新型冠状病毒信息简报

第 103 期（2021 年 5 月 08-21 日报）

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

1. 2021 年 5 月 20 日疫情

数据来源：WHO

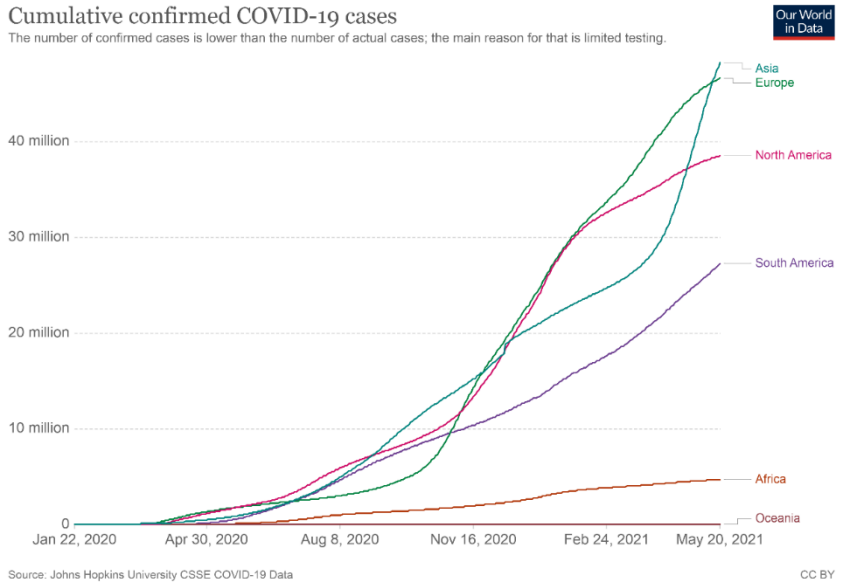
发布时间：2021 年 5 月 20 日北京时间下午 4 点

根据 WHO 提供的数据，2021 年 5 月 20 日全球累计确诊新型冠状病毒病人 **164, 523, 894** 例，当日新增确诊 **638, 247** 例，累计死亡 **3, 412, 032** 例，当日新增死亡 **13, 247**。全球至少接种一剂疫苗的人数为 **657, 768, 699**。

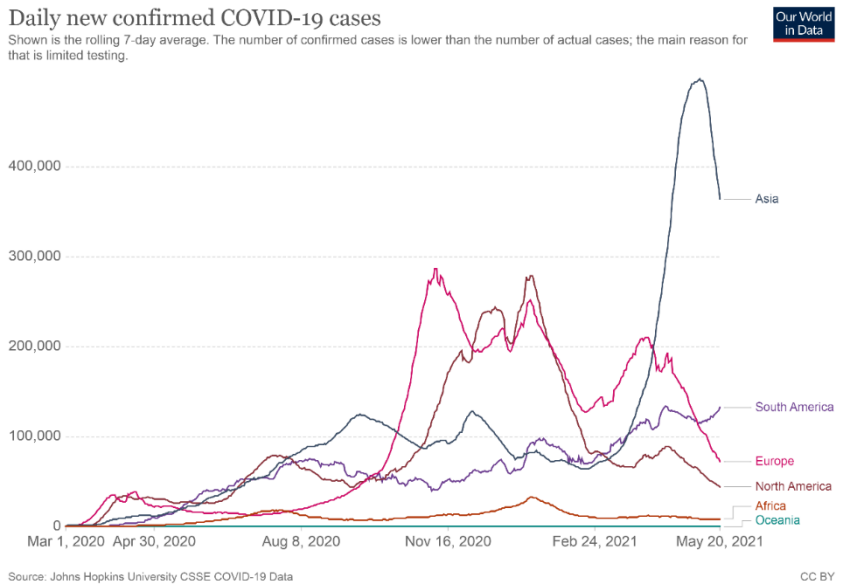
中国累计确诊 **105, 647** 例，累计死亡 **4, 861** 例，当日新增确诊 **317** 例（其中台湾地区新增 292 例），新增死亡 **1** 例。

截至 2021 年 5 月 20 日，31 个省（自治区、直辖市）和新疆生产建设兵团累计报告接种新冠病毒疫苗 46669.8 万剂次。

(http://www.nhc.gov.cn/xcs/yqfkdt/202105/61ca087702164c328e87f2ed3516a77f.shtml)

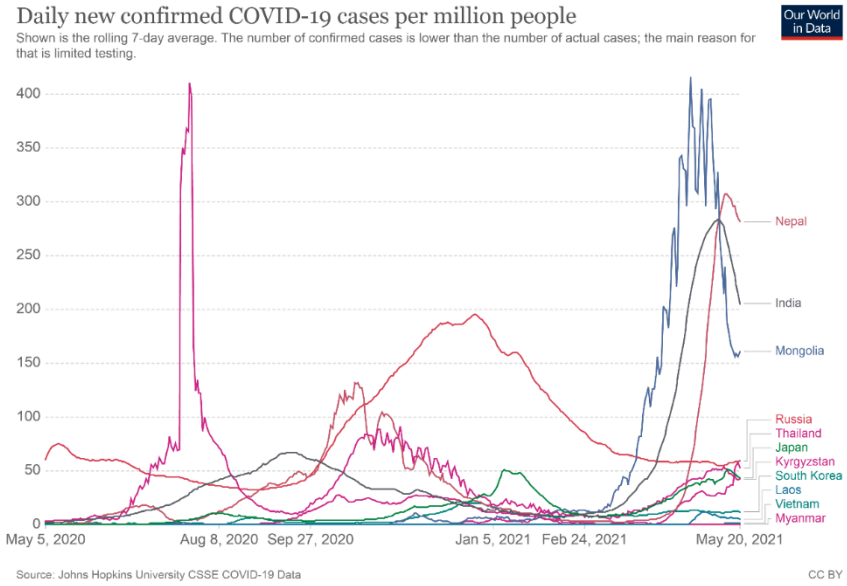


世界各洲确诊人数分布图（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）

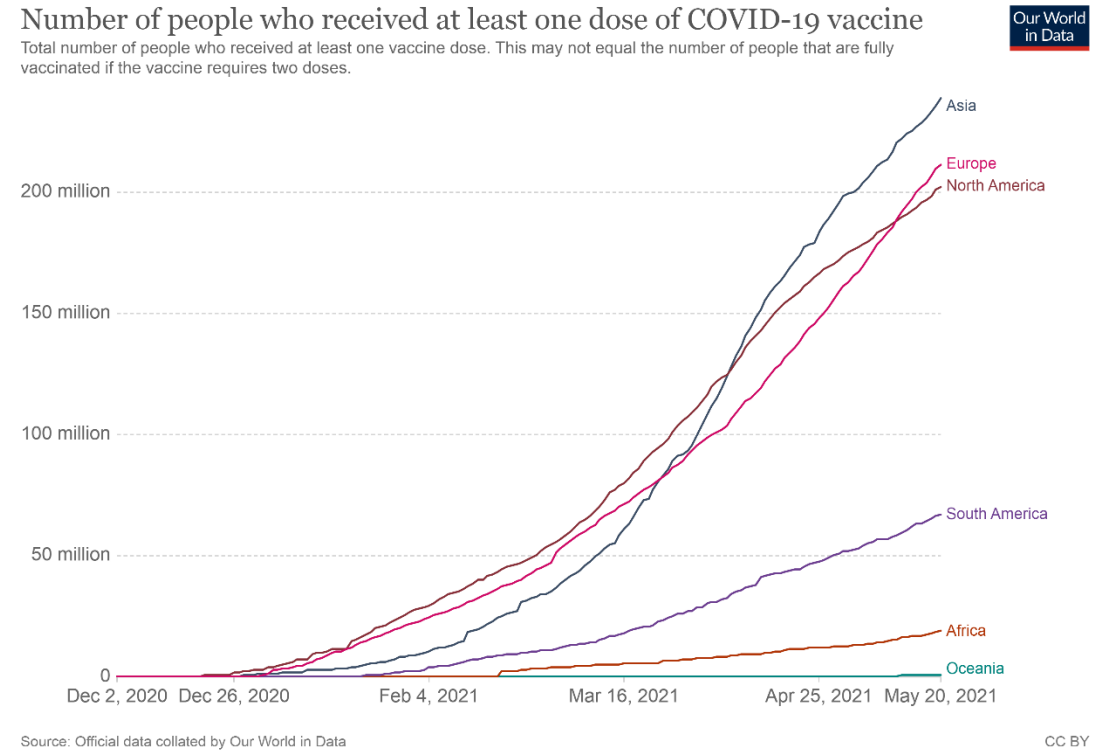


世界各洲每日新增确诊人数分布图（https://ourworldindata.org/covid-

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



中国周边国家每日新增确诊人数分布图（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



世界各洲接受至少一剂 COVID-19 疫苗的人群比例（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（5 月 20 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 全国累计接种新冠疫苗超过 4 亿！

来源：新化社微信公众号

发布时间：2021-05-16

链接：https://mp.weixin.qq.com/s/o7FroHkVaZpdWEoAHfMyaw

根据新化社公众号消息，截至 2021 年 5 月 16 日，全国各地累计接种新冠疫苗 4 亿剂。

3. 发现两种全新的可感染人类的冠状病毒，分别来自狗和猪

来源：生物世界公众号

发布时间：2021-05-22

转载链接：https://mp.weixin.qq.com/s/rzlwVO4hB8sG2_wSJoiCVg

撰文 | 王聪

编辑 | nagashi

排版 | 水成文

摘要:

2021 年 5 月 20 日，Science 发布了一篇题为：Two more coronaviruses can infect people, studies suggest 的新闻，称**发现了两种全新的可感染人类的冠状病毒**。

在此之前，只知道有 **7 种**可以感染人类的冠状病毒，1966 年，科学家发现了第一种可感染人类的冠状病毒 HCoV-229E，之后又陆续发现了 HCoV-OC43、HCoV-NL63、HCoV-HKU1，**这四种冠状病毒均可感染人类，但是致病性较低，仅会引起感冒样症状。**

然而，2011 年发现的 SARS-CoV、2012 年发现的 MERS-CoV，以及 2019 年发现的 SARS-CoV-2，**这三种冠状病毒不仅会感染人类，还可能导致严重症状，甚至死亡。**

仅仅在近十年内，就接连出现了三种高致病性的冠状病毒，因此，持续观测可能感染人类的冠状病毒显得非常重要。

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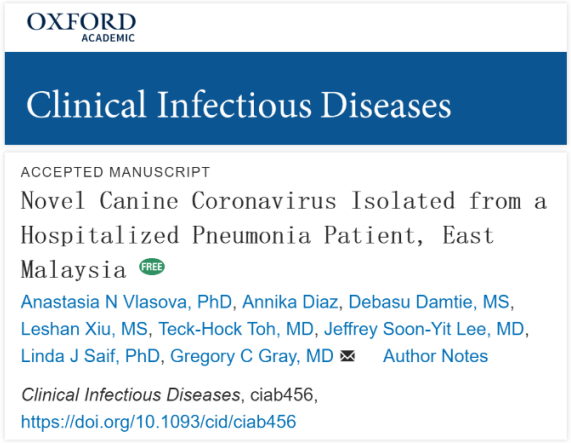
2021 年 5 月 20 日，美国杜克大学、俄亥俄州立大学的研究人员在 Clinical Infectious Diseases 期刊发表了一项题为：Novel Canine Coronavirus Isolated from a Hospitalized Pneumonia Patient, East Malaysia 的研究论文。


OXFORD ACADEMIC

Clinical Infectious Diseases

ACCEPTED MANUSCRIPT

Novel Canine Coronavirus Isolated from a Hospitalized Pneumonia Patient, East Malaysia

Anastasia N Vlasova, PhD, Annika Diaz, Debasu Damtie, MS, Leshan Xiu, MS, Teck-Hock Toh, MD, Jeffrey Soon-Yit Lee, MD, Linda J Saif, PhD, Gregory C Gray, MD Author Notes

Clinical Infectious Diseases, ciab456, https://doi.org/10.1093/cid/ciab456

研究团队对 2017-2018 年期间在马来西亚砂拉越邦医院住院的肺炎患者的 301 个样本重新进行了检测，从其中 8 个样本中检测到一种全新的犬冠状病毒。

这 8 个检测到全新冠状病毒感染的孩子生活在马来西亚砂拉越邦农村地区，当地医院没有针对肺炎和其他呼吸系统疾病的标准诊断程序，因此当时并没有发现是冠状病毒感染。

研究团队对其进行完整基因组测序后将其确定为一种**新型犬猫重组 α 冠状病毒**，并命名为 **CCoV-HuPn-2018**，**这是首次发现犬冠状病毒能够感染人类**。

这项研究提醒了我们，犬、猫冠状病毒可能并不像之前认为的那样不会感染人类，目前还没有证据表明这种冠状病毒能够在人与人之间传播，但是它们可能会在动物或人类内发展出这种能力，因此需要警惕。

到目前为止，威胁生命的三种冠状病毒：SARS-CoV、SARS-CoV-2、MERS-CoV 都是 β -冠状病毒，尚未发现会导致人类严重疾病的 α -冠状病毒。

这是从人肺炎患者中分离出的新型犬猫重组 α 冠状病毒的首次报道。如果该冠状病毒被确认为人类病原体，那么它**将成为已知会导致人类疾病的第八种冠状病毒**。这些发现强调了动物冠状病毒对公共健康的威胁，需要对其进行更好的监视。

在今年 3 月 25 日，美国佛罗里达大学的研究人员在预印本 **medRxiv** 发表了一项题为：Emergence of porcine delta-coronavirus pathogenic infections among children in Haiti through independent zoonoses and convergent evolution 的研究论文。

研究团队在 2014-2015 年的 3 名发烧的海地儿童的血清里发现了一种**猪冠状病毒**，研究人员将血清样品转移到猴细胞中，并能够生长出与已知猪冠状病毒遗传匹配的病毒。（该工作已提交至同行评议期刊）。


Comment on this paper

Emergence of porcine delta-coronavirus pathogenic infections among children in Haiti through independent zoonoses and convergent evolution

John A. Lednicky, Massimiliano S. Tagliamonte, Sarah K. White, Maha A. Elbadry, Md. Mahbubul Alam, Caroline J. Stephenson, Tania S. Bonny, Julia C. Loeb, Taina Telisma, Sonese Chavannes, David A. Ostrov, Carla Mavian, Valerie Madsen Beau De Rochars, Marco Salemi, J. Glenn Morris Jr.

doi: https://doi.org/10.1101/2021.03.19.21253391

这种猪冠状病毒属于 **δ -冠状病毒**，之前 **δ -冠状病毒**被认为只感染鸟类，之后在猪体内发现了感染，这表明该病毒已经跳出了鸟类，开始感染哺乳动物。

冠状病毒研究权威专家 **Ralph Baric** 教授表示，这是**目前唯一知道的既能感染鸟类又能感染哺乳动物的冠状病毒**。而且之后的研究表明，在体外培养条件下，该病毒可以感染人类细胞系。

这两项研究共同指出了动物疾病在公共卫生中的重要性，也提示了我们我们对家养动物使用冠状病毒疫苗的需求。

最后，**Ralph Baric** 教授表示，这些研究清楚地表明，迫切需要进行更多的研究来评估有关跨物种冠状病毒传播频率，以及它们在人与人之间传播潜力的关键问题。

参考资料：https://www.sciencemag.org/news/2021/05/two-more-coronaviruses-can-infect-people-studies-suggesthttps://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab456/6278597

https://www.medrxiv.org/content/10.1101/2021.03.19.21253391v1

4. 别再用咽拭子了：荷兰一家公司声称，他们的呼气式检测器可以帮助嗅出 COVID-19

Forget throat swabs: Dutch company claims its breathalyzer can help sniff out COVID-19

来源：Science

发布时间：2020-05-17

链接：https://www.sciencemag.org/news/2021/05/forget-throat-swabs-dutch-company-claims-its-breathalyzer-can-help-sniff-out-covid-19

第一作者：Jop de Vrieze (a science journalist in Amsterdam)

通讯作者：

通讯作者单位：

DOI 或 PUBMED ID：doi:10.1126/science.abj5103

编译者：宋张悦

中文摘要：

今年 2 月，在阿姆斯特丹公共卫生服务中心(GGD)接受 COVID-19 检测，他们是世界上第一批使用呼气测酒器进行检测的人，该仪器可以根据患者呼出的化学成分的混合物嗅出疾病。这种方法承诺比鼻拭子或咽拭子更快、更不舒服，而且更便宜。但在首次亮相后不久，25 人的检测结果为阴性，最终被证实患有 COVID-19，阿姆斯特丹停止了这种仪器的使用。然而，荷兰政府已经认定该装置本身是无辜的，并没有撤回其授权。一家商业测试公司正在广泛使用它，例如，明天在鹿特丹举行的欧洲歌唱大赛(Eurovision Song Contest)上，它被用于筛选工作人员。

SpiroNose 并不意味着可以确诊感染；相反，它的目的是尽可能多地排除这种可能性。对于剩下的人，测试结果是“不确定的”，这些人接受聚合酶链反应(PCR)或抗原测试。生产该设备的荷兰公司 Breathomix 的首席运营官里安·德·弗里斯(Rianne de Vries)表示：“我们想要的是尽可能多的排除被病毒感染的人，以减少检测负担，提高检测的意愿。”

Abstract:

People seeking to get tested for COVID-19 by Amsterdam’s Public Health Service (GGD) in February were pioneers: They were the first in the world to be tested using a “breathalyzer” that can sniff out the disease based on a mix of chemical components exhaled by the patient.

The approach promises to be faster and less unpleasant than a nose or throat swab, and cheaper. But soon after its premiere, 25 people who tested negative turned out to have COVID-19 after all, and Amsterdam halted its use. The Dutch government has decided the device itself was innocent, however, and has not withdrawn its authorization. A commercial testing company is now deploying it widely—for example to screen workers at the Eurovision Song Contest, which

begins tomorrow in Rotterdam.

SpiroNose isn't meant to definitively diagnose infection; instead it aims to rule it out in as many cases as possible. For the remainder, the test yields an "inconclusive," and those people receive a polymerase chain reaction (PCR) or antigen test. "What we want is to exclude as many people as possible who might be infected with the coronavirus, to reduce the testing burden and increase the willingness to test," says Rianne de Vries, chief operating officer of Breathomix, the Dutch company that makes the device.

5. COVID-19 重症与非 SARS-CoV-2 致重症肺炎的不同免疫学特征

Distinct immunological signatures discriminate severe COVID-19 from non-SARS-CoV-2-driven critical pneumonia

来源：Immunity

发布时间：2021-05-09

链接：https://www.cell.com/immunity/fulltext/S1074-7613(21)00208-9

第一作者：Stefanie Kreutmair

通讯作者：Burkhard Becher

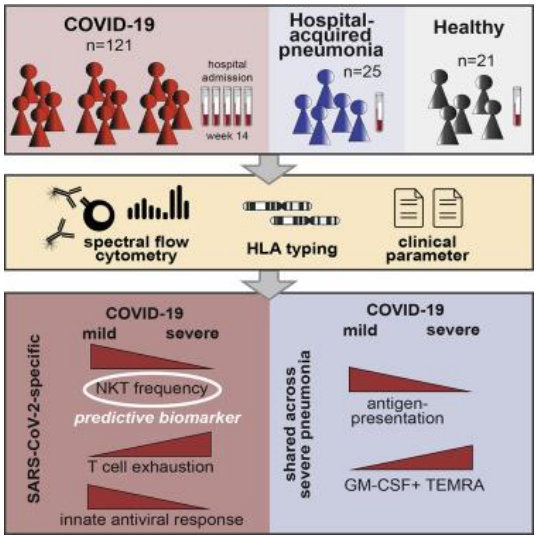
通讯作者单位：Institute of Experimental Immunology, University of Zurich, 5057 Zurich, Switzerland

DOI 或 PUBMED ID：https://doi.org/10.1016/j.immuni.2021.05.002

编译者：王玮

中文摘要：

COVID-19 患者的免疫特征为先天性和适应性免疫的许多改变。但是，这些变化究竟是 SARS-CoV-2 的特异性改变，还是由重症肺炎患者共同的炎症反应所驱动，目前尚不清楚。该研究使用纵向、高维单细胞光谱细胞术和算法引导分析比较了重症 COVID-19 与非 SARS-CoV-2 肺炎 ICU 患者的免疫状况。COVID-19 和非 SARS-CoV-2 肺炎均显示出紧急骨髓生成的增加，并表现出适应性免疫麻痹的特征。但是，T 细胞衰竭的病理免疫特征是 COVID-19 独有的。单细胞谱分析与 SARS-CoV-2 多肽预测的结合能力与患者 HLA 谱的整合进一步将 COVID-19 免疫病理学与病毒识别能力降低联系在一起。进行临床转化时，循环 NKT 细胞频率被确定为患者预后的预测生物标志物。这一比较性免疫图谱可用于解释治疗策略，从而干扰 COVID-19 重症特有的免疫病理级联反应。



Abstract:
Immune profiling of COVID-19 patients has identified numerous alterations in both innate and adaptive immunity. However, whether those changes are specific to SARS-CoV-2 or driven by a general inflammatory response shared across severely ill pneumonia patients remains unknown. Here, we compared the immune profile of severe COVID-19 with non-SARS-CoV-2 pneumonia ICU patients using longitudinal, high-dimensional single-cell spectral cytometry and algorithm-guided analysis. COVID-19 and non-SARS-CoV-2 pneumonia both showed increased emergency myelopoiesis and displayed features of adaptive immune paralysis. However, pathological immune signatures suggestive of T cell exhaustion were exclusive to COVID-19. The integration of single-cell profiling with a predicted binding capacity of SARS-CoV-2-petides to the patients' HLA profile further linked the COVID-19 immunopathology to impaired virus recognition. Towards clinical translation, circulating NKT cell frequency was identified as a predictive biomarker for patient outcome. Our comparative immune map serves to delineate treatment strategies to interfere with the immunopathologic cascade exclusive to severe COVID-19.

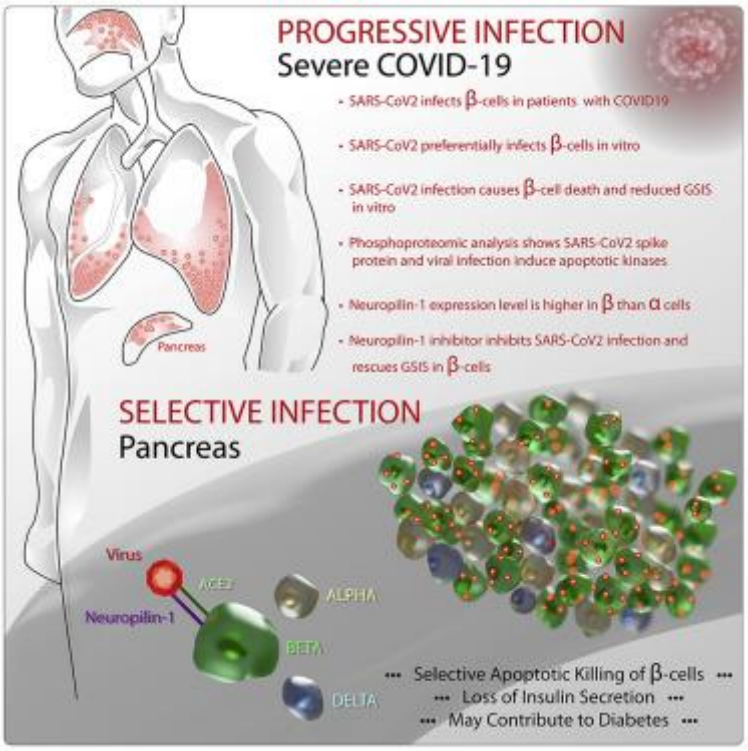
6. SARS-CoV-2 感染人胰腺 β 细胞并且损害 β 细胞

SARS-CoV-2 infects human pancreatic β-cells and elicits β-cell impairment
来源：cell metabolism
发布时间：2021-05-18
链接：https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00230-8
第一作者：Chien-Ting Wu
通讯作者：Peter K. Jackson
通讯作者单位: Stanford University School of Medicine
DOI: https://doi.org/10.1016/j.cmet.2021.05.013
要点：
SARS-CoV2 在体外可以感染人胰岛，在 COVID-19 病人中感染胰腺 β 细胞
SARS-CoV2 感染引起 β 细胞死亡并且降低体外的糖促胰岛素分泌
磷酸蛋白质组显示 SARS-CoV2 的刺突蛋白以及病毒会诱导凋亡激酶
高水平的 Neuropilin-1 是 SARS-CoV-2 选择性感染胰腺 β 细胞的原因，其抑制剂可以阻断感染 β 细胞感染和凋亡
总结
越来越多的证据表明 COVID-19 疫情和糖尿病存在复杂的关系。虽然先发糖尿病和重症 COVID-19 发生有关，不是很清楚重症 COVID-19 是糖尿病的因还是果。为了从机制上理解 COVID-19 和糖尿病的联系，我们检测了产生胰岛素的胰腺 β 细胞是否能被 SARS-CoV-2 感染，以及 SARS-CoV-2 是否会引起 β 细胞的丢失。我们发现 SARS-CoV-2 感染降低了胰腺的胰岛素水平以及胰岛素的分泌，诱导了 β 细胞程序性凋亡，抑制 NRP1 进行防止感染以及 β 细胞程序性凋亡。对感染的胰岛的蛋白磷酸化通路分析表明发生程序性坏死的 β 细胞信号和 1 型糖尿病里观察到的信号相似。总结而言，我们的研究表明 SARS-CoV-2 可以直接诱导 β 细胞死亡。
Highlights
SARS-CoV2 infects β-cells in COVID19 patients and in human islets in vitro

SARS-CoV2 infection causes β-cell death and reduced GSIS in vitro
Phosphoproteomics shows SARS-CoV2 spike protein and virus induce apoptotic kinases
High Neuropilin-1 levels support β-cell selectivity and inhibitors block infection

Summary
Emerging evidence points towards an intricate relationship between the pandemic of coronavirus disease 2019 (COVID-19) and diabetes. While pre-existing diabetes is associated with severe COVID-19, it is unclear if COVID-19 severity is a cause or consequence of diabetes. To mechanistically link COVID-19 to diabetes, we tested whether insulin-producing pancreatic β-cells can be infected by SARS-CoV-2 and cause β-cell depletion.
We found that the SARS-CoV-2 receptor, ACE2 and related entry factors (TMPRSS2, NRP1, TRFC) are expressed in β-cells, with selectively high expression of NRP1. We discovered that SARS-CoV-2 infects human pancreatic β-cells in patients who succumbed to COVID-19 and selectively infects human islet β-cells in vitro.
We demonstrated SARS-CoV-2 infection attenuates pancreatic insulin levels and secretion, and induces β-cell apoptosis, each rescued by NRP1 inhibition. Phosphoproteomic pathway analysis of infected islets indicates apoptotic β-cell signaling, similar to that observed in Type 1 diabetes (T1D). In summary, our study shows SARS-CoV-2 can directly induce β-cell killing.

该文图示摘要



7. SARS-CoV-2 感染诱导 β 细胞转分化

SARS-CoV-2 Infection Induces Beta Cell Transdifferentiation

来源：cell metabolism
发布时间：2021-05-19
链接：https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00232-1
第一作者：Xuming Tang
通讯作者：Shubing Chen
通讯作者单位： Weill Cornell Medicine
DOI: https://doi.org/10.1016/j.cmet.2021.05.015

要点

在 COVID-19 病人的尸检的 β 细胞中检测到了 SARS-CoV-2 病毒抗原

SARS-CoV-2 感染可以引起 β 细胞转分化

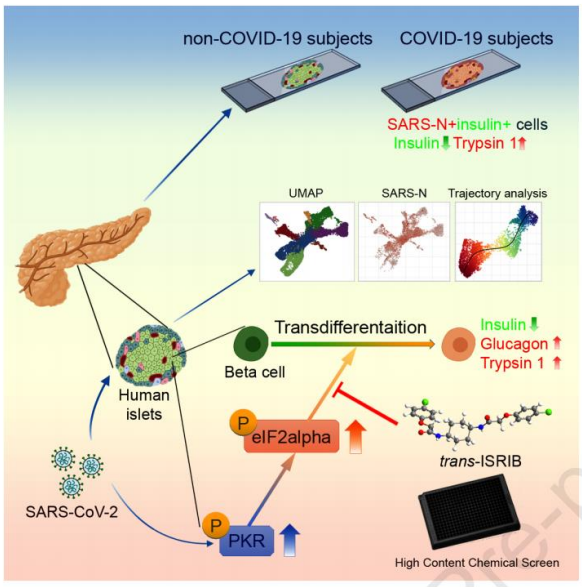
SARS-CoV-2 诱导的 β 细胞转分化是 Eif2 通路介导的

反式-ISRIB 可以反转 SARS-CoV-2 感染诱导的 β 细胞转分化

中文摘要

最近的临床数据显示 COVID-19 和糖尿病之间存在相关性。这里，我们阐述了在 COVID-19 病人的尸检样品中的胰岛 β 细胞中检测到了 SARS-CoV-2 病毒抗原。对于离体感染样品进行单细胞 RNA 测序以及免疫染色证明多种类型的胰岛细胞易感 SARS-CoV-2，SARS-CoV-2 可以诱导细胞应激反应以及诱导趋化因子。SARS-CoV-2 感染后，β 细胞的胰岛素表达水平下降、alpha 和 acinar 细胞的标记物包括胰高血糖素和胰蛋白酶表达却升高，这些一起提示发生了细胞转分化。细胞轨迹分析显示 SARS-CoV-2 诱导了 eIF2 通路介导的 β 细胞转分化。这个现象可以被反式整合的应激反应抑制剂反转（trans-ISRIB）。总结而言，这个研究揭示了 SARS-CoV-2 感染可以改变细胞命运，这个发现为解释 COVID-19 的病理学机制提供了更深入的解释。

图示摘要



Highlights

SARS-CoV-2 viral antigen is detected in beta cells of autopsies of COVID-19 subjects.

SARS-CoV-2 infection causes beta cell transdifferentiation.

SARS-CoV-2 induced beta cell transdifferentiation is mediated by eIF2 pathway.

Trans-ISRIB reverses SARS-CoV-2 infection induced beta cell transdifferentiation.

Abstract
Recent clinical data has suggested a correlation between Coronavirus disease 19 (COVID-19) and diabetes. Here, we describe the detection of SARS-CoV-2 viral antigen in pancreatic beta cells in autopsy samples from individuals with COVID-19.
Single-cell RNA-sequencing and immunostaining from ex vivo infections confirmed that multiple types of pancreatic islet cells were susceptible to SARS-CoV-2, eliciting a cellular stress response and the induction of chemokines.
Upon SARS-CoV-2 infection, beta cells showed a lower expression of insulin and a higher expression of alpha and acinar cell markers, including glucagon and trypsin1, respectively, suggesting cellular transdifferentiation.
Trajectory analysis indicated that SARS-CoV-2 induced eIF2 pathway-mediated beta cell transdifferentiation, a phenotype that could be reversed with trans-integrated stress response inhibitor (trans-ISRIB). All together, this study demonstrates an example of SARS-CoV-2 infection causing cell fate change, which provides further insight into the pathomechanisms of COVID-19.

8. BNT162b2 疫苗能够诱导产生针对新的 SARS-CoV-2 Spike 变异株的中和反应

BNT162b2-Elicited Neutralization against New SARS-CoV-2 Spike Variants

来源：NEJM
发布时间：2020-05-12
链接：https://www.nejm.org/doi/full/10.1056/NEJMc2106083?query=featured_home
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DOI：10.1056/NEJMc2106083
编译者：宋珂

中文摘要：
SARS-CoV-2 病毒持续进化的速度非常快，产生了一些引起人们关注的病毒新变异株。例如首次在加利福尼亚（B.1.429 谱系）和纽约（B.1.526 谱系）发现的变异株正引起美国的关注。最初在英国（B.1.1.7 谱系）检测到的变异株正在全球范围内扩散，现在也已经发生了 E484K 突变，使病毒据有了对某些单克隆抗体的抗性。
据作者报道，BNT162b2 疫苗对 COVID-19 的预防有效率能够达到 95%。BNT162b2 是一种表达 SARS-CoV-2 病毒融合前的稳定全长 spike 糖蛋白（S）的 mRNA 疫苗，其使用的 SARS-CoV-2 病毒株分离自武汉-Hu-1（GenBank accession number, MN908947.3）。此外，作者还发现，接种 BNT162b2 疫苗后产生的血浆，对携带 B.1.1.7 变异株 S 基因的重组 SARS-CoV-2 病毒和病毒 P.1 变异株仍然具有中和能力。不过对 B.1.1.7 变异株的中和能力有所下降。其中，B.1.1.7 变异株（B.1.351 谱系）首先发现于南非，而 P.1 变异株（P.1 谱系）首先发现于巴西。
为了明确 BNT162b2 疫苗诱导产生的中和作用对新近出现的病毒变异株是否仍然有效，作者利用基因工程将病毒变异株的完整 S 基因插入 USA-WA1/2020（分离于 2020 年 1 月）的遗传本底，生成了三种重组病毒。
在受试者第一次接种 BNT162b2 疫苗 3 周后，进行第二剂 30 μg 的注射。在 2 周或 4 周后，收集了 15 人的血清样本，利用 50% PRNT 实验对所有重组病毒进行了分析。所有中和性血清

样本与 USA-WA1/2020 和病毒变异株的滴度比例为 1:80 或更高。
依据现有数据，由重要疫苗诱导产生的免疫因子（中和抗体）对新出现的 B.1.526，B.1.429 和 B.1.1.7+E484K 病毒变异株仍然有效，同时证实了通过大规模接种目前已授权使用的高效疫苗而产生免疫力，并以此作为结束 COVID-19 疫情主要策略的重要性。

Abstract:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to evolve at a rapid pace, generating new variants that arouse concern. Variants that were first detected in California (B.1.429 lineage) and New York (B.1.526 lineage) are causing concern in the United States. A variant that was first detected in the United Kingdom (B.1.1.7 lineage) is spreading globally and has now acquired an E484K substitution, which confers resistance to certain monoclonal antibodies. We and our colleagues reported that BNT162b2, a messenger RNA vaccine that expresses the prefusion stabilized full spike glycoprotein (S) of SARS-CoV-2 isolate Wuhan-Hu-1 (GenBank accession number, MN908947.3), is 95% effective against coronavirus disease 2019 (Covid-19). In addition, we reported that recombinant SARS-CoV-2 bearing S genes from the B.1.1.7 variant, the variant first identified in South Africa (B.1.351 lineage), and the variant first identified in Brazil (P.1 lineage) remained susceptible to BNT162b2 vaccine-elicited serum neutralization, although at a reduced level for the B.1.351 variant.
To determine whether variants that have emerged more recently are also susceptible to BNT162b2-elicited neutralization, we engineered the complete S genes of the variant viruses into the genetic background of USA-WA1/2020 (isolated in January 2020), which resulted in three recombinant viruses.
All the recombinant viruses were analyzed by means of 50% plaque reduction neutralization testing with 20 human serum samples, collected from 15 persons 2 or 4 weeks after the second dose of 30 μg of BNT162b2, which was administered 3 weeks after the first immunization2. All the serum samples neutralized USA-WA1/2020 and the variant viruses at titers of 1:80 or higher.
Because these data show that the newly emerged B.1.526, B.1.429, and B.1.1.7+E484K variants remain susceptible to an important vaccine-elicited immune effector (neutralizing antibody), they confirm the importance of mass immunization with current, highly effective, authorized vaccines as a central strategy to end the Covid-19 pandemic.

9. SARS-CoV-2b.1.617 的出现及对疫苗诱导抗体的敏感性

SARS-CoV-2 B.1.617 emergence and sensitivity to vaccine-elicited antibodies
来源：bioRxiv
发布时间：2021-05-09
链接：https://www.biorxiv.org/content/10.1101/2021.05.08.443253v1
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通讯作者：V.S. Radhakrishnan,
通讯作者单位：印度 SARS-CoV-2 基因组学联合会（INSACOG），COVID-19 英国基因组学联合会(COG-UK)

DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：
B.1.617 变种于 2020 年底在印度马哈拉施特拉邦出现，并已蔓延到印度全国和至少 40 个国家。有人担心在受体结合域 L452R 和 E484Q 中发现的两个关键突变会对逃避中和抗体产生附加效应。在这里，作者描绘了 B.1.617 的系统发育和 spike 突变频率，在其他携带 L452R 的背景下。B.1.617.1spike 的决定性突变是 RBD 中与 ACE2 相互作用的 L452R 和 E484Q，是中和抗体的靶点。所有 B.1.617 病毒在 spike 的多碱性裂解位点区域都有 P681R 突变。我们报告，与武汉 1 号相比，B.1.617.1 携带 L452R、E484Q 和 P681R 的 spike 介导的进入细胞的效率略有降低。该 spike 使 BNT162b2 mRNA 疫苗诱导的抗体的敏感性一定程度降低，其程度与 L452R 或 E484Q 单独引起的敏感性降低相似。此外，我们还发现 P681R 突变显著增强了 B.1.617.1 spike 蛋白上合胞体的形成，可能导致仓鼠发病率增加和人类感染率增加。
Abstract:
The B.1.617 variant emerged in the Indian state of Maharashtra in late 2020 and has spread throughout India and to at least 40 countries. There have been fears that two key mutations seen in the receptor binding domain L452R and E484Q would have additive effects on evasion of neutralising antibodies. Here we delineate the phylogenetics of B.1.617 and spike mutation frequencies, in the context of others bearing L452R. The defining mutations in B.1.617.1 spike are L452R and E484Q in the RBD that interacts with ACE2 and is the target of neutralising antibodies. All B.1.617 viruses have the P681R mutation in the polybasic cleavage site region in spike. We report that B.1.617.1 spike bearing L452R, E484Q and P681R mediates entry into cells with slightly reduced efficiency compared to Wuhan-1. This spike confers modestly reduced sensitivity to BNT162b2 mRNA vaccine-elicited antibodies that is similar in magnitude to the loss of sensitivity conferred by L452R or E484Q alone. Furthermore, we show that the P681R mutation significantly augments syncytium formation upon the B.1.617.1 spike protein, potentially contributing to increased pathogenesis observed in hamsters and infection growth rates observed in humans.

10. SARS-CoV-2 变种 B.1.617 对 Bamlanivimab 耐药，并逃避了由感染和疫苗接种诱导的抗体

SARS-CoV-2 variant B.1.617 is resistant to Bamlanivimab and evades antibodies induced by infection and vaccination
来源：bioRxiv
发布时间：2021-05-05
链接：https://www.biorxiv.org/content/10.1101/2021.05.04.442663v1
第一作者：Markus Hoffmann
通讯作者：Stefan Pöhlmann
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DOI 或 PUBMED ID：
编译者：张鹏伟
中文摘要：

SARS-CoV-2 变体的出现威胁了遏制 COVID-19 大流行的努力。 近几周来，印度的 COVID-19 病例数和死亡人数急剧上升，一种新型的 SARS-CoV-2 变种 B.1.617 被认为是造成这些病例的主要原因。 B.1.617 的刺突蛋白在受体结合结构域中具有两个突变，该突变与 ACE2 受体相互作用并构成中和抗体的主要靶标。 因此，我们分析了 B.1.617 是否更擅长进入细胞和/或逃避抗体反应。 B.1.617 以稍微提高的效率进入了八种细胞系中的两种，并被进入抑制剂所阻断。 相反，B.1.617 对用于 COVID-19 治疗的抗体 Bamlanivimab 有抗性。 最后，尽管效率中等，但 B.1.617 却避开了由感染或疫苗接种诱导的抗体。 总的来说，我们的研究表明 B.1.617 对抗体的逃避可能有助于这种变异的迅速传播。

Abstract:

The emergence of SARS-CoV-2 variants threatens efforts to contain the COVID-19 pandemic. The number of COVID-19 cases and deaths in India has risen steeply in recent weeks and a novel SARS-CoV-2 variant, B.1.617, is believed to be responsible for many of these cases. The spike protein of B.1.617 harbors two mutations in the receptor binding domain, which interacts with the ACE2 receptor and constitutes the main target of neutralizing antibodies. Therefore, we analyzed whether B.1.617 is more adept in entering cells and/or evades antibody responses. B.1.617 entered two out of eight cell lines tested with slightly increased efficiency and was blocked by entry inhibitors. In contrast, B.1.617 was resistant against Bamlanivimab, an antibody used for COVID-19 treatment. Finally, B.1.617 evaded antibodies induced by infection or vaccination, although with moderate efficiency. Collectively, our study reveals that antibody evasion of B.1.617 may contribute to the rapid spread of this variant.

11. COVID-19 mRNA 疫苗在孕妇和哺乳期妇女中的免疫原性研究

Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women

来源：JAMA.

发布时间：2021-05-13

链接：

https://jamanetwork.com/journals/jama/fullarticle/2780202?guestAccessKey=af39f2e3-942b-4692-9554-508bcab77554&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=051321

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DOI 或 PUBMED ID：10.1001/jama.2021.7563

编译者：张丽双

中文摘要：

一项探索性、描述性、前瞻性队列研究纳入了 103 名从 2020 年 12 月至 2021 年 3 月接种了 COVID-19 疫苗的妇女和 28 名从 2020 年 4 月至 2021 年 3 月确认感染了 SARS-CoV-2 的妇女（最后一次随访日期为 2021 年 3 月 26 日）。其中 30 名孕妇和 16 名哺乳期妇女。结果：结合、中和和功能性非中和抗体反应以及 CD4 和 CD8 T 细胞反应在接种疫苗后的孕妇、哺乳期妇女和非妊娠妇女中都存在。在婴儿脐血和母乳中也观察到结合和中和抗体。对 SARS COV-2 突变株 B.1.1.7 和 B.1.351 的结合和中和抗体滴度均降低，但对突变株保持了 T 细胞应

答。这意味着在这个小样本中，COVID-19 mRNA 疫苗对孕妇和哺乳期妇女具有免疫原性，并可诱导对 SARS-CoV-2 突变株的免疫应答。

Abstract:
Question What is the immunogenicity of COVID-19 messenger RNA (mRNA) vaccines in pregnant and lactating women?
Findings In this cohort study involving 103 women who received a COVID-19 mRNA vaccine, 30 of whom were pregnant and 16 of whom were lactating, immunogenicity was demonstrated in all, and vaccine-elicited antibodies were found in infant cord blood and breast milk. Pregnant and nonpregnant vaccinated women developed cross-reactive immune responses against SARS-CoV-2 variants of concern.
Meaning In a small convenience sample, COVID-19 mRNA vaccines were immunogenic in pregnant and lactating women and induced immune responses against SARS-CoV-2 variants.

12. 妊娠期严重急性呼吸综合征冠状病毒 2 (SARS-CoV-2)疫苗接种

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy

来源：Obstetrics & Gynecology
发布时间：2021-05-11

文章链接：
https://journals.lww.com/greenjournal/Fulltext/9900/Severe_Acute_Respiratory_Syndrome_Coronavirus_2.206.aspx

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doi: 10.1097/AOG.0000000000004457

编译者：张怡

中文摘要：
针对严重急性呼吸系统综合症冠状病毒 2 (SARS-CoV-2)的疫苗已被批准用于紧急情况，但尽管严重疾病的风险增加，孕妇被排除在导致其获得批准的临床试验之外。胎盘发现可以提示潜在的临床风险，可能是罕见损伤的早期信号，只有在广泛使用后，才会看到在怀孕人群。
孕产妇 SARS-CoV-2 感染与蜕膜动脉病变、胎儿血管灌注不良和慢性组织细胞绒毛间炎相关。mRNA 疫苗通过激活 TLR3 诱导免疫反应，TLR3 在小鼠模型中与蜕膜动脉病变、生长限制、早产和胎儿丢失有关。研究的目的是评估在妊娠期间接受 SARS-CoV-2 疫苗接种的患者发生这些关键胎盘病变的频率。

Abstract
Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been approved for emergency use, but, despite elevated risk of severe disease, pregnant women were excluded from the clinical trials that led to their authorization. Placental findings can indicate potential clinical risk and could be an early signal for rare injury seen only after widespread use in the pregnant population.
Maternal SARS-CoV-2 infection has been associated with decidual arteriopathy,

fetal vascular malperfusion, and chronic histiocytic intervillositis. mRNA vaccines induce an immune response through activation of TLR3, which has been linked to decidual arteriopathy, growth restriction, preterm delivery, and fetal loss in mouse models.
Our objective was to evaluate the frequency of these key placental lesions in patients who received SARS-CoV-2 vaccination in pregnancy.

13. 推迟 COVID 疫苗的第二次接种时间可增强免疫反应

Delaying a COVID vaccine’s second dose boosts immune response
来源：Nature news
发布时间：2021-05-13
链接：https://www.nature.com/articles/d41586-021-01299-y?utm_source=Nature+Briefing&utm_campaign=ac23da77ef-briefing-dy-20210514&utm_medium=email&utm_term=0_c9dfd39373-ac23da77ef-46052274
作者：Heidi Ledford
编译者：孔娟
中文摘要：
面对有限的疫苗供应，联合王国于 2020 年底开始了一项大胆的公共卫生实验:推迟第二剂新冠肺炎疫苗。一项研究表明，对于 80 岁以上的患者，延迟第二次接种辉瑞-生物泰克 mRNA 疫苗可以使抗体应答增强三倍以上。作者表示，这是首次直接研究这种延迟如何影响冠状病毒抗体水平，并可能为其他国家的疫苗计划决策提供信息。12 月 30 日，联合王国宣布将第二次给药推迟至第一次给药后 12 周。为了确定延迟是否更有效，Amirthalingam 等人进行了相关研究，在预印版本发表 “Extended interval BNT162b2 vaccination enhances peak antibody generation in older people”，此研究纳入了 175 名 80 岁以上的疫苗接受者，他们在第一次给药后 3 周或 11-12 周接受了第二次辉瑞疫苗，随后测试了受试者抗 S 蛋白抗体水平，并评估了 T 细胞的免疫细胞(有助于随着时间保持抗体水平)对疫苗接种的反应。结果显示，两次接种间隔 12 周的受试者的抗体水平是间隔 3 周接种的 3.5 倍。间隔时间延长者的 T 细胞反应较低。但在强化注射后的九周内，并没有导致抗体水平下降得更快。 世界卫生组织免疫战略专家咨询小组主席亚历杭德罗·克拉维托(Alejandro Cravioto)表示，这些结果令人放心，但仅针对辉瑞疫苗，而这种疫苗在许多中低收入国家并不具备。他说，各国将需要考虑，在本国特定地区流行的变异病毒仅注射一剂疫苗后，是否可能增加感染风险。
Abstract
Facing a limited vaccine supply, the United Kingdom embarked on a bold public-health experiment at the end of 2020: delaying second doses of COVID-19 vaccines in a bid to maximize the number of people who would be at least partially protected from hospitalization and death. Now, a study suggests that delaying the second dose of the Pfizer–BioNTech mRNA vaccine could boost antibody responses after the second inoculation more than threefold in those older than 80. It is the first direct study of how such a delay affects coronavirus antibody levels, and could inform vaccine scheduling decisions in other countries, the authors say. “This study further supports a growing body of evidence that the approach taken in the UK for delaying that second dose has really paid off,” Gayatri Amirthalingam, an epidemiologist at Public Health England in London and

a co-author of the preprint, said during a press briefing. But for some existing vaccines, a longer wait between first and second doses yields a stronger immune response. Delaying the COVID-19 booster shots could also expand partial immunity among a greater swathe of the population than could the shorter dosing schedule. On 30 December, the United Kingdom announced that it would delay the second dose by up to 12 weeks after the first. To determine whether the delay paid off, Amirthalingam and her colleagues studied 175 vaccine recipients older than 80 who received their second dose of the Pfizer vaccine either 3 weeks or 11–12 weeks after the first dose. The team measured recipients' levels of antibodies against the SARS-CoV-2 spike protein and assessed how immune cells called T cells, which can help to maintain antibody levels over time, responded to vaccination. Peak antibody levels were 3.5 times higher in those who waited 12 weeks for their booster shot than were those in people who waited only 3 weeks. Peak T-cell response was lower in those with the extended interval. But this did not cause antibody levels to decline more quickly over the nine weeks after the booster shot. The results are reassuring, but are specific to the Pfizer vaccine, which is not available in many low-to-middle income countries, says Alejandro Cravioto, chair of the World Health Organization's Strategic Advisory Group of Experts on Immunization. Countries will need to consider whether the variants that are circulating in their particular region might raise infection risk after only one vaccine dose, he says.

14. 康泰生物：关于新型冠状病毒灭活疫苗纳入紧急使用的提示性公告

Shenzhen Kangtai Biological Products Co., Ltd. Indicative Announcement on the Authorization of the Inactivated COVID-19 Vaccine for Emergency Use

来源：深圳证券交易所

发布时间：2021-05-14

链接：http://www.szse.cn/disclosure/listed/bulletinDetail/index.html?45874cf8-53f2-4beb-9f2a-44cf71bfc6e6

作者单位：深圳康泰生物制品股份有限公司

编译者：张鹏伟

中文摘要：

深圳康泰生物制品股份有限公司（以下简称“公司”）近日收到国务院联防联控机制科研攻关组疫苗研发专班的通知，根据《中华人民共和国疫苗管理法》第二十条有关规定，公司研发的新型冠状病毒灭活疫苗经国家卫生健康委提出建议，国家药品监督管理局组织论证同意紧急使用。

一、产品简介 公司自主研发的新型冠状病毒灭活疫苗用于预防由新型冠状病毒感染引起的流行性疾病，属于预防用生物制品第 1.1 类。新型冠状病毒灭活疫苗于 2021 年 2 月完成Ⅰ、Ⅱ期临床试验。目前，公司已启动开展新型冠状病毒灭活疫苗 III 期临床试验相关工作。

二、对公司的影响 公司新型冠状病毒灭活疫苗此次纳入紧急使用，若后续被国家相关部门规模化采购使用将对公司的经营业绩产生积极影响，进一步提高公司的核心竞争力。

三、风险提示 1、根据《中华人民共和国疫苗管理法》第二十条规定，出现特别重大突发公共卫生事件或者其他严重威胁公众健康的紧急事件，国务院卫生健康主管部门根据传染病预防、控制需要提出紧急使用疫苗的建议，经国务院药品监督管理部门组织论证同意后可以在

一定范围和期限内紧急使用。 2、疫苗研发是一项复杂严谨的科学活动，在上市销售前需要申请临床试验、进行临床试验、申请生产文号、产品批签发。公司新型冠状病毒灭活疫苗仍处于临床试验阶段，后续研发及行政审批阶段具有一定的不确定性，公司将持续按国家有关部门规定推动项目进展并按照相关规定履行信息披露义务。敬请广大投资者谨慎决策，注意投资风险。

Abstract:

Shenzhen Kangtai Biological Products Co., Ltd. (hereinafter referred to as "the Company") recently received a notice from the vaccine R&D group of the scientific research and development innovation team of the Joint Prevention and Control Mechanism of the State Council, according to the relevant provisions of Article 20 of the Vaccine Administration Law of the People's Republic of China, the inactivated COVID-19 vaccine developed by the Company have been put into emergency use after the recommendations of the National Health Commission of the People's Republic of China and the evaluation by National Medical Products Administration. Ⅰ. Product Introduction The inactivated COVID-19 vaccine independently developed by the Company is used to prevent epidemic diseases caused by COVID-19, which belongs to Category 1.1 of Preventive Biological Products. Phases I and II clinical trials of the inactivated COVID-19 vaccine have been completed in February 2021. Currently, the Company has started related work of Phase III clinical trial of inactivated COVID-19 vaccine. Ⅱ. Impact on Company The Company's inactivated COVID-19 vaccine has been included in the emergency use listing. If the vaccine is subsequently procured and used on a large scale by the relevant national departments, a positive impact will be exerted on the Company's business performance and the Company's core competitiveness will be further improved. Ⅲ. Risk Warning The Company and all members of the Board of Directors warrant that the information disclosed is authentic, accurate and complete, and there are no false representations, misleading statements or material omissions. 1. According to Article 20 of Vaccine Administration Law of the People's Republic of China, in the event of a major public health emergency or other emergencies that seriously threaten public health, the competent health authorities under the State Council may propose the emergency use of vaccines based on the needs for prevention and control of infectious diseases, and then the vaccine will be used within a certain scope and period of time with the consent of the drug regulatory agency of the State Council. 2. Vaccine research & development is complex and rigorous, which requires application for clinical trials, conduction of clinical trials, application for market authorization, and batch release before product launch. Company's Inactivated COVID-19 vaccine is still in the clinical trial stage, so there is a certain degree of uncertainty in the subsequent development and regulatory approval stages. The Company will continue to promote the progress of the project and fulfill information disclosure obligations in accordance with the regulations of the relevant state authorities. Investors are urged to make cautious decisions and pay attention to investment risks.

15. 赛诺菲和 GSK COVID-19 候选疫苗在 2 期临床试验中证明对所有成年组均有较强的免疫反应

Sanofi and GSK COVID-19 vaccine candidate demonstrates strong immune responses across all adult age groups in Phase 2 trial

来源：Sanofi

发布时间：2021-05-21

链接：https://www.sanofi.com/en/media-room/press-releases/2021/2021-05-17-07-30-00-2230312

编译者：刘焕珍

中文摘要：

赛诺菲和葛兰素史克佐剂重组 COVID-19 候选疫苗在一项针对 722 名志愿者的 2 期临床研究中，在所有成年年龄组中，中和抗体应答率都很高，与从 COVID-19 中康复者中测得的抗体应答率一致。一项全球关键的三期临床研究预计将在未来几周开始。二期临床的中期结果显示，所有年龄组（18 至 95 岁）和所有剂量的第二次注射后，血清转化率均为 95%至 100%，耐受性可接受且无安全性问题。总体而言，候选疫苗引起的中和抗体水平很强，与自然感染产生的抗体水平相当，在年轻人（18 至 59 岁）中观察到更高的中和抗体水平。单次注射后，有证据表明曾感染过 SARS-CoV-2 的受试者体内产生了高水平的中和抗体，这表明作为一种增强疫苗的发展潜力很大。根据这些积极的第 2 阶段中期结果，公司计划在未来几周内启动一项全球 3 期随机双盲研究。预计该 3 期试验将招募来自各国的 35000 多名成年参与者，并将评估包括 D614（武汉）和 B.1.351（南非）变体在内的两种疫苗制剂的功效。同时，这些公司打算对各种不同的配方进行增强剂研究，以评估低剂量疫苗产生强大增强剂反应的能力，而不管最初的疫苗平台是什么。在第三阶段取得积极成果和监管审查之前，该疫苗有望在 2021 年第四季度获得批准。

Abstract:

The Sanofi and GSK adjuvanted recombinant COVID-19 vaccine candidate achieved strong rates of neutralizing antibody responses, in line with those measured in people who have recovered from COVID-19, in all adult age groups in a Phase 2 study with 722 volunteers. A global pivotal Phase 3 study is expected to start in the coming weeks. The Phase 2 interim results showed 95% to 100% seroconversion following a second injection in all age groups (18 to 95 years old) and across all doses, with acceptable tolerability and with no safety concerns. Overall, the vaccine candidate elicited strong neutralizing antibody levels that were comparable to those generated by natural infection, with higher levels observed in younger adults (18 to 59 years old). After a single injection, high neutralizing antibody levels were generated in participants with evidence of prior SARS-CoV-2 infection, suggesting strong potential for development as a booster vaccine. Based on these positive Phase 2 interim results, the companies plan to initiate a global Phase 3, randomized, double-blind study with the 10μg dose, in combination with GSK's pandemic adjuvant, in the coming weeks. This Phase 3 trial is expected to enroll more than 35,000 adult participants from a broad range of countries and will assess the efficacy of two vaccine formulations including the D614 (Wuhan) and B.1.351 (South African) variants. In parallel, the companies intend to conduct booster studies with various variant formulations in order to assess the ability of a lower dose of the vaccine to generate a strong

booster response regardless of the initial vaccine platform received.Pending positive Phase 3 outcomes and regulatory reviews, the vaccine is expected to be approved in the fourth quarter of 2021.

16. IgG 抗体对 SARS-CoV-2 spike 蛋白非 RBD 区域表位的普遍性、保护性和集中性的识别

Prevalent, protective, and convergent IgG recognition of SARS-CoV-2 non-RBD spike epitopes

来源：Science

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链接：https://science.sciencemag.org/content/early/2021/05/03/science.abg5268

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DOI 或 PUBMED ID：10.1126/science.abg5268

编译者：宋珂

中文摘要：

目前，人们尚不清楚在感染 SARS-CoV-2 患者的血浆中的循环免疫球蛋白 G（IgG）抗体的分子组成和结合表位。对来自康复期的受试者体内针对 spike 糖蛋白的 IgG 抗体组库的进行蛋白质组学退卷积分析，发现该免疫响应主要（>80％）定位于受体结合结构域（RBD）以外的表位。在一个受试者中，仅四个 IgG 谱系就覆盖了 93.5％的免疫响应。其中包括一个定位于 N 端结构域（NTD）的抗体，该抗体能够在面对致命病毒的挑战时提供保护作用。对多宿主来源类别的“公共”抗体进行遗传、结构和功能表征，发现了一个 NTD 表位，该表位在引起关注的新兴 SARS-CoV-2 变异株中反复突变。这些数据表明，定位“公共”NTD 和其他非 RBD 区域表位的血浆抗体非常普遍，并且能够影响抗体逃逸和针对 SARS-CoV-2 的保护作用。

Abstract:

The molecular composition and binding epitopes of the immunoglobulin G (IgG) antibodies that circulate in blood plasma following SARS-CoV-2 infection are unknown. Proteomic deconvolution of the IgG repertoire to the spike glycoprotein in convalescent subjects revealed that the response is directed predominantly (>80%) against epitopes residing outside the receptor-binding domain (RBD). In one subject, just four IgG lineages accounted for 93.5% of the response, including an N-terminal domain (NTD)-directed antibody that was protective against lethal viral challenge. Genetic, structural, and functional characterization of a multi-donor class of “public” antibodies revealed an NTD epitope that is recurrently mutated among emerging SARS-CoV-2 variants of concern. These data show that “public” NTD-directed and other non-RBD plasma antibodies are prevalent and have implications for SARS-CoV-2 protection and antibody escape.

17. 欧洲流感病毒基因组档案揭示了 1918 年流感大流行期间的基因组和表型变异

Archival influenza virus genomes from Europe reveal genomic and phenotypic variability during the 1918 pandemic

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第一作者：Livia Victoria Patrono, Bram Vrancken, Matthias Budt
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Viral Evolution, Robert Koch Institute, Berlin, Germany
DOI 或 PUBMED ID：
编译者：王玮
中文摘要：
1918 年的流感大流行是 20 世纪最致命的呼吸道大流行，它决定了随后的人甲型流感病毒（human influenza A viruses，IAV）的基因组组成。该研究分析了 1918 年欧洲第一个 IAV 基因组，以及第一次，更温和的流行浪潮。1918 年 IAV 基因组多样性与局部传播和频繁的远距离传播事件一致，体外聚合酶鉴定表明潜在的表型变异性。第一和第二波基因组的比较显示，核蛋白基因中的两个位点与宿主抗病毒反应的抗性相关，表明 1918 年 IAV 可能对人类的适应性。最后，基于扩展分子钟模型的系统发育估计表明，季节性 H1N1 IAV 的单纯大流行性下降可替代亚型内重新分配起源的假设。
Abstract:
The 1918 influenza pandemic was the deadliest respiratory pandemic of the 20th century and determined the genomic make-up of subsequent human influenza A viruses (IAV). Here, we analyze the first 1918 IAV genomes from Europe and from the first, milder wave of the pandemic. 1918 IAV genomic diversity is consistent with local transmission and frequent long-distance dispersal events and in vitro polymerase characterization suggests potential phenotypic variability. Comparison of first and second wave genomes shows variation at two sites in the nucleoprotein gene associated with resistance to host antiviral response, pointing at a possible adaptation of 1918 IAV to humans. Finally, phylogenetic estimates based on extended molecular clock modelling suggests a pure pandemic descent of seasonal H1N1 IAV as an alternative to the hypothesis of an intrasubtype reassortment origin.

18. 逆转录的 SARS-CoV-2 RNA 可以整合到培养的人类细胞基因组中，并可以在患者来源的组织中表达

Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues
来源：PNAS
发布时间：2021-05-06
链接：https://www.pnas.org/content/118/21/e2105968118
第一作者：Liguo Zhang
通讯作者：Rudolf Jaenisch
通讯作者单位：Whitehead Institute for Biomedical Research, Cambridge, MA 02142
DOI 或 PUBMED ID：https://doi.org/10.1073/pnas.2105968118
编译者：宋张悦

中文摘要：
在 COVID-19 康复后的患者中，长时间检测 SARS-CoV-2 RNA 和 PCR 阳性检测复发已被广泛报道，但其中一些患者似乎没有传播传染性病毒。我们研究了 SARS-CoV-2 RNA 可以被逆转录并整合到培养的人类细胞 DNA 中的可能性，以及整合序列的转录可能解释了在患者中看到的一些阳性 PCR 测试。为了支持这一假设，我们发现 SARS-CoV-2 序列的 DNA 拷贝可以整合到受感染人类细胞的基因组中。我们发现病毒序列的侧翼有目标位点重复，整合位点上有一致的 LINE1 内切酶识别序列，与 LINE1 逆转录转座子介导的、目标引导的逆转录和逆转录的机制一致。我们还发现，在一些患者来源的组织中，有证据表明，很大一部分病毒序列是从病毒序列的整合 DNA 拷贝转录而来，产生病毒-宿主嵌合转录本。因此，病毒序列的整合和转录有助于 PCR 检测感染后和临床康复患者的病毒 RNA。由于我们只检测到主要来自整合到宿主细胞 DNA 中的病毒基因组 3’端亚基因组序列，因此不能从整合的 SARS-CoV-2 亚基因组序列中产生传染性病毒。

意义：
SARS-CoV-2 疾病尚未解决的一个问题是，在缺乏病毒复制证据的情况下，患者在最初感染数周后，通过 PCR 检测到的病毒 RNA 往往仍呈阳性。我们在此表明，SARS-CoV-2 RNA 可以逆转录并整合到受感染细胞的基因组中，并以病毒与细胞序列融合的嵌合转录本表达。重要的是，这种嵌合转录物可以在患者来源的组织中检测到。我们的数据表明，在一些患者组织中，大多数病毒转录本来自于整合序列。我们的数据为了解 SARS-CoV-2 感染的后果提供了一个见解，这可能有助于解释为什么患者在康复后可以继续产生病毒 RNA。

编者注：
在第 84 期新型冠状病毒信息简报的第 15 条中已经报道过此研究的预印本。

Abstract:
Prolonged detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA and recurrence of PCR-positive tests have been widely reported in patients after recovery from COVID-19, but some of these patients do not appear to shed infectious virus. We investigated the possibility that SARS-CoV-2 RNAs can be reverse-transcribed and integrated into the DNA of human cells in culture and that transcription of the integrated sequences might account for some of the positive PCR tests seen in patients. In support of this hypothesis, we found that DNA copies of SARS-CoV-2 sequences can be integrated into the genome of infected human cells. We found target site duplications flanking the viral sequences and consensus LINE1 endonuclease recognition sequences at the integration sites, consistent with a LINE1 retrotransposon-mediated, target-primed reverse transcription and retroposition mechanism. We also found, in some patient-derived tissues, evidence suggesting that a large fraction of the viral sequences is transcribed from integrated DNA copies of viral sequences, generating viral–host chimeric transcripts. The integration and transcription of viral sequences may thus contribute to the detection of viral RNA by PCR in patients after infection and clinical recovery. Because we have detected only subgenomic sequences derived mainly from the 3′ end of the viral genome integrated into the DNA of the host cell, infectious virus cannot be produced from the integrated subgenomic SARS-CoV-2 sequences.

Significance
An unresolved issue of SARS-CoV-2 disease is that patients often remain positive

for viral RNA as detected by PCR many weeks after the initial infection in the absence of evidence for viral replication. We show here that SARS-CoV-2 RNA can be reverse-transcribed and integrated into the genome of the infected cell and be expressed as chimeric transcripts fusing viral with cellular sequences. Importantly, such chimeric transcripts are detected in patient-derived tissues. Our data suggest that, in some patient tissues, the majority of all viral transcripts are derived from integrated sequences. Our data provide an insight into the consequence of SARS-CoV-2 infections that may help to explain why patients can continue to produce viral RNA after recovery.

19. FDA 发布 COVID-19 药品和疫苗主方案的最终指南

FDA Issues Final Master Protocols Guidance for COVID-19 Drugs and Vaccines

来源：biospace

发表时间：2021-05-17

链 接 ： https://www.biospace.com/article/fda-issues-final-master-protocols-guidance-for-covid-19-drugs-and-vaccines/

作者：Gail Dutton

编译者：雷颖

中文摘要：

美国食品和药物管理局（FDA）周一发布了有关评估 COVID-19 预防和治疗方案的主方案的最终指南。该指南将立即生效，并将在整个大流行中保持有效。该文件，COVID-19：评估药品和生物制品用于治疗或预防主方案的行业指南，给行业带来了从大流行中学到的临床试验设计和执行的最佳实践。该新指南特别侧重于评估治疗或预防 COVID-19 的疗法的策略。主方案旨在纳入多个子研究，这些子研究需要协同努力，以一种或多种目标评估一种或多种疾病亚型中的一种或多种研究药物，所有这些研究均在同一总体试验结构内进行。本指南的重点是伞式试验（可同时评估一种疾病的多种疗法）和平台试验（可持续不断地评估多种疗法）。它还向 COVID-19 药物主方案的发起人提供行政和程序建议。

该指南的重点是：

- 包括一个适当的随机比较臂，以说明护理标准的变化。
- 当该药物用作背景治疗或作为控制臂的一部分时，请获得机构的同意以进行更改。
- 设计方案中要防止研究参与者被随机分配到他们不符合资格接受的药物中。
- 将盲法纳入试验中，可能使用多种虚拟设计或每种药物使用不同的安慰剂对照。如果不切实际，请设计一个客观的端点。
- 在药物意图影响疾病不同方面的情况下，设计多个特定于干预措施的终点。
- 在考虑针对改用药物的安全性和毒性数据的选择性方法时，请与 FDA 一起确定在这些新情况下需要哪些数据。
- 关于统计数据的收集和分析，该指南建议：
- 尽早与 FDA 讨论包括复杂的自适应或贝叶斯设计的任何计划。
- 给定研究药物的统计分析基础是仅与同时随机分组的对照组的比较。
- 如果某些参与者仅在试验中符合某些治疗条件，则给定治疗的统计分析应仅包括符合条件的参与者。
- 如果试验期间对研究药物及其比较药剂的总体随机分配率发生变化，则应根据各种随机分配率的时间段对它们之间的比较进行分层。
- 为了减少总体试验或平台试验中的相关误差，在确定有效性时，应从单个比较中考虑 p

值以外的因素。

- 防止对一种研究药物的结果进行分析和交流，以防无意间散布有关其他药物的信息，从而损害试验的完整性。

Abstract

The U.S. Food and Drug Administration (FDA) issued final guidance Monday on master protocols for evaluating prevention and treatment options for COVID-19. The guidance takes effect immediately and will remain in effect throughout the pandemic.The document, COVID-19: Master Protocols Evaluating Drugs and Biological Products for Treatment or Prevention Guidance for Industry, brings industry best practices learned during the pandemic to bear on the design and execution of clinical trials. This new guidance focuses specifically on strategies to evaluate therapeutics to treat or prevent COVID-19.Master protocols are designed to incorporate multiple sub-studies involving coordinated efforts to evaluate one or more investigational drugs in one or more disease subtypes, with one or more objectives, all within the same overall trial structure.This guidance focuses on umbrella trials (which simultaneously evaluate multiple therapies for a single disease) and platform trials (which evaluate multiple therapies perpetually). It also provides administrative and procedural recommendations to sponsors of master protocols for COVID-19 drugs.

Key points in the guidance are to:

- Include an appropriate randomized comparator arm that account for changes in standard of care.
- Obtain Agency concurrence for changes when the drug is used as background therapy or as part of the control arm.
- Design protocols to prevent study participants from being randomized to drugs they are not eligible to receive.
- Incorporate blinding into trials, perhaps using a multiple-dummy design, or a distinct placebo control for each drug. If impractical, design an objective end-point.
- Design multiple intervention-specific endpoints in cases where drugs are intended to affect different aspects of the disease.
- When considering a selective approach to safety and toxicity data for repurposed drugs, work with the FDA to identify which data is necessary in these new circumstances.

In terms of statistical data collection and analysis, the guidance recommends:

- Early on, discuss with the FDA any plans to include complex adaptive or Bayesian designs.
- Base statistical analyses for a given investigational drug on comparisons against only those control arm participants who were concurrently randomized.
- When some participants are eligible for only some treatment arms in the trial, statistical analyses for a given treatment should only include eligible participants.
- If the overall randomization ratio to an investigational drug and its comparator changes during the trial, comparisons between them should be

stratified by the time periods of the various randomization ratios.

- To reduce correlation errors in umbrella or platform trials, include considerations beyond the p-value from a single comparison in determining effectiveness.
- Prevent the analysis and communication of results for one investigational drug from inadvertently disseminating information regarding other drugs and thus compromising trial integrity.

20. 美国各州市全力以赴采取激励措施，鼓励接种新冠疫苗

Cities and States Go All Out on Incentives to Encourage COVID-19 Vaccination

来源：BioSpace 新闻稿

发布时间：2021-05-12

链 接 ： https://www.biospace.com/article/cities-and-states-offer-money-beer-and-other-incentives-to-bolster-covid-19-vaccinations/

作者：Brandon May

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中文摘要：

目前正在开展一项全球努力，以提高新冠疫苗接种率。在美国，许多州、组织和雇主正在使用独特的策略来提高疫苗接种率。《华尔街日报》报道称，纽约市计划向城市游客提供新冠肺炎疫苗。根据这一倡议，将在中央公园、帝国大厦和纽约游客经常光顾的其他地方设立流动货车和公共汽车，以便游客接种疫苗。目前，该计划是在纽约市弹出窗口的地点使用单次注射强生(J&J)疫苗。减少游客两周后返回接受另一剂疫苗的需要。如果这些计划获得批准，接种车将于本周末前往时代广场、布鲁克林大桥公园和城市的其他地方。周一，纽约州州长安德鲁·科莫宣布，该州将在几个行政区的地铁站和通勤站提供额外的 J&J·新冠肺炎疫苗接种点。根据疾病控制和预防中心的数据，到目前为止，美国超过 58%的成年人已经达到 70%的疫苗接种里程碑。此外，超过 44%的美国成年人已完全接种新型冠状病毒疫苗。在新泽西州，州长考虑向居民支付疫苗费用，以推动该州到 6 月份的疫苗接种率达到 70%。州长上周发起的“泽西夏季行动”为接种疫苗提供了不同的激励。新泽西州 21 岁及以上的居民如果接种了新冠肺炎疫苗，将获得免费啤酒。马里兰州计划支付新冠疫苗接种者高达 100 美元，西弗吉尼亚州，年龄在 16 岁至 35 岁之间的居民如果接种了新冠肺炎疫苗，可以获得 100 美元的储蓄债券。康涅狄格州长将向新冠疫苗接种者提供免费饮料。其它活动诸如获得免费树苗等。虽然免费项目可能会在一定程度上鼓励和提高疫苗接种率，但一些批评者认为，更实际的激励措施，如获得疫苗的带薪休假，可能会进一步提高新冠肺炎全国的疫苗接种率。华盛顿大学医学院生物伦理学教授南希·杰克(NancyJecker)在接受彭博城市实验室(Bloomberg CityLab)采访时说：“激励的一种方式是支付交通费用，或者补偿人们的休假……这样人们就不会因为做了正确的事情而产生费用。”。“对我来说，这是一种在不产生不当诱因的情况下支付费用的方式，也是一种让最弱势人群更容易获得疫苗接种的方式。”

Abstract

A global effort is currently underway to improve coronavirus disease 2019 (COVID-19) vaccination rates. In the U.S., many states, organizations and employers are using unique tactics to improve vaccination rates. The Wall Street Journal reports New York City plans to offer COVID-19 vaccines to city tourists, an effort initiated by Mayor Bill de Blasio to increase and revive the tourism industry. Currently, the plan is to use the single-shot Johnson & Johnson (J&J)

vaccine at the New York City pop-up locations. So far, over 58% of adults in America have reached the 70% vaccination milestone, according to the Centers for Disease Control and Prevention. Additionally, more than 44% of US adults have been fully vaccinated against the novel coronavirus. In New Jersey, Governor Phil Murphy considers paying residents to get a vaccine to push the state's vaccination rate to 70% by June. As part of this program, residents of New Jersey aged 21 years and older can be offered a free beer if they received the COVID-19 vaccine, as reported by Fox News. Maryland and West Virginia have also joined the ranks of New Jersey and other states in offering incentives to residents for getting immunized. Maryland plans to pay state employees up to $100 if they become fully vaccinated. At West Virginia, residents aged 16 to 35 years can earn a $100 savings bond if they get vaccinated against COVID-19. While free items may somewhat encourage and improve vaccination rates, some critics suggest more practical incentives like paid time off to get the vaccine could further bolster COVID-19 vaccination rates across the country. "One way to incentivize is to cover transportation costs, or reimburse people for their time off…so that people don't incur expenses by doing the right thing," said Nancy Jecker, a professor of bioethics at the University of Washington School of Medicine, in an interview with Bloomberg CityLab. "That, to me, is a way of covering costs without creating undue inducement, and it's also a way of making vaccination more accessible to those who are most vulnerable."

21. 美国疾控中心 CDC 终于更新了 COVID-19 会通过空气传播的指南，

After Months of Prodding, CDC Updates Guidance on COVID-19 Airborne Transmission

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Abstract

On Friday, the Centers for Disease Control and Prevention (CDC) published updated guidance communicating to the public that the coronavirus disease 2019 (COVID-19) is an airborne threat, explicitly stating that transmission and subsequent infection with the novel coronavirus can occur via inhalation of very fine respiratory droplets as well as aerosolized particles. This updated guidance offers validation for scientists worldwide, many of whom have criticized the agency for being too vague in its wording on infection risk. Previously, the CDC had a position that the majority of infections occurred via "close contact, not airborne transmission," causing some concern among individuals in the scientific community who claimed accumulating evidence established the airborne threat.

中文摘要：经过几个月的督促之后，美国疾控中心 CDC 终于更新了 COVID-19 会通过空气传播的指南，此前该机构一直强调 COVID-19 是通过接触传播

22. 新冠信息简报暂时停止更新说明

作为一种新发疫情，自发生以来，新冠疫情迅速吸引了全世界科学家从疫情防控相关的流行病学、消杀防控技术、病毒学、病理学、检测技术、药物研发、疫苗研发等各方面对其进行研究。包括我校在内的我国高校和科研院所第一时间投入战“疫”行动。为了帮助我校科学家更好跟踪新冠的研究进展，帮助广大师生更好了解到疫情各方面的知识以及疫情发生情况，疫情开始不久后我们采用编译、转发其他来源文章等方式制作了新冠信息简报共 103 期。

时至今日，多款疫苗上市，全球正在积极推进疫苗的接种工作，在部分防控措施有力的国家特别是我国疫情得到了有效的控制。全球范围内疫情防控的步调不一、水平差异导致疫情不可避免地成为一个长期化、常态化的问题。各国科学家对新冠疫情防控的方方面面获得了大量数据，让我们对新冠病毒以及疫情有了丰富的认识。鉴于此，我们将暂时停止新冠相关信息的收集和汇总工作，更加紧张地投入到各项日常科研工作中去。

感谢校领导对新冠信息简报的指导和关心，感谢 EHS 同事们帮忙将简报发布于 EHS 的网站，感谢免化所、ihuman 研究所、生科院各位同事们对新冠信息简报提供建议反馈、鼓励支持、资源推荐甚至文章编译，最后也特别感谢一直坚持编译相关文章的免化所平台各位同事。

谨祝大家安康幸福，工作顺利！