新型冠状病毒信息简报

第 76 期（2020 年 10 月 17-23 日周报）

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

联系人：蒋立春 jianglch@shanghaitech.edu.cn

内容介绍

分类	标题名称
疫情播报	1. 2020 年 10 月 22 日疫情 2. 转:多国疫情急剧恶化，“封城”潮再次开始
流行病学	3. SARS-CoV 和 SARS-CoV-2 通过空气在雪貂之间超过 1 米的距离进行传播 4. 在美国进行透析的大规模全国样本患者中 SARS-CoV-2 抗体的存在情况:横断面研究
疾病检测	5. 截至 2020 年 10 月 23 日国家药监局已批准 49 个新型冠状病毒检测产品
疾病病理	6. COVID 感染患病的低风险个体在长期观察中出现了多器官损伤 7. SARS-CoV-2 感染对多个重要器官，运动能力，认知，生活质量和精神健康，医院出院的中期影响 8. 与对照组相比，COVID-19 康复者的认知缺陷
疫苗研发	9. 对一种先进候选疫苗中的全长 SARS-CoV-2 Spike 蛋白的结构分析 10. 辉瑞公司首席执行官预计 11 月下旬 COVID-19 疫苗将获得 EUA
药物研发	11. 美国 FDA 于 22 日批准了 Veklury(瑞德西韦)治疗 COVID-19—
临床试验	12. NEJM ｜ 托珠单抗未能减少住院 Covid-19 患者插管或死亡 13. 褪黑素与插管 COVID-19 患者的存活率显著相关 14. 数十人在英国将进行“人类挑战”试验被故意感染冠状病毒 15. 铁蛋白与降钙素原比值在鉴别新冠肺炎病患者和细菌性肺炎患者中的诊断价值:一项多中心研究 16. SARS-CoV-2 灭活疫苗 BBIBP-CorV 的安全性和免疫原性：一项随机、双盲、安慰剂对照的 1/2 期试验 17. 针对 COVID-19 的药物重定位抗病毒药物 - WHO SOLIDARITY 中期试验结果
基础研究	18. 通过对感染 SARS-CoV-2 的雪貂组织进行 3D 重构，阐明了病毒在上呼吸道中的病灶感染模式 19. 通过对比宿主-冠状病毒的蛋白相互作用网络揭示了泛病毒性疾病的机理 20. CRISPR 全基因组水平筛选揭示 SARS-CoV-2 感染的关键因子 21. 单细胞 RNA 测序揭示了与慢性肺病患者 SARS-CoV-2 严重程度和预后相关的分子程序的失调 22. 10 月 20 日 Science 两篇背靠背文章发现新膜蛋白帮助新冠病毒感染细胞
其他	23. COVID-19 会是一次完美的帕金森病风暴吗？ 24. 某些 COVID-19 疫苗会使人们更容易感染艾滋病病毒吗？ 25. 5 型腺病毒载体疫苗的应用：一个警示故事

医院或者咨询医生。

1. 2020 年 10 月 22 日疫情

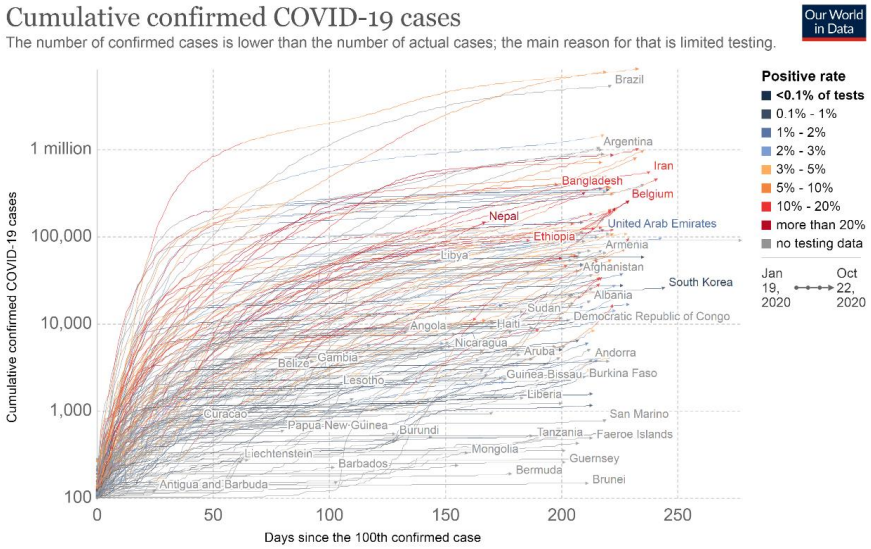
数据来源：WHO

发布时间：2020 年 10 月 22 日北京时间下午 4 点

链接：https://covid19.who.int/

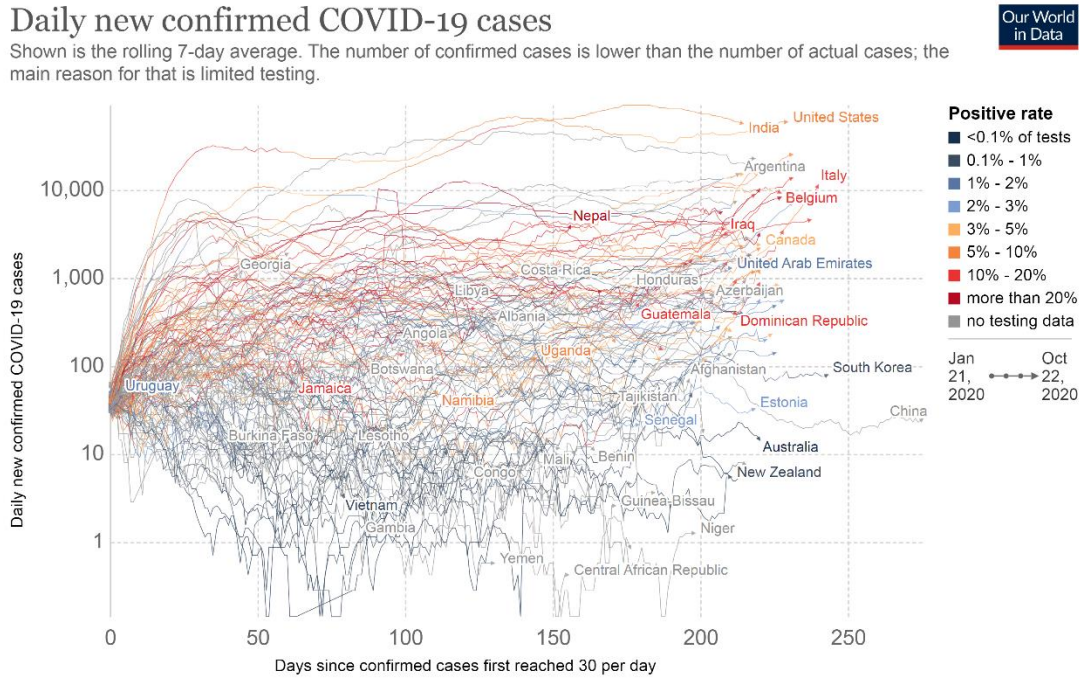
根据 WHO 提供的数据，2020 年 10 月 22 日全球累计确诊新型冠状病毒病人 **41,104,946** 例，当日新增确诊 **423,819** 例，累计死亡 **1,128,325** 例，当日新增死亡 **6,424**。

中国累计确诊 91,588 例，累计死亡 4,746 例，当日新增确诊 23 例，新增死亡 0 例。



Source: European CDC – Situation Update Worldwide – Last updated 22 October, 10:34 (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 22 October, 10:34 (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（10 月 22 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 转:多国疫情急剧恶化，“封城”潮再次开始

医学中文网公众号文章：https://mp.weixin.qq.com/s/t1AOVqF9LuwWTfEkI2Ze_g

摘要：根据世卫组织最新实时统计数据，截至欧洲中部夏令时间 10 月 23 日 15 时 34 分（北京时间 10 月 23 日 21 时 34 分），全球累计新冠肺炎确诊病例 41570883 例，累计死亡病例 1134940 例。全球新冠肺炎确诊病例新增 445419 例，单日新增病例数量**再次突破疫情以来最高纪录，死亡新增 6512 例。**

3. SARS-CoV 和 SARS-CoV-2 通过空气在雪貂之间超过 1 米的距离进行传播

SARS-CoV and SARS-CoV-2 are transmitted through the air between ferrets over more than one meter distance

来源：bioRxiv

发布时间：2020-10-19

链接：https://www.biorxiv.org/content/10.1101/2020.10.19.345363v1

第一作者：Jasmin S Kutter

通讯作者：Sander Herfst

通讯作者单位：Department of Viroscience, Erasmus University Medical Center, Rotterdam, The Netherlands

DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

作者们用一个新开发的实验装置来研究 SARS-CoV 和 SARS-CoV-2 通过空气在雪貂之间超过一米的距离进行传播。实验中，SARS-CoV-2 传播给 4 只间接受体雪貂中的 2 只，SARS-CoV

传播给所有 4 只雪貂。虽然实验没有区分通过小气溶胶、大液滴和污染物的传播，但这些结果表明，SARS-CoV 和 SARS-CoV-2 在空气中传播时仍然具有传染性。雪貂可能是研究如何防止病毒传播的干预措施的敏感模型。

4. 在美国进行透析的大规模全国样本患者中 SARS-CoV-2 抗体的存在情况:横断面研究

Prevalence of SARS-CoV-2 antibodies in a large nationwide sample of patients on dialysis in the USA: a cross-sectional study

来源：lancet

发布时间：2020.09.25

文章链接： https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32009-2/fulltext

第一作者：Shuchi Anand

通讯作者：Shuchi Anand

通讯作者单位：斯坦福大学医学院肾脏病学系

doi：https://doi.org/10.1016/ S0140-6736(20)32009-2

编译者：张怡

中文摘要：

方法 在这项横断面研究中，作者与一个中心实验室合作，该实验室从全美约 1300 家透析机构接收了样本，作者使用一个刺突蛋白受体结合域总抗体化学发光检测(敏感性 100%,特异性 99.8%)。作者从匿名电子健康记录中提取了年龄、性别、种族和民族、居住地和邮政编码等数据，将患者的居住地数据与每 10 万人的累计病例和每日死亡病例以及鼻拭子检测阳性率联系起来。作者根据美国整体透析和成人人口的情况标准化了患病率的估计，并对四个预先指定的(年龄、性别、地区、种族和民族)进行了估计。

发现 抽样的人群与美国透析人群有相似的年龄、性别、种族和民族分布，老年人、男性和居住在黑人和西班牙裔社区的人口比例高于美国成年人。在样本中，SARS-CoV-2 的血清亲和力为 8.0% (95% CI 7.7 - 8.4)，在美国透析人群中为 8.3%(8.0-8.6)，在美国成人人群中为 9.3%(8.8 - 9.9)。当对美国透析人群进行标准化时，血清阳性率从西部的 3.5%(3.1-3.9)到东北部的 27.2%(25.9 - 28.5)不等。比较每 10 万人口的血清阳性率和病例数，我们发现有 9.2%(8.7-9.8)的血清阳性患者被诊断。与其他测量 SARS-CoV-2 传播的方法相比，血清阳性率与每 10 万人口死亡人数的相关性最好(斯皮尔曼 ρ=0.77)。与以非西班牙裔为主的白人社区居民相比，非西班牙裔黑人社区和西班牙裔社区居民的血清阳性率更高(优势比 3.9 [95% CI 3.4-4.6]和 2.3[1.9 - 2.6])。与居住在最低人口密度五分位数的居民相比，居住在人口密度最高五分位数的居民血清阳性率增加(10.3[8.7-12.2])。2020 年 3 月初，由于交通限制，工作访问减少了至少 5%，与 2020 年 7 月血清阳性率降低(0.4[0.3-0.5])相比，降低率不到 5%。

Abstract

Methods For this cross-sectional study, in partnership with a central laboratory that receives samples from approximately 1300 dialysis facilities across the USA, using a spike protein receptor binding domain total antibody chemiluminescence assay (100% sensitivity, 99.8% specificity). We extracted data on age, sex, race and ethnicity, and residence and facility ZIP codes from the anonymised electronic health records, linking patient-level residence data with cumulative and daily cases and deaths per 100 000 population and with nasal swab test positivity rates. We standardised prevalence estimates according to the overall

US dialysis and adult population, and present estimates for four prespecified strata (age, sex, region, and race and ethnicity).
Findings The sampled population had similar age, sex, and race and ethnicity distribution to the US dialysis population, with a higher proportion of older people, men, and people living in majority Black and Hispanic neighbourhoods than in the US adult population. Seroprevalence of SARS-CoV-2 was 8.0% (95% CI 7.7–8.4) in the sample, 8.3% (8.0–8.6) when standardised to the US dialysis population, and 9.3% (8.8–9.9) when standardised to the US adult population. When standardised to the US dialysis population, seroprevalence ranged from 3.5% (3.1–3.9) in the west to 27.2% (25.9–28.5) in the northeast. Comparing seroprevalent and case counts per 100 000 population, we found that 9.2% (8.7–9.8) of seropositive patients were diagnosed. When compared with other measures of SARS-CoV-2 spread, seroprevalence correlated best with deaths per 100 000 population (Spearman's ρ=0.77). Residents of non-Hispanic Black and Hispanic neighbourhoods experienced higher odds of seropositivity (odds ratio 3.9 [95% CI 3.4–4.6] and 2.3 [1.9–2.6], respectively) compared with residents of predominantly nonHispanic white neighbourhoods. Residents of neighbourhoods in the highest population density quintile experienced increased odds of seropositivity (10.3 [8.7–12.2]) compared with residents of the lowest density quintile. County mobility restrictions that reduced workplace visits by at least 5% in early March, 2020, were associated with lower odds of seropositivity in July, 2020 (0.4 [0.3–0.5]) when compared with a reduction of less than 5%.

5. 截至 2020 年 10 月 23 日国家药监局已批准 49 个新型冠状病毒检测产品

来源：国家药品监督管理局
链接：https://www.nmpa.gov.cn/zhuanti/xgqxchpxx/index.html
编译者：宋张悦
截至 2020 年 10 月 23 日，国家药监局已批准 49 个新型冠状病毒检测产品，其中新冠病毒核酸检测试剂 24 个，抗体检测试剂 25 个。详见参考文件："国家药监局新型冠状病毒检测试剂注册信息_20201023.xlsx"。

6. COVID 感染患病的低风险个体在长期观察中出现了多器官损伤

Multi-organ impairment in low-risk individuals with long COVID
来源：medRxiv
发布时间：2020-10-16
链接：https://www.medrxiv.org/content/10.1101/2020.10.14.20212555v1
第一作者：Andrea Dennis
通讯作者：Amitava Banerjee[7], Rajarshi Banerjee[1]
通讯作者单位：7 Institute of Health Informatics, University College London, 222 Euston Road, London, UK; 1 Perspectum, 5520 John Smith Drive, Oxford, OX4 2LL, UK
DOI 或 PUBMED ID：Preprint
编译者：宋张悦
中文摘要：

背景： SARS-CoV-2 病毒感染在老年人和有基础疾病的人群中影响较大。目前的研究多集中在医院的短期结局和单个器官损伤上。因此，长期 COVID（long COVID，感染后症状持续三个月）对低风险个体多器官的影响尚待评估。
方法：对急性 SARS-CoV-2 感染后出现症状的个体进行了一项持续的前瞻性、纵向、双中心、观察性研究。通过标准化问卷(EQ-5D-5L, Dyspnoea-12)、血液调查和定量磁共振成像对症状和器官功能(心、肺、肾、肝、胰、脾)进行评估，根据共识定义确定单器官和多器官损伤。
结果：2020 年 4 月至 9 月，201 人(平均年龄 44 岁(SD 为 11.0 岁)，70%为女性，87%为白人，31%为医护人员)在 SARS-CoV-2 感染后完成了评估(中位数 140 天,IQR 105-160 天后出现症状)。既往疾病的患病率(肥胖:20%，高血压:6%;糖尿病:2%;心脏病发病率(4%)较低，只有 18%的人因感染 COVID-19 而住院。疲劳(98%)、肌肉疼痛(88%)、呼吸困难(87%)和头痛(83%)是最常见的报告症状。持续的心肺系统(92%)和胃肠系统(73%)症状很常见，42%的人有 10 种以上症状。心脏(32%)、肺(33%)、肾脏(12%)、肝脏(10%)、胰腺(17%)和脾脏(6%)均有轻度器官损伤。单器官损伤(66%)和多器官损伤(25%)，与 COVID-19 住院风险显著相关($p<0.05$)。
解释：在有持续症状的年轻、低风险人群中，大约 70%的人在首次出现 SARS-CoV-2 感染症状四个月后，一个或多个器官出现损伤。这不仅对长期 COVID 患病的负担有影响，而且对没有合并症的年轻人承担低风险的公共卫生策略也有影响。

Abstract
Background: Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection has disproportionately affected older individuals and those with underlying medical conditions. Research has focused on short-term outcomes in hospital, and single organ involvement. Consequently, impact of long COVID (persistent symptoms three months post-infection) across multiple organs in low-risk individuals is yet to be assessed.
Methods: An ongoing prospective, longitudinal, two-centre, observational study was performed in individuals symptomatic after recovery from acute SARS-CoV-2 infection. Symptoms and organ function (heart, lungs, kidneys, liver, pancreas, spleen) were assessed by standardised questionnaires (EQ-5D-5L, Dyspnoea-12), blood investigations and quantitative magnetic resonance imaging, defining single and multi-organ impairment by consensus definitions.
Findings: Between April and September 2020, 201 individuals (mean age 44 (SD 11.0) years, 70% female, 87% white, 31% healthcare workers) completed assessments following SARS-CoV-2 infection (median 140, IQR 105-160 days after initial symptoms). The prevalence of pre-existing conditions (obesity: 20%, hypertension: 6%; diabetes: 2%; heart disease: 4%) was low, and only 18% of individuals had been hospitalised with COVID-19. Fatigue (98%), muscle aches (88%), breathlessness (87%), and headaches (83%) were the most frequently reported symptoms. Ongoing cardiorespiratory (92%) and gastrointestinal (73%) symptoms were common, and 42% of individuals had ten or more symptoms. There was evidence of mild organ impairment in heart (32%), lungs (33%), kidneys (12%), liver (10%), pancreas (17%), and spleen (6%). Single (66%) and multi-organ (25%) impairment was observed, and was significantly associated with risk of prior COVID-19 hospitalisation ($p<0.05$).

Interpretation: In a young, low-risk population with ongoing symptoms, almost 70% of individuals have impairment in one or more organs four months after initial symptoms of SARS-CoV-2 infection. There are implications not only for burden of long COVID but also public health approaches which have assumed low risk in young people with no comorbidities.

7. SARS-CoV-2 感染对多个重要器官，运动能力，认知，生活质量和精神健康，医院出院的中期影响

Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge

来源：medRxiv

发布时间：2020-10-18

链接：https://www.medrxiv.org/content/10.1101/2020.10.15.20205054v1

第一作者：Betty Raman, DPhil

通讯作者：Betty Raman, DPhil

通讯作者单位：Division of Cardiovascular Medicine, Radcliffe Department of Medicine, National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), University of Oxford, Oxford, United Kingdom

DOI 或 PUBMED ID：

编译者：张鹏伟

中文摘要：

背景 人们对冠状病毒病（COVID-19）对多器官健康，运动能力，认知，生活质量和精神健康的中期影响知之甚少。

方法 前瞻性招募了 58 名 COVID-19 患者出院后和 30 位合并症患者，进行了多器官（大脑，肺，心脏，肝和肾脏）磁共振成像（MRI），肺活量测定，六分钟步行测试，心肺运动训练 测试（CPET），生活质量，认知和心理健康评估。

发现 发病后 2-3 个月，有 64％的患者持续呼吸困难，而 55％的患者则表现出明显的疲劳感。在 MRI 上，患者的肺部（60％），心脏（26％），肝脏（10％）和肾脏（29％）出现组织信号异常。COVID-19 患者在脑部 MRI 上还表现出丘脑，丘脑后部辐射和矢状层的组织变化，并且认知能力受损，尤其是在相对于对照组的执行和视觉空间领域。患者的运动耐力（CPET 的最大耗氧量和通气效率）和六分钟步行距离（对照组为 405±118m vs 517±106m，p <0.0001）显着降低。肺部 MRI 异常程度和运动耐量与持续炎症的血清标志物和急性疾病的严重程度相关。与对照组相比，患者更有可能报告中度至重度焦虑症状（35％vs 10％，p = 0.012）和抑郁（39％vs 17％，p = 0.036），并且在生活质量的所有方面均存在明显的损害。

解释 从医院出院的 COVID-19 患者中，很大一部分在发病后 2-3 个月内出现持续的呼吸困难，疲劳，焦虑，抑郁和运动受限的症状。持续性肺和肺外器官 MRI 表现很常见。在 COVID-19 幸存者中，慢性炎症可能是多器官异常的基础，并导致生活质量受损。

Abstract:

Background The medium-term effects of Coronavirus disease (COVID-19) on multiple organ health, exercise capacity, cognition, quality of life and mental health are poorly understood.

Methods Fifty-eight COVID-19 patients post-hospital discharge and 30 comorbidity-matched controls were prospectively enrolled for multiorgan (brain, lungs, heart, liver and kidneys) magnetic resonance imaging (MRI), spirometry, six-minute walk

test, cardiopulmonary exercise test (CPET), quality of life, cognitive and mental health assessments.
Findings At 2-3 months from disease-onset, 64% of patients experienced persistent breathlessness and 55% complained of significant fatigue. On MRI, tissue signal abnormalities were seen in the lungs (60%), heart (26%), liver (10%) and kidneys (29%) of patients. COVID-19 patients also exhibited tissue changes in the thalamus, posterior thalamic radiations and sagittal stratum on brain MRI and demonstrated impaired cognitive performance, specifically in the executive and visuospatial domain relative to controls. Exercise tolerance (maximal oxygen consumption and ventilatory efficiency on CPET) and six-minute walk distance (405±118m vs 517±106m in controls, $p<0.0001$) were significantly reduced in patients. The extent of extra-pulmonary MRI abnormalities and exercise tolerance correlated with serum markers of ongoing inflammation and severity of acute illness. Patients were more likely to report symptoms of moderate to severe anxiety (35% versus 10%, $p=0.012$) and depression (39% versus 17%, $p=0.036$) and significant impairment in all domains of quality of life compared to controls.
Interpretation A significant proportion of COVID-19 patients discharged from hospital experience ongoing symptoms of breathlessness, fatigue, anxiety, depression and exercise limitation at 2-3 months from disease-onset. Persistent lung and extra-pulmonary organ MRI findings are common. In COVID-19 survivors, chronic inflammation may underlie multiorgan abnormalities and contribute to impaired quality of life.

8. 与对照组相比，COVID-19 康复者的认知缺陷

Cognitive deficits in people who have recovered from COVID-19 relative to controls: An N=84,285 online study
来源：medRxiv
发布时间：2020-10-21
链接：https://www.medrxiv.org/content/10.1101/2020.10.20.20215863v1
第一作者：Adam Hampshire
通讯作者：Adam Hampshire
通讯作者单位：英国伦敦帝国理工学院
DOI 或 PUBMED ID：https://doi.org/10.1101/2020.10.20.20215863
编译者：刘焕珍
中文摘要：
案例研究表明，COVID-19 重症患者存在神经系统问题。但是，关于感染后或整个严重程度的认知问题的性质和更广泛的患病率方面的信息很少。本文分析了 84285 名英国智能测验参与者的认知测验数据，这些参与者完成了有关疑似和生物学证实的 COVID-19 感染的问卷调查，康复者表现出明显的认知缺陷。性能的细粒度分析支持以下假设：COVID-19 对人类认知具有多系统影响。
Abstract:
Case studies have revealed neurological problems in severely affected COVID-19 patients. However, there is little information regarding the nature and broader prevalence of cognitive problems postinfection or across the full spread of

severity. We analysed cognitive test data from 84,285 Great British Intelligence Test participants who completed a questionnaire regarding suspected and biologically confirmed COVID-19 infection. People who had recovered, including those no longer reporting symptoms, exhibited significant cognitive deficits when controlling for age, gender, education level, income, racial-ethnic group and pre-existing medical disorders. They were of substantial effect size for people who had been hospitalised, but also for mild but biologically confirmed cases who reported no breathing difficulty. Finer grained analyses of performance support the hypothesis that COVID-19 has a multi-system impact on human cognition.

9. 对一种先进候选疫苗中的全长 SARS-CoV-2 Spike 蛋白的结构分析

Structural analysis of full-length SARS-CoV-2 spike protein from an advanced vaccine candidate

8 月 14 日第 23 条报道过该研究的预印本。该研究中的疫苗出自于美国马里兰州的 Novavax 公司，在 9 月底进入了三期临床试验。

原文链接：https://science.sciencemag.org/content/early/2020/10/19/science.abe1502

10. 辉瑞公司首席执行官预计 11 月下旬 COVID-19 疫苗将获得 EUA

Pfizer CEO Anticipates EUA for COVID-19 Vaccine in Late November

发布时间：2020.10.16

文章链接：https://www.biospace.com/article/pfizer-ceo-anticipates-eua-for-vaccine-in-late-november/

编译者：张怡

中文摘要：

辉瑞（Pfizer）公司首席执行官 Albert Bourla 先生在公司官网上发布了一封公开信，对该公司和 BioNTech 公司联合开发的新冠候选疫苗的开发时间线进行了进一步的解释。Albert Bourla 先生表示，虽然该公司可能在 10 月底获得候选新冠疫苗的保护效力数据，但是仍然需要时间获得候选疫苗的安全性数据，如果数据积极，该公司最早将在 11 月的第三周向美国 FDA 递交紧急使用授权（EUA）申请。

与所有疫苗一样，必须证明在三个关键领域取得了成功，才能获得批准用于大众。首先，疫苗必须被证明是有效的，这意味着它可以在至少大多数接种疫苗的患者中帮助预防 COVID-19 疾病；其次，同样重要的是，疫苗必须通过从成千上万的患者中产生的可靠安全性数据，被证明是安全的；最后，我们必须证明疫苗能够以最高质量标准持续生产。

Abstract

Pfizer will not seek Emergency Use Authorization (EUA) for its COVID-19 vaccine until the end of November even if the readout from a Phase III study expected later this month is positive.

Pfizer Chief Executive Officer Albert Bourla posted an open letter on the company's website explaining three key metrics the experimental vaccine for the novel coronavirus must meet before the company and its partner, Germany's BioNTech will seek EUA. The vaccine must be effective in preventing COVID-19 in at least a majority of vaccinated patients. Bourla also stressed that the vaccine must meet safety standards. The third metric is the companies must demonstrate they can consistently manufacture the vaccine while meeting quality control

standards.

11. 美国 FDA 于 22 日批准了 Veklury(瑞德西韦)治疗 COVID-19—关于其安全性和有效性的科学

FDA’s approval of Veklury (remdesivir) for the treatment of COVID-19—The Science of Safety and Effectiveness

来源：FDA

发布时间：2020-10-22

链接:

https://www.fda.gov/drugs/drug-safety-and-availability/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness

美国 FDA 于 22 日批准了 Veklury(瑞德西韦)治疗 COVID-19，这个 FDA 批准的第一个治疗 COVID-19 的药物。FDA 批准 Veklury 用于需要住院的体重至少 40kg（88 磅）的成年人以及 12 岁以上的儿童患者。

该批准并不包括之前 Veklury 针对全人群的紧急授权使用（EUA），这两个批准不是同一个。FDA 也修改了 5 月 1 日针对 Veklury 的紧急授权使用，准许该药物紧急使用于体重 3.5 千克到 40 千克之间的检测确认或者疑似住院儿童病患，或者住院的 12 岁以下的体重至少 3.5 千克的儿童病患。

…Today, FDA approved Veklury (remdesivir), the first drug approved to treat COVID-19, for use in adults and pediatric patients 12 years of age and older and weighing at least 40 kg (about 88 pounds) requiring hospitalization.

This approval does not include the entire population that had been authorized to use Veklury under a mechanism called emergency use authorization (EUA), which is not the same as approval. FDA also revised the EUA for Veklury, originally issued on May 1, 2020, to permit the drug’s use for treatment of suspected or laboratory confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg *or* hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

…

12. NEJM ｜ 托珠单抗未能减少住院 Covid-19 患者插管或死亡

公众号 NEJM 医学前沿发布 NEMJ 最近一项托珠单抗在住院 COVID-19 病人中疗效文章的评论性文章。

评论文章链接：https://mp.weixin.qq.com/s/F5hy1NoFxZVdCu4mXiq7Yw

NEMJ 原文:

住院 COVID-19 中托珠单抗缺乏疗效

Efficacy of Tocilizumab in Patients Hospitalized with Covid-19

链接：

https://www.nejm.org/doi/full/10.1056/NEJMoa2028836?query=featured_coronavirus

13. 褪黑素与插管 COVID-19 患者的存活率显著相关

Melatonin is significantly associated with survival of intubated COVID-19 patients

链接：https://www.medrxiv.org/content/10.1101/2020.10.15.20213546v1
编译者：雷颖
在这项回顾性研究中，作者使用生存分析来确定在纽约长老会/哥伦比亚大学欧文医学中心接受治疗的患者中，插管后死亡率是否与激素暴露相关。文中作者报告了插管和机械通气患者插管前后每种激素的总体危害比，发现插管后使用褪黑激素与 COVID-19 和非 COVID-19 患者的存活率显著相关，在需要机械通气的 COVID-19 患者中，插管后使用褪黑激素与存活率也显著相关。

14. 数十人在英国将在“人类挑战”试验被故意感染冠状病毒

Dozens to be deliberately infected with coronavirus in UK ‘human challenge’ trials
来源：Nature News
发布时间： 2020-10-20
链接：https://www.nature.com/articles/d41586-020-02821-4
作者：Ewen Callaway
编译者：孔娟
中文摘要：
10 月 20 日，英国政府和一家开展此类研究的公司宣布，在首次“人类挑战试验”中，年轻健康志愿者被故意感染新冠病毒。如果获得最终的监管和伦理批准，该实验将于明年 1 月在伦敦一家医院的高级隔离病房进行开始，旨在加速开发可能结束这一流行病的疫苗。
人类挑战性研究已经用于疟疾、伤寒和流感等疾病的疫苗和治疗的研究。英国的试验将试图确定可用于未来疫苗试验的合适剂量的 SARS-CoV-2 病毒。相关免疫学家和研究人员认为挑战性研究有可能加速新药和疫苗的开发并降低其风险。但是，此做法确实涉及一些未知的医学和生物伦理领域。并且三期试验可能无法提供明确的证据证明疫苗是否对老年人有效，因为他们在这些试验中的参与率很低。
这项研究的精确设计尚未最终确定。但很可能少数参与者将接受非常低剂量的 SARS-CoV-2 “挑战毒株”，这种毒株来自目前正在传播的病毒，并在严格的条件下生长。如果没有或很少参与者被感染，研究人员将寻求独立安全监督委员会的许可，让参与者暴露在更高的剂量下。卡奇波尔说，这一过程将会重复，直到研究人员发现一种剂量可以感染大多数暴露者。感染剂量一经确定，后续会进行一系列挑战性的试验来测试几种疫苗。
Catchpole 说“他的团队将采取一切预防措施，防止最初试验的参与者患上严重疾病。一旦鼻拭子对 SARS-CoV-2 遗传物质的结果呈阳性，志愿者将接受抗病毒治疗。除了年龄和健康，参与者还将接受与严重新冠肺炎相关的风险因素筛查”。选择风险最低的参与者是进行挑战性试验最重要的安全步骤。此项计划将招募大约 500 名参与者，计划为志愿者支付 4000 英镑左右。
新泽西新布伦瑞克罗格斯大学的生物伦理学家尼尔.艾尔说，有人担心人们会为了钱而参与，而不会意识到风险。他认为新冠肺炎挑战赛可以安全、合乎伦理地进行。但他说，例如，一个设计良好的在线课程可以确保参与者了解风险。
Abstract：
Young, healthy people will be intentionally exposed to the virus responsible for COVID-19 in a first-of-its kind ‘human challenge trial’, the UK government and a company that runs such studies announced on 20 October. The experiment, set to begin in January in a London hospital if it receives final regulatory and ethical approval, aims to accelerate the development of vaccines that could end the

pandemic.

Human challenge trials have a history of providing insight into diseases such as malaria and influenza. The UK trial will try to identify a suitable dose of the SARS-CoV-2 virus that could be used in future vaccine trials. But the prospect of deliberately infecting people — even those at low risk of severe disease — with SARS-CoV-2, a deadly pathogen that has few proven treatments, is uncharted medical and bioethical territory.

The precise design of the study has not been finalized. But it is likely that a small number of participants will receive a very low dose of a SARS-CoV-2 'challenge strain' derived from a currently circulating virus and grown under stringent conditions. If none or few of the participants become infected, the researchers will seek permission from an independent safety monitoring board to expose participants to higher doses. This process will be repeated until researchers identify a dose that infects most of those exposed, says Catchpole.

Catchpole says that his team will take every precaution against participants in the initial trial developing severe disease. Volunteers will be treated with an antiviral, such as remdesevir, once a nasal swab gives a positive result for SARS-CoV-2 genetic material. In addition to age and health, participants will be screened for risk factors that have been associated with severe COVID-19.

Selecting participants at the lowest risk is the most important safety step in running a challenge trial, says Matt Memoli, an infectious-disease physician and virologist at the US National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland. "Once you've given that virus to the person, anything's possible," he says. "You can't control it, you can only react to it." It will aim to recruit around 500 participants altogether, Open Orphan typically pays volunteers around £4,000 for their time, says Catchpole.

Ethical issues

There is a concern that people will participate for the money without appreciating the risks, says Nir Eyal, a bioethicist at Rutgers University in New Brunswick, New Jersey, who has argued that COVID-19 challenge trials can be run safely and ethically. But a well-designed online course, for instance, could ensure participants understand the risks, he says.

15. 铁蛋白与降钙素原比值在鉴别新冠肺炎病患者和细菌性肺炎患者中的诊断价值:一项多中心研究

Diagnostic utility of a Ferritin-to-Procalcitonin Ratio to differentiate patients with COVID-19 from those with Bacterial Pneumonia: A multicenter study

来源：medRxiv

发布时间：2020-10-22

链接：https://www.medrxiv.org/content/10.1101/2020.10.20.20216309v1

第一作者：Amal A. Gharamti, MD

通讯作者：Andrés F. Henao-Martínez

通讯作者单位：University of Colorado Denver

DOI 或 PUBMED ID：preprint
编译者：孔娟
中文摘要：
重要性:在诊断测试可用之前，在临床表现时开发区分新冠肺炎和细菌性肺炎的检测方法尤为必要。
目的:确定铁蛋白与降钙素原的比值(F/P)能否用于鉴别新冠肺炎病和细菌性肺炎。
设计:这项病例对照研究比较了 2020 年 3 月 1 日至 5 月 31 日期间收治的新冠肺炎或细菌性肺炎患者。排除新冠肺炎病和细菌性肺炎合并感染的患者。
背景:该项多中心研究在三家医院进行，研究对象包括 242 例新冠肺炎感染患者和 34 例细菌性肺炎对照。
主要结果和措施:比较新冠肺炎或细菌性肺炎患者铁蛋白与降钙素原的比值(F/P)。接收器操作特性分析确定了用于诊断新冠肺炎与细菌性肺炎的铁蛋白与降钙素原的比值(F/P)的敏感性和特异性。
结果与细菌性肺炎患者相比，新冠肺炎肺炎患者的平均年龄较低(57.11 岁 vs 64.4 岁，p=0.02)，体重指数较高(30.74 公斤 vs 27.15 公斤/平方米，p=0.02)。病例组和对照组的女性比例相似(47%对 53%，p=0.5)，新冠肺炎患者的糖尿病患病率较高(32.6% vs 12%，p=0.01)。新冠肺炎病患者的中位 F/P 比值 (4037.5)明显高于细菌性肺炎患者的中位 F/P 比值 (802，p<0.001)。用于诊断新冠肺炎的 F/P ≥ 877，灵敏度为 85%，特异性为 56%，阳性预测值为 93.2%，似然比为 1.92。在多变量分析中，F/P ≥ 877 与识别新冠肺炎病例的更大几率相关(OR: 11.27，置信区间:4-31.2，p<0.001)。
结论和相关性:与细菌性肺炎相比，F/P ≥ 877 增加新冠肺炎的可能性。需要进一步的研究来确定在临床表现时同时获得铁蛋白和降钙素原是否提高了诊断价值。其他问题包括连续 F/P 的升高和或连续升高是否与新冠肺炎病的发生和严重程度相关。
Abstract:
Importance: There is a need to develop tools to differentiate COVID-19 from bacterial pneumonia at the time of clinical presentation before diagnostic testing is available.
Objective: To determine if the Ferritin-to-Procalcitonin ratio (F/P) can be used to differentiate COVID-19 from bacterial pneumonia.
Design: This case-control study compared patients with either COVID-19 or bacterial pneumonia, admitted between March 1 and May 31, 2020. Patients with COVID-19 and bacterial pneumonia co-infection were excluded. Setting: A multicenter study conducted at three hospitals that included UCHealth and Phoebe Putney Memorial Hospital in the United States, and Yichang Central People's Hospital in China. Participants: A total of 242 cases with COVID-19 infection and 34 controls with bacterial pneumonia.
Main Outcomes and Measures: The F/P in patients with COVID-19 or with bacterial pneumonia were compared. Receiver operating characteristic analysis determined the sensitivity and specificity of various cut-off F/P values for the diagnosis of COVID-19 versus bacterial pneumonia.
Results Patients with COVID-19 pneumonia had a lower mean age (57.11 vs 64.4 years, p=0.02) and a higher BMI (30.74 vs 27.15 kg/m2, p=0.02) compared to patients with bacterial pneumonia. Cases and controls had a similar proportion of women (47% vs 53%, p=0.5) and COVID-19 patients had a higher prevalence of

diabetes mellitus (32.6% vs 12%, p=0.01). The median F/P was significantly higher in patients with COVID-19 (4037.5) compared to the F/P in bacterial pneumonia (802, p<0.001). An F/P ≥ 877 used to diagnose COVID-19 resulted in a sensitivity of 85% and a specificity of 56%, with a positive predictive value of 93.2%, and a likelihood ratio of 1.92. In multivariable analyses, an F/P ≥ 877 was associated with greater odds of identifying a COVID-19 case (OR: 11.27, CI: 4-31.2, p<0.001).

Conclusions and Relevance: An F/P ≥ 877 increases the likelihood of COVID-19 pneumonia compared to bacterial pneumonia. Further research is needed to determine if obtaining ferritin and procalcitonin simultaneously at the time of clinical presentation has improved diagnostic value. Additional questions include whether an increased F/P and/or serial F/P associates with COVID-19 disease severity or outcomes.

16. SARS-CoV-2 灭活疫苗 BBIBP-CorV 的安全性和免疫原性：一项随机、双盲、安慰剂对照的 1/2 期试验

Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV a randomised, double-blind, placebo-controlled, phase 1/2 trial

来源：THE LANCET
发布时间：2020-10-15
链接：https://www.sciencedirect.com/science/article/pii/S1473309920308318?via%3Dihub#!
第一作者：夏胜利
通讯作者：杨晓明
通讯作者单位：河南省疾病预防控制中心、北京生物制品研究所
DOI 或 PUBMED ID：https://doi.org/10.1016/S1473-3099(20)30831-8
编译者：张丽双
中文摘要：

灭活的 SARS-CoV-2 疫苗 BBIBP-CorV 是安全的，并且在两个年龄段的所有测试剂量下均具有良好的耐受性。在第 42 天在所有疫苗接种者中诱导出针对 SARS-CoV-2 的体液应答。在第 0 天和第 21 天或第 0 天和第 28 天用 4μg 疫苗进行两剂免疫接种的中和抗体效价高于单剂 8μg 或 4μg 在第 0 天和第 14 天服药。

Abstract:

The inactivated SARS-CoV-2 vaccine, BBIBP-CorV, is safe and well tolerated at all tested doses in two age groups. Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 μg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 μg dose or 4 μg dose on days 0 and 14.

17. 针对 COVID-19 的药物重定位抗病毒药物 - WHO SOLIDARITY 中期试验结果

Repurposed antiviral drugs for COVID-19 - interim WHO SOLIDARITY trial results

来源：medRxiv
发布时间：2020-10-15

链接：https://www.medrxiv.org/content/10.1101/2020.10.15.20209817v1
第一作者：Hongchao Pan
通讯作者：Hongchao Pan
通讯作者单位：Nuffield Department of Population Health, University of Oxford, Oxford
DOI 或 PUBMED ID：
编译者：张鹏伟
中文摘要：
背景：世卫组织专家组建议对住院的 COVID-19 进行四种改用抗病毒药物的死亡率试验。
方法：研究药物为 Remdesivir, Hydroxychloroquine, Lopinavir（与 Ritonavir 固定剂量联合用药）和干扰素β1a（主要是皮下注射，最初用 Lopinavir，后来没有）。COVID-19 住院患者在当地可用的研究药物和开放对照（最多 5 个选项：4 个有效和当地标准护理）之间进行平等随机分组。意向性治疗的主要分析是每种研究药物与对照药物的 4 组成对比较中的院内死亡率（尽管可获得，但同时分配了不使用该药物的相同管理）。Kaplan-Meier 的 28 天风险未分层； 对数死亡率的比率（RRs）按年龄和进入时的通气进行分层。
结果：在 30 个国家的 405 家医院中，11266 名成人被随机分配，其中 2750 名分配了 Remdesivir，954 名 Hydroxychloroquine，1411 名 Lopinavir，651 名干扰素加 Lopinavir ，1412 名仅使用干扰素，4088 名没有研究药物。治疗期间依从性为 94-96%，交叉治疗为 2-6%。据报道有 1253 例死亡（中位数第 8 天，IQR 4-14）。Kaplan-Meier 28 天死亡率为 12%（如果在随机分组时已经通气，则为 39%，否则为 10%）。死亡率（95%CI 和死亡/随机数，每种药物相对于对照）的死亡率为：Remdesivir RR = 0.95（0.81-1.11，p = 0.50； 301/2743 活性对 303/2708 对照），HydroxychloroquineRR = 1.19 （0.89-1.59，p = 0.23； 104/947 vs 84/906），Lopinavir RR = 1.00（0.79-1.25，p = 0.97； 148/1399 vs 146/1372）和干扰素 RR = 1.16（0.96-1.39，p = 0.11； 243/2050 对 216/2050）。没有研究药物能明显降低死亡率（在未通气患者或任何其他进入特征的亚组）、开始通气或住院时间。
结论：从总体死亡率、通气开始时间和住院时间来看，这些 Remdesivir, Hydroxychloroquine, Lopinavir 和干扰素方案对住院的 COVID-19 几乎没有影响。死亡率调查结果包含了大部分关于 Remdesivir 和干扰素的随机证据，并且与所有主要试验中死亡率的荟萃分析相一致。
Abstract:
BACKGROUND WHO expert groups recommended mortality trials in hospitalized COVID-19 of four re-purposed antiviral drugs.
METHODS Study drugs were Remdesivir, Hydroxychloroquine, Lopinavir (fixed-dose combination with Ritonavir) and Interferon-β1a (mainly subcutaneous; initially with Lopinavir, later not). COVID-19 inpatients were randomized equally between whichever study drugs were locally available and open control (up to 5 options: 4 active and local standard-of-care). The intent-to-treat primary analyses are of in-hospital mortality in the 4 pairwise comparisons of each study drug vs its controls (concurrently allocated the same management without that drug, despite availability). Kaplan-Meier 28-day risks are unstratified; log-rank death rate ratios (RRs) are stratified for age and ventilation at entry.
RESULTS In 405 hospitals in 30 countries 11,266 adults were randomized, with 2750 allocated Remdesivir, 954 Hydroxychloroquine, 1411 Lopinavir, 651 Interferon plus Lopinavir, 1412 only Interferon, and 4088 no study drug. Compliance was 94-96% midway through treatment, with 2-6% crossover. 1253 deaths were reported (at

median day 8, IQR 4-14). Kaplan-Meier 28-day mortality was 12% (39% if already ventilated at randomization, 10% otherwise). Death rate ratios (with 95% CIs and numbers dead/randomized, each drug vs its control) were: Remdesivir RR=0.95 (0.81-1.11, p=0.50; 301/2743 active vs 303/2708 control), Hydroxychloroquine RR=1.19 (0.89-1.59, p=0.23; 104/947 vs 84/906), Lopinavir RR=1.00 (0.79-1.25, p=0.97; 148/1399 vs 146/1372) and Interferon RR=1.16 (0.96-1.39, p=0.11; 243/2050 vs 216/2050). No study drug definitely reduced mortality (in unventilated patients or any other subgroup of entry characteristics), initiation of ventilation or hospitalisation duration. CONCLUSIONS These Remdesivir, Hydroxychloroquine, Lopinavir and Interferon regimens appeared to have little or no effect on hospitalized COVID-19, as indicated by overall mortality, initiation of ventilation and duration of hospital stay. The mortality findings contain most of the randomized evidence on Remdesivir and Interferon, and are consistent with meta-analyses of mortality in all major trials.

18. 通过对感染 SARS-CoV-2 的雪貂组织进行 3D 重构，阐明了病毒在上呼吸道中的病灶感染模式

3D reconstruction of SARS-CoV-2 infection in ferrets emphasizes focal infection pattern in the upper respiratory tract

来源：bioRxiv
发布时间：2020-10-18
链接：https://www.biorxiv.org/content/10.1101/2020.10.17.339051v1
第一作者：Luca M. Zaeck
通讯作者：Stefan Finke
通讯作者单位：
Institute of Molecular Virology and Cell Biology, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, 17493 Greifswald, Isle of Riems, Germany
DOI 或 PUBMED ID：
编译者：宋珂

中文摘要：

对被感染组织中的病毒病原体进行可视化分析，是了解病毒在体内的空间分布，位置和细胞趋向性的重要工具。通常，需要在石蜡包埋的薄组织切片中使用常规免疫组织化学方法对病毒感染的组织进行分析。本文中，作者证实了利用生物组织光透明技术和光片显微镜技术进行体三维（3D）免疫荧光成像的使用性。并利用该技术在介观尺度上研究了流行性 SARS-CoV-2 病毒在雪貂体内的宿主-病原体相互作用。在大型完整样本（>150 mm^3）的优越的空间背景下，允许研究人员对相关参数进行详细量化。例如，病灶到病灶间的距离，或 SARS-CoV-2 感染的区域，从而有助于更深入地描述 SARS-CoV-2 感染病灶。因此，作者可以确定出 SARS-CoV-2 病毒在雪貂上呼吸道中的优先感染位置，并阐明了病毒在鼻甲中独特的病灶感染模式。综上，作者进行了一项概念验证实验，研究了非常重要的呼吸道病原体的空间组织形态，并展示了第一个 SARS-CoV-2 感染组织的详细 3D 可视化结构。

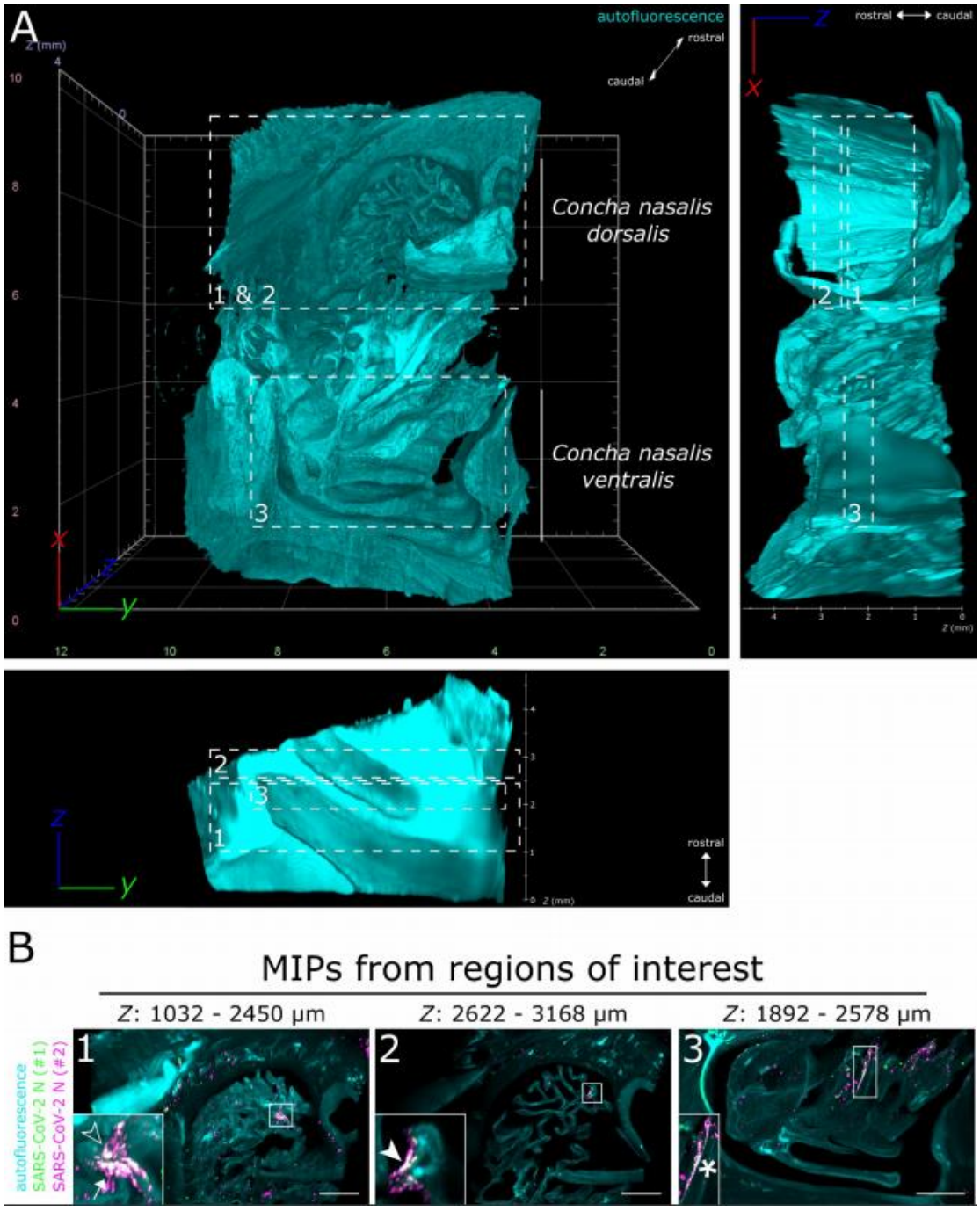


Figure 2: LSFM is able to visualize SARS-CoV-2 infection in nasal turbinates within a high spatial context. (A) The tissue structure of the nasal conchae (> 200mm^3; 4 days post-infection) was reconstructed using tissue autofluorescence (cyan) and is depicted as volumetric projection from three viewing angles. Anatomical terms of location are provided for orientation. Edge length of grid squares = 2 mm. Total magnification = 1.26x. **(B)** Maximum intensity projections of the regions of interest (1-3) highlighted in (A). SARS-CoV-2 infection is characterized by colocalization of both SARS-CoV-2 N stainings (#1, green; #2, magenta) and results in white coloring (inset). Four distinct SARS-CoV-2 infection foci are highlighted (filled-in arrowhead [A1], outlined arrowhead [A5], arrow [A7], and asterisk). Foci will hereafter be referred to via their respective indicator or designation in square brackets. Ranges of the MIPs in the z-dimension are provided above the respective image. MIP = maximum intensity projection. Scale bar = 1 mm.

Abstract:
The visualization of viral pathogens in infected tissues is an invaluable tool to understand spatial virus distribution, localization, and cell tropism in vivo. Commonly, virus-infected tissues are analyzed using conventional immunohistochemistry in paraffin-embedded thin sections. Here, we demonstrate the utility of volumetric three-dimensional (3D) immunofluorescence imaging using tissue optical clearing and light sheet microscopy to investigate host-pathogen interactions of pandemic SARS-CoV-2 in ferrets at a mesoscopic scale. The superior spatial context of large, intact samples (> 150 mm3) allowed detailed quantification of interrelated parameters like focus-to-focus distance or SARS-CoV-2-infected area, facilitating an in-depth description of SARS-CoV-2 infection foci. Accordingly, we could confirm a preferential infection of the ferret upper respiratory tract by SARS-CoV-2 and emphasize a distinct focal infection pattern in nasal turbinates. Conclusively, we present a proof-of-concept study for investigating critically important respiratory pathogens in their spatial tissue morphology and demonstrate the first specific 3D visualization of SARS-CoV-2 infection.

19. 通过对比宿主-冠状病毒的蛋白相互作用网络揭示了泛病毒性疾病的机理

Comparative host-coronavirus protein interaction networks reveal pan-viral disease mechanisms

来源：Science

发布时间：2020-10-15

链接：https://science.sciencemag.org/content/early/2020/10/14/science.abe9403

第一作者：David E. Gordon et.al

通讯作者： Nevan Krogan et.al

通讯作者单位：USC et.al

编译者：宋珂

中文摘要：

由 SARS-CoV-2 冠状病毒引起的 COVID-19 疫情对全球经济和公共卫生造成了重大威胁。SARS-CoV-2 病毒与致死性更强，但传播能力较弱的其他冠状病毒，如：SARS-CoV-1 和 MERS-CoV 的关系密切。本文中，作者对以上三种病毒进行了病毒与人体之间的蛋白-蛋白相互作用网络的对比研究，以及病毒蛋白的定位分析。在随后的功能遗传筛选实验中，确定了在功能上影响冠状病毒增殖的宿主因子，包括 Tom70，一种与 SARS-CoV-1 和 SARS-CoV-2 Orf9b 存在相互作用的线粒体伴侣蛋白。作者进一步利用 cryo-EM 技术在结构上证实了这种相互作用的存在。将经过基因验证的宿主因子与 COVID-19 患者的遗传数据，以及医疗记录相结合，发现了重要的分子机制和潜在的药物治疗方法，值得进一步的分子和临床研究。

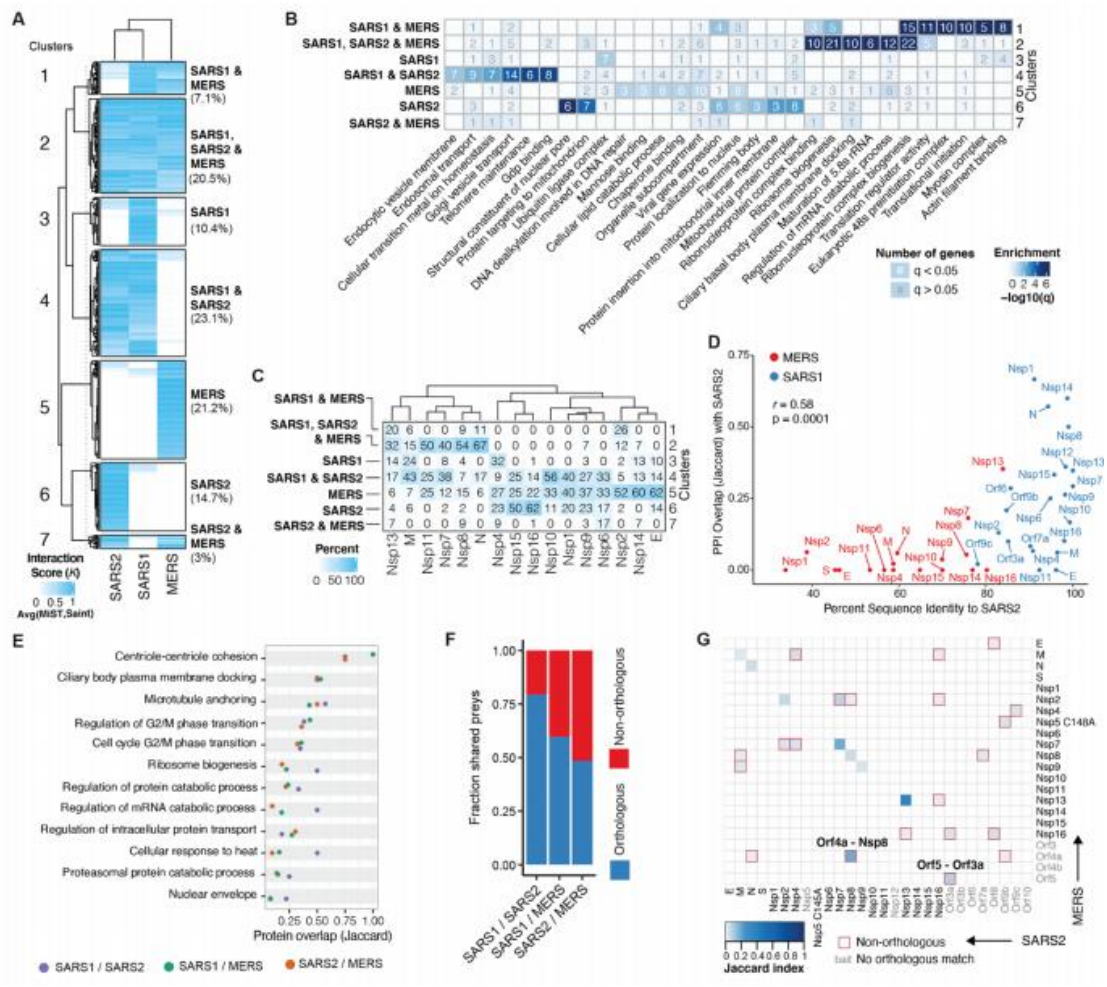


Fig. 3. Comparative analysis of coronavirus-host interactomes. (A) Clustering analysis (k-means) of interactors from SARS-CoV-2, SARS-CoV-1, and MERS-CoV weighted according to the average between their MIST and Saint scores (interaction score K) and percentages of total interactions. Included are only viral protein baits represented amongst all three viruses and interactions that pass the high-confidence scoring threshold for at least one virus. Seven clusters highlight all possible scenarios of shared versus unique interactions. **(B)** GO enrichment analysis of each cluster from A, with the top six most significant terms per cluster. Color indicates -log10(q) and number of genes with significant ($q<0.05$; white) or nonsignificant enrichment ($q>0.05$; grey) is shown. **(C)** Percentage of interactions for each viral protein belonging to each cluster identified in A. **(D)** Correlation between protein sequence identity and PPI overlap (Jaccard index) comparing SARS-CoV-2 and SARS-CoV-1 (blue) or MERS-CoV (red). Interactions for PPI overlap are derived from the final thresholded list of interactions per virus. **(E)** GO biological process terms significantly enriched ($q<0.05$) for all three virus PPIs with Jaccard index indicating overlap of genes from each term for pairwise comparisons between SARS-CoV-1 and SARS-CoV-2 (purple), SARS-CoV-1 and MERS-CoV (green) and SARS-CoV-2 and MERS-CoV (orange). **(F)** Fraction of shared preys between orthologous (blue) versus non-orthologous (red) viral protein baits. **(G)** Heatmap depicting overlap in PPIs (Jaccard index) between each bait from SARS-CoV-2 and MERS-CoV. Baits in grey were not assessed, do not exist, or do not have highconfidence interactors in the compared virus. Non-orthologous bait interactions are highlighted with a red square. GO = Gene Ontology; PPI = protein-protein interaction; SARS2 = SARS-CoV-2; SARS1 = SARS-CoV-1; MERS =

MERS-CoV.

Abstract:

The COVID-19 (Coronavirus disease-2019) pandemic, caused by the SARS-CoV-2 coronavirus, is a significant threat to public health and the global economy. SARS-CoV-2 is closely related to the more lethal but less transmissible coronaviruses SARS-CoV-1 and MERS-CoV. Here, we have carried out comparative viral-human protein-protein interaction and viral protein localization analysis for all three viruses. Subsequent functional genetic screening identified host factors that functionally impinge on coronavirus proliferation, including Tom70, a mitochondrial chaperone protein that interacts with both SARS-CoV-1 and SARS-CoV-2 Orf9b, an interaction we structurally characterized using cryo-EM. Combining genetically-validated host factors with both COVID-19 patient genetic data and medical billing records identified important molecular mechanisms and potential drug treatments that merit further molecular and clinical study.

20. CRISPR 全基因组水平筛选揭示 SARS-CoV-2 感染的关键因子

Genome-wide CRISPR screens reveal host factors critical for SARS-CoV-2 infection

来源：cell

发布时间：2020-10-20

链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31392-1

第一作者：Jin Wei

通讯作者：G. Doench*3 , Craig B. Wilen*1,2,14,18

通讯作者单位：1Department of Laboratory Medicine, Yale School of Medicine, New Haven, CT 06520, USA

2Department of Immunobiology, Yale School of Medicine, New Haven, CT 06520, USA

3Genetic Perturbation Platform, Broad Institute of MIT and Harvard, Cambridge, MA 02142, USA

14Yale Cancer Center, Yale School of Medicine, New Haven, CT 06520, USA

18Lead Contact

DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2020.10.028

编译者：王玮

中文摘要：

亮点

建立猴 CRISPR 文库，筛选感染致病性冠状病毒的 Vero-E6 细胞。

筛选出 SARS-CoV-2-、MERS-CoV-和泛冠状病毒特异的基因。

治疗靶点包括 SARS-CoV-2 感染相关的 SMARCA4。

HMGB1 是 ACE2 表达的新调控因子，对病毒进入具有重要意义。

SARS-CoV-2 感染的宿主基因的鉴定可能揭示新的治疗靶点，并且能为我们了解 COVID-19 的发病机制提供依据。该文章在 Vero-E6 细胞中进行全基因组的 CRISPR 筛选，其中 SARS-CoV-2、MERS-CoV、表达 SARS-CoV-1 刺突蛋白的蝙蝠冠状病毒 HKU5，表达 SARS-CoV-2 刺突蛋白的 VSV。鉴定出了已知的 SARS-CoV-2 宿主因子，包括受体 ACE2 和 protease Cathepsin L。该研究还发现 pro-viral 基因和途径，包括 HMGB1 和 SWI/SNF 染色质重构复合体，分别具有

SARS 家族和泛冠状病毒特异性。HMGB1 调节 ACE2 的表达，对 SARS-CoV-2、SARS-CoV-1 和 NL63 的病毒入侵宿主具有重要意义。被鉴定出来的基因的小分子拮抗剂能够抑制猴和人类细胞中 SARS-CoV-2 感染，证明了这些基因在不同物种间的遗传保守作用。这些工作确定了 SARS-CoV-2 的潜在治疗靶点，揭示了 SARS 家族特异性和泛冠状病毒宿主因子，这些因子调节了对高致病性冠状病毒的敏感性。

Abstract:

Highlights

Developed monkey CRISPR library to screen pathogenic coronaviruses in Vero-E6 cells.

Screens identified genes that are SARS-CoV-2-, MERS-CoV-, and pan-coronavirus-specific.

Therapeutic targets including SMARCA4 identified for SARS-CoV-2 infection.

HMGB1 is novel regulator of ACE2 expression and critical for viral entry.

Identification of host genes essential for SARS-CoV-2 infection may reveal novel therapeutic targets and inform our understanding of COVID-19 pathogenesis. Here, we performed genome-wide CRISPR screens in Vero-E6 cells with SARS-CoV-2, MERS-CoV, bat coronavirus HKU5 expressing the SARS-CoV-1 spike, and VSV expressing the SARS-CoV-2 spike. We identify known SARS-CoV-2 host factors including the receptor ACE2 and protease Cathepsin L. We additionally discovered pro-viral genes and pathways including HMGB1 and the SWI/SNF chromatin remodeling complex that are SARS-lineage and pan-coronavirus specific, respectively. We show HMGB1 regulates ACE2 expression and is critical for viral entry of SARS-CoV-2, SARS-CoV-1, and NL63. We also show that small molecule antagonists of identified gene products inhibited SARS-CoV-2 infection in monkey and human cells, demonstrating the conserved role of these genetic hits across species. Together this identifies potential therapeutic targets for SARS-CoV-2 and reveals SARS-lineage specific and pan-coronavirus host factors that regulate susceptibility to highly pathogenic coronaviruses.

21. 单细胞 RNA 测序揭示了与慢性肺病患者 SARS-CoV-2 严重程度和预后相关的分子程序的失调

Single-cell RNA-sequencing reveals dysregulation of molecular programs associated with SARS-CoV-2 severity and outcomes in patients with chronic lung disease

来源：bioRxiv

发布时间：2020-10-20

链接：https://www.biorxiv.org/content/10.1101/2020.10.20.347187v1

第一作者：Linh T. Bui, Nichelle I. Winters

通讯作者：Linh T. Bui, Nicholas E. Banovich

通讯作者单位：Translational Genomics Research Institute, Phoenix, AZ, USA

DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

基本原理：慢性肺部疾病患者发生 COVID-19 重症和不良预后的风险增加。
目的：确定可能导致慢性肺部疾病患者 COVID-19 预后恶化的病变肺上皮和免疫细胞的分子特征。
方法：我们分析了从健康的 79 例和患病的人类肺(31 例慢性阻塞性肺疾病(COPD)、82 例特发性肺纤维化(IPF)和 18 例非 IPF 间质性肺疾病)中分离的 605,904 个单细胞的转录组。
测量和主要结果：SARS-CoV-2 进入因子(ACE2, TMPRSS2)在疾病和控制肺部的细胞分布和相对表达相似。从患病肺中分离出来的上皮细胞表达了更高水平的与病毒复制效率和先天免疫反应直接相关的基因。每个诊断组在 II 型肺泡细胞中都发现了独特的 ACE2 相关基因集。与对照组相比，患病肺部的 CD4、CD8 和 NK 细胞比例显著增加。干扰素途径、IL6 细胞因子途径和主要组织相容性复合体(MHC) II 类基因的成分在几种患病的免疫细胞类型中上调。这些炎症基因表达程序的差异突出了慢性肺部疾病在病毒暴露于周围肺时如何改变炎症微环境。
结论：慢性肺部疾病伴随着细胞型特异性基因表达程序的改变，这些基因表达程序引发肺上皮细胞并影响对 SARS-CoV-2 感染的先天性和适应性免疫反应。

Abstract
Rationale: Patients with chronic lung disease have an increased risk for severe coronavirus disease-19 (COVID-19) and poor outcomes.
Objectives: To identify molecular characteristics of diseased lung epithelial and immune cells that may account for worse COVID-19 outcomes in patients with chronic lung diseases.
Methods: We analyzed the transcriptomes of 605,904 single cells isolated from healthy (79 samples) and diseased human lungs (31 chronic obstructive pulmonary disease (COPD), 82 idiopathic pulmonary fibrosis (IPF) and 18 non-IPF interstitial lung disease samples).
Measurements and Main Results: Cellular distribution and relative expression of SARS-CoV-2 entry factors (ACE2, TMPRSS2) was similar in disease and control lungs. Epithelial cells isolated from diseased lungs expressed higher levels of genes linked directly to efficiency of viral replication and the innate immune response. Unique ACE2-correlated gene sets were identified for each diagnosis group in the type II alveolar cells. Diseased lungs have a significant increase in the proportion of CD4, CD8 and NK cells compared to control lungs. Components of the interferon pathway, the IL6 cytokine pathway and the major histocompatibility complex (MHC) class II genes are upregulated in several diseased immune cell types. These differences in inflammatory gene expression programs highlight how chronic lung disease alters the inflammatory microenvironment encountered upon viral exposure to the peripheral lung.
Conclusions: Chronic lung disease is accompanied by changes in cell-type-specific gene expression programs that prime the lung epithelium for and influence innate and adaptive immune responses to SARS-CoV-2 infection.

22. 10 月 20 日 Science 两篇背靠背文章发现新膜蛋白帮助新冠病毒感染细胞
https://mp.weixin.qq.com/s/S9YLNpZvYSkT6zLo9k2Fgw
简报 6 月 12 日第 38 条报道过这两项研究的预印本

neuropilin-1 (NRP1)参与了 SARS-COV-2 侵袭中枢神经系统
原文链接：
https://science.sciencemag.org/content/early/2020/10/19/science.abd3072
https://science.sciencemag.org/content/early/2020/10/19/science.abd2985

23. COVID-19 会是一次完美的帕金森病风暴吗？

Is COVID-19 a perfect storm for Parkinson's disease?
来源：cell
发布时间：2020-10
链接：https://www.cell.com/trends/neurosciences/fulltext/S0166-2236(20)30242-3
第一作者：Patrik Brundin
通讯作者: Patrik Brundin
通讯作者单位：Van Andel Research Institute
DOI 或 PUBMED ID：Journal Pre-proof
编译者：蒋立春
中文摘要：
最近出现了三例病人罹患 COVID-19 之后发展出急性帕金森症状的报道。该评论文章中塔伦了可能的细胞和分子机制，以及 COVID-19 是否可能和长期的的帕金森病发病率提高相关。
以下是作者提出的可能的细胞和分子机制模型

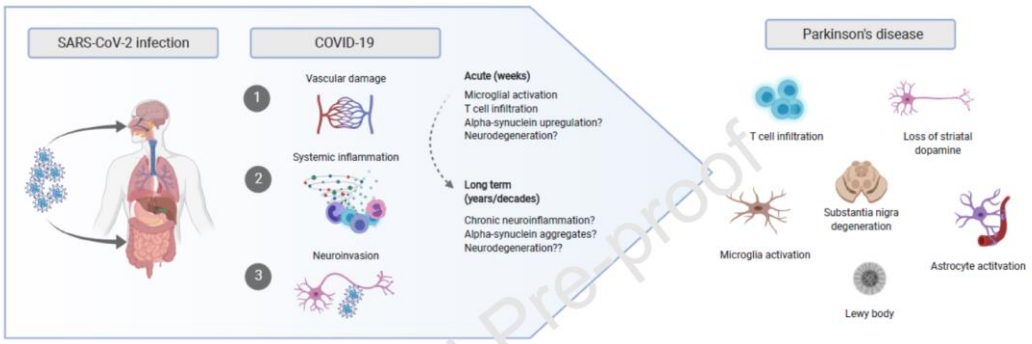


Figure 1

Fig1 Schematic illustration of how SARS-CoV-2 infection might lead to increased PD risk
图示 SARS-CoV-2 感染会怎样导致 PD 风险升高

Abstract:
Three recent case reports describe the development of acute parkinsonism following COVID-19. We discuss possible underlying cellular and molecular mechanisms, and whether COVID-19 might be associated with elevated long-term risk of Parkinson's disease.

24. 某些 COVID-19 疫苗会使人们更容易感染艾滋病病毒吗？

Could certain COVID-19 vaccines leave people more vulnerable to the AIDS virus?

来源：Science

发布时间：2020-10-19
链接：https://www.sciencemag.org/news/2020/10/could-certain-covid-19-vaccines-leave-people-more-vulnerable-aids-virus
第一作者：Jon Cohen
通讯作者：Jon Cohen
通讯作者单位：Science
DOI 或 PUBMED ID：10.1126/science.abf3359
编译者：张丽双
中文摘要：
2007 年，默克公司的腺病毒载体疫苗 STEP 临床试验发现疫苗增加了 HIV 感染风险，一些研究人员警告说，某些 COVID-19 候选疫苗可能会增加对 HIV 的易感性，部分原因是对这些候选人的试验可能很快就会在南非等艾滋病流行明显的地区开始。
默克公司的 Ad5 疫苗究竟是如何同步增加艾滋病病毒传播的风险的，目前仍不清楚，《柳叶刀》的社论阐述了几种可能性，包括抑制针对艾滋病病毒的免疫力，增强艾滋病病毒的复制，或者为它建立更多的靶细胞。
目前几种领先的疫苗，包括中国陈薇团队、强生公司和阿斯利康/牛津大学生产的疫苗，都使用不同的腺病毒作为载体。但没有证据表明这些腺病毒会增加感染艾滋病毒的风险。
Abstract:
Certain COVID-19 vaccine candidates could increase susceptibility to HIV, warns a group of researchers who in 2007 learned that an experimental HIV vaccine had raised in some people the risk for infection with the AIDS virus. These concerns have percolated in the background of the race for a vaccine to stem the coronavirus pandemic, but now the researchers have gone public with a “cautionary tale,” in part because trials of those candidates may soon begin in locales that have pronounced HIV epidemics, such as South Africa.
Precisely how Merck’s Ad5 vaccine increased the risk of HIV transmission in STEP and Phambili remains murky. The Lancet editorial spells out several possibilities, including dampening of HIV immunity, enhancing replication of the AIDS virus, or setting up more target cells for it.
In addition to the Ad5 COVID-19 vaccine candidates, several other leading vaccines, including ones made by Johnson & Johnson and AstraZeneca/the University of Oxford, use different adenoviruses as vectors. There’s no evidence that any of those adenoviruses increases the risks of an HIV infection.

25. 5 型腺病毒载体疫苗的应用：一个警示故事
Use of adenovirus type-5 vectored vaccines: a cautionary tale
来源：sciencedirect
发布时间：2020-10-19
链接：
https://www.sciencedirect.com/science/article/pii/S0140673620321565?via%3Dihub
第一作者：Susan PBuchbinder
通讯作者：Susan PBuchbinder
通讯作者单位：加利福尼亚大学，旧金山公共卫生部
DOI 或 PUBMED ID：https://doi.org/10.1016/S0140-6736(20)32156-5

编译者：刘焕珍

中文摘要：

十多年前，我们完成了 Step and Phambili 临床 2b 期研究，评估了三种免疫接种中使用 Ad5 载体的 HIV-1 疫苗对 HIV-1 获得的有效性。两项国际研究都发现，接种疫苗的男性感染 HIV-1 的风险增加。Step 试验发现，在最初 18 个月的随访中，Ad5 血清阳性且未进行包皮环切的男性感染 HIV-1 的风险较高。在参加 Phambili 研究的异性恋男性中也观察到类似的 HIV 感染风险增加。我们担心使用 Ad5 载体进行针对严重急性呼吸综合征冠状病毒 2（SARS-CoV-2）的免疫接种可能同样增加接种疫苗的男性获得 HIV-1 的风险。在进一步开发用于 SARS-CoV-2 的 Ad5 疫苗之前，应该对这一重要的安全性进行彻底的评估。

Abstract:

Over a decade ago, we completed the Step and Phambili phase 2b studies that evaluated an Ad5 vectored HIV-1 vaccine administered in three immunisations for efficacy against HIV-1 acquisition. Both international studies found an increased risk of HIV-1 acquisition among vaccinated men. The Step trial found that men who were Ad5 seropositive and uncircumcised on entry into the trial were at elevated risk of HIV-1 acquisition during the first 18 months of follow-up. A similar increased risk of HIV infection was also observed in heterosexual men who enrolled in the Phambili study. We are concerned that use of an Ad5 vector for immunisation against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could similarly increase the risk of HIV-1 acquisition among men who receive the vaccine. This important safety consideration should be thoroughly evaluated before further development of Ad5 vaccines for SARS-CoV-2.