamic topologies
Multiple site-specific interactions between host and virus RNAs
An arch around the ribosomal frameshifting element is under purifying selection



21. 用相关的多模态多尺度冷冻成像揭示 SARS-CoV-2 组装和出胞的通路
SARS-CoV-2 Assembly and Egress Pathway Revealed by Correlative Multi-modal Multi-scale Cryo-imaging
来源：biorxiv
发布时间：2020-11-05

链接：https://www.biorxiv.org/content/10.1101/2020.11.05.370239v1
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SARS-CoV-2 疫情爆发以来，已经有相当多的纯化的重组病毒成分以及失活病毒的结构研究。但是对天然感染细胞状态下的 SARS-CoV-2 的结构研究很少，所以我们对 SARS-CoV-2 复制周期缺乏全面的认识。病毒基因组的复制、病毒的组装和出胞是由多个步骤以及许多病毒和细胞的蛋白参与的过程。了解这个过程对找到阻止感染的医学干预手段至关重要。在这个研究中作者在近乎天然状态的水化冷冻条件下对绿猴细胞中 SARS-CoV-2 复制进行了研究。采用独特的相关性多模态、多尺度的冷冻成像方法，结合软 X 射线冷冻断层成像以及一系列冷冻聚焦离子束显微镜/扫描电镜对整个 SARS-CoV-2 感染的细胞进行 3 维成像。其中采用冷冻电子断层技术对细胞片层和细胞边缘进行成像，采用断层扫描图平均化对病毒成分的结构进行解析。该研究揭示了 SARS-CoV-2 感染带来的复杂全细胞水平的细胞毒性。比如该研究揭示了细胞质中负责 RNA 合成和病毒组装的大量异质性的囊泡的结构，另外也研究了病毒出胞以及大量细胞质进入细胞核的膜通道形成的过程。对细胞片层的冷冻电子断层成像揭示了病毒 RNA 是怎样被从合成以及组装它们的双层膜囊泡转运出来；病毒的刺突核和核糖体蛋白怎么帮助病毒组装和出芽；以及组装完成的病毒颗粒怎么从细胞中出去；从而构建了 SARS-CoV-2 基因组复制、病毒组装以及出胞通路的模型。

Since the outbreak of the SARS-CoV-2 pandemic, there have been intense structural studies on purified recombinant viral components and inactivated viruses. However, investigation of the SARS-CoV-2 infection in the native cellular context is scarce, and there is a lack of comprehensive knowledge on SARS-CoV-2 replicative cycle. Understanding the genome replication, assembly and egress of SARS-CoV-2, a multistage process that involves different cellular compartments and the activity of many viral and cellular proteins, is critically important as it bears the means of medical intervention to stop infection. Here, we investigated SARS-CoV-2 replication in Vero cells under the near-native frozen-hydrated condition using a unique correlative multi-modal, multi-scale cryo-imaging approach combining soft X-ray cryo-tomography and serial cryoFIB/SEM volume imaging of the entire SARS-CoV-2 infected cell with cryo-electron tomography (cryoET) of cellular lamellae and cell periphery, as well as structure determination of viral components by subtomogram averaging. Our results reveal at the whole cell level profound cytopathic effects of SARS-CoV-2 infection, exemplified by a large amount of heterogeneous vesicles in the cytoplasm for RNA synthesis and virus assembly, formation of membrane tunnels through which viruses exit, and drastic cytoplasm invasion into nucleus. Furthermore, cryoET of cell lamellae reveals how viral RNAs are transported from double-membrane vesicles where they are synthesized to viral assembly sites; how viral spikes and RNPs assist in virus assembly and budding; and how fully assembled virus particles exit the cell, thus stablishing a model of SARS-CoV-2 genome replication, virus assembly and egress pathways.

22. K18-hACE2 小鼠中 COVID-19 的治疗和发病机制，包括嗅觉丧失

COVID-19 treatments and pathogenesis including anosmia in K18-hA CE2 mice

来源：Nature
发布时间：2020-11-09
链接：https://www.nature.com/articles/s41586-020-2943-z

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DOI 或 PUBMED ID：https://doi.org/10.1038/s41586-020-2943-z

编译者：宋张悦

中文摘要：

COVID-19 大流行与大量发病率和死亡率相关。虽然在大流行的头几个月已经了解了许多情况，但 COVID-19 发病机理的许多特征仍有待确定。例如，嗅觉丧失是一种常见的表现，许多有这种症状的病人没有或只有轻微的呼吸道症状。在实验性感染导致 COVID-19 的 SARS-CoV-2 病毒的动物中进行的研究，为研究该病不易在人类患者中调查的方面提供了机会。尽管 COVID-19 的严重程度从无症状到致死不等，但大多数实验性感染为轻度疾病提供了认识。在这里，使用 K18-hACE2 小鼠（最初为非典研究而开发），我们证明感染 SARS-CoV-2 导致严重的肺部疾病，在一些小鼠中，导致严重的大脑疾病。在患有严重肺炎的小鼠中检测到血栓形成和血管炎的证据。此外，我们还证明，从 COVID-19 患者的康复期注入血浆可以预防致命疾病。小鼠在感染后早期就出现嗅觉丧失。值得注意的是，虽然用恢复期血浆进行预处理可以预防明显的临床疾病，但不能预防嗅觉丧失。因此，K18-hACE2 小鼠为研究轻度和致命性 COVID-19 的病理基础以及评估治疗干预措施提供了一个有用的模型。

Abstract

The ongoing COVID-19 pandemic is associated with substantial morbidity and mortality. Although much has been learned in the first months of the pandemic, many features of COVID-19 pathogenesis remain to be determined. For example, anosmia is a common presentation and many patients with this finding show no or only minor respiratory signs[1]. Studies in animals experimentally infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of COVID-19, provide opportunities to study aspects of the disease not easily investigated in human patients. Although COVID-19 severity ranges from asymptomatic to lethal[2], most experimental infections provide insights into mild disease[3]. Here, using K18-hACE2 mice that we originally developed for SARS studies[4], we show that infection with SARS-CoV-2 causes severe disease in the lung, and in some mice, the brain. Evidence of thrombosis and vasculitis was detected in mice with severe pneumonia. Furthermore, we show that infusion of convalescent plasma from a recovered patient with COVID-19 protected against lethal disease. Mice developed anosmia at early times after infection. Notably, although pre-treatment with convalescent plasma prevented notable clinical disease, it did not prevent anosmia. Thus, K18-hACE2 mice provide a useful model for studying the pathological underpinnings of both mild and lethal COVID-19 and for assessing therapeutic interventions.

23. 促进关于 COVID-19 的网络药理学研究的资源整合工作流程

A Workflow of Integrated Resources to Catalyze Network Pharmacology Driven COVID-19 Research

来源：biorxiv
发布时间：2020-11-05
链接：https://www.biorxiv.org/content/10.1101/2020.11.04.369041v1

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DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

背景 当新出现的病原体引起的暴发时，时间对于控制或减轻疾病的传播至关重要。药物重新定位是一种具有潜力的相对快速地提供治疗的策略。SARS-CoV-2 大流行表明，整合关键的数据资源来推动药物重新定位研究，包括宿主-宿主、宿主-病原体和药物-靶点相互作用，仍然是一项耗时的工作，这可能会导致治疗方法的开发和提供出现延误。

结果 该研究描述了一个为快速出现的数据集的半自动集成而设计的工作流，这类数据集可应用于网络药理学研究。该工作流程构建了一个以 COVID-19 为中心的多模态网络，该网络集成了 487 个宿主-病原体、74805 个宿主-宿主蛋白和 1265 个药物-靶点相互作用。生成了名为“Neo4COVID19”的 Neo4j 图形数据库，该数据库可以通过 web 界面和基于 Bolt 协议的 API 调用进行访问。Neo4COVID19 数据库将成为科学界的宝贵资产，并将促进发现治疗 COVID-19 的药物。

网站地址 https://neo4covid19.ncats.io

Abstract:

Motivation In the event of an outbreak due to an emerging pathogen, time is of the essence to contain or to mitigate the spread of the disease. Drug repositioning is one of the strategies that has the potential to deliver therapeutics relatively quickly. The SARS-CoV-2 pandemic has shown that integrating critical data resources to drive drug-repositioning studies, involving host-host, hostpathogen and drug-target interactions, remains a time-consuming effort that translates to a delay in the development and delivery of a life-saving therapy.

Results Here, we describe a workflow we designed for a semi-automated integration of rapidly emerging datasets that can be generally adopted in a broad network pharmacology research setting. The workflow was used to construct a COVID-19 focused multimodal network that integrates 487 host-pathogen, 74,805 host-host protein and 1,265 drug-target interactions. The resultant Neo4j graph database

named “Neo4COVID19” is accessible via a web interface and via API calls based on the Bolt protocol. We believe that our Neo4COVID19 database will be a valuable asset to the research community and will catalyze the discovery of therapeutics to fight COVID-19.

Availability https://neo4covid19.ncats.io

24. 为什么 COVID 的死亡率正在下降呢？

Why do COVID death rates seem to be falling?

来源：Nature

发布时间：2020-11-11

链接：https://www.nature.com/articles/d41586-020-03132-4

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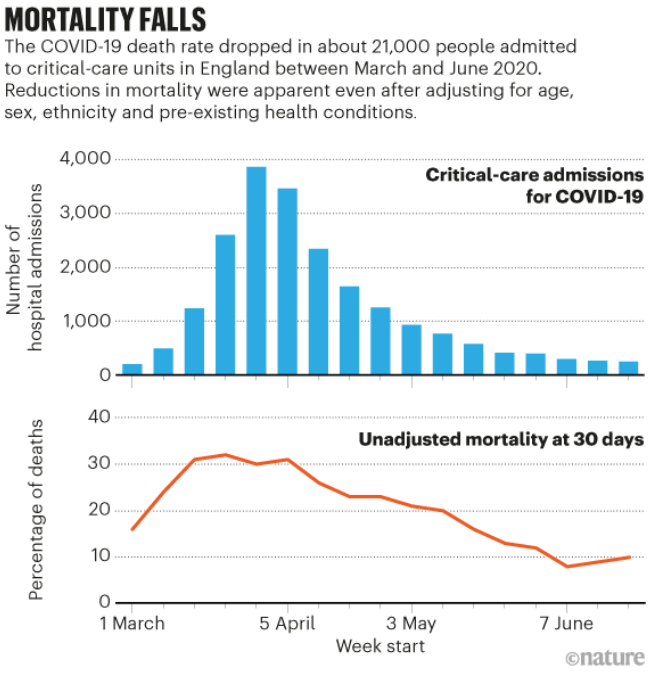
中文摘要：

维杰亚拉加万(Vijayaraghavan)在 Apollo Main Hospital 担任重症监护室专科医生，他指出一个亮点是重症监护室死亡率的下降。今年 4 月，新冠肺炎患者中高达 35%的患者死亡，使用呼吸机的患者中约 70%死亡。现在，重症监护病人的死亡率下降到 30%，使用呼吸机的病人的死亡率大约是 45-50%。

在世界各地，类似的故事正在上演。英国剑桥大学的重症监护医生夏洛特·萨默斯说，英国国家医疗服务系统(NHS)收集的数据显示死亡率有所下降(见“死亡率下降”)。宾夕法尼亚州匹兹堡大学(University of Pittsburgh)的重症监护医生德里克·安格斯(Derek Angus)表示，他所在医院的统计团队也发现，随着时间的推移，死亡率有所下降。

这种疾病已经在全世界感染了 5000 多万人，并导致 120 多万人死亡，在治疗策略方面没有取得重大进展，也没有什么特效药、新技术。死亡率下降的原因可能和来之不易的经验、不断变化的人口结构以及减轻医院压力有关。



Abstract
Hard-won experience, changing demographics and reduced strain on hospitals are all possibilities — but no one knows how long the change will last.

One shining light that he can point to is his intensive-care unit's dwindling fatality rate. In April, up to 35% of those in the unit with COVID-19 perished, and about 70% of those on ventilators died. Now, the intensive-care mortality rate for people with the illness is down to 30%, and for those on ventilators it is around 45–50%. "This itself was a relief," says Vijayaraghavan.

Around the world, similar stories are emerging. Charlotte Summers, an intensive-care physician at the University of Cambridge, UK, says that data collected by the country's National Health Service (NHS) show a decline in death rates1 (see 'Mortality falls'). Critical-care physician Derek Angus at the University of Pittsburgh in Pennsylvania says that his hospital's statistics team also saw reductions over time. "Without question, we've noticed a drop in mortality," says Angus. "All things being equal, patients have a better chance of getting out alive."