新型冠状病毒信息简报

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上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

联系人：蒋立春 jianglch@shanghaitech.edu.cn

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免责申明：

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

1. 2020 年 10 月 15 日疫情

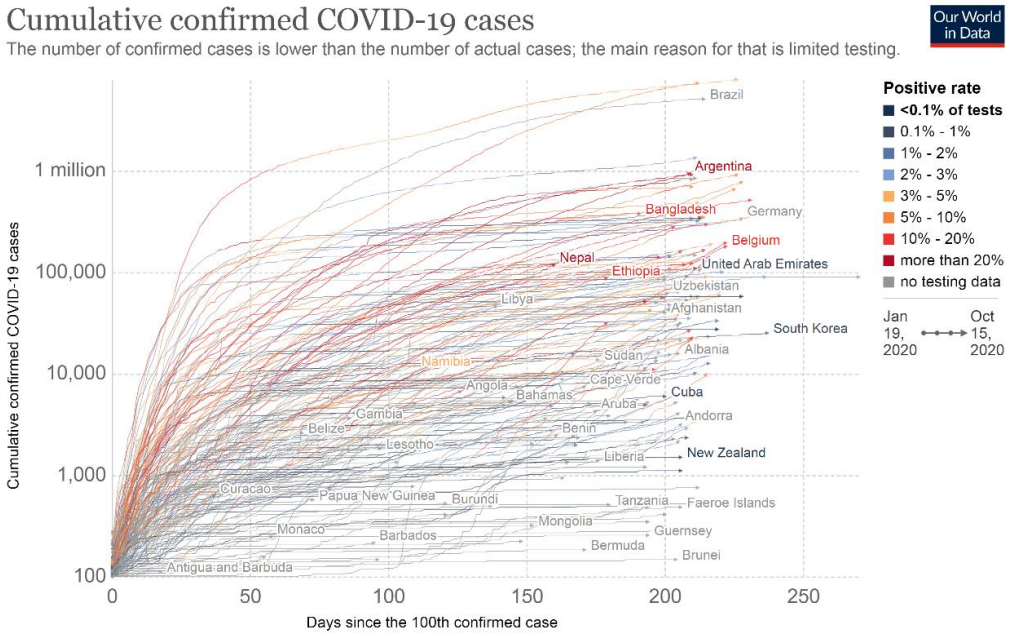
数据来源：WHO

发布时间：2020 年 10 月 15 日北京时间下午 4 点

链接：https://covid19.who.int/

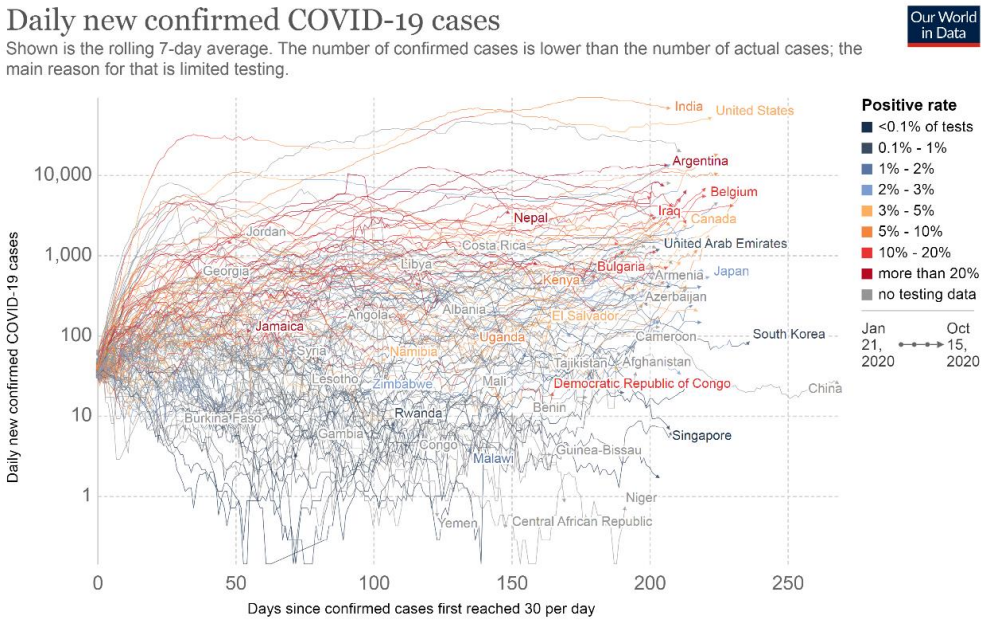
根据 WHO 提供的数据，2020 年 10 月 15 日全球累计确诊新型冠状病毒病人 **38,394,169** 例，当日新增确诊 **336,515** 例，累计死亡 **1,089,047** 例，当日新增死亡 **5,297**。

中国累计确诊 91,399 例，累计死亡 4,746 例，当日新增确诊 11 例，新增死亡 0 例。



Source: European CDC – Situation Update Worldwide – Last updated 15 October, 10:05 (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 15 October, 10:05 (London time), Official data collated by Our World in Data
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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 15 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

转载：青岛市 6 例新冠肺炎无症状感染者转为确诊病例
新华社公众号相关链接：https://mp.weixin.qq.com/s/QjFw771ETut8kS88xLlhNA
我国青岛地区国庆节前后和一家医院关联的确诊，目前已经完全全市核酸检测排查，除小范围感染外，没有检出其他阳性病例。已经查明医院关联感染是由于诊治境外人员的 CT 消毒不规范造成其他病患和护工等感染。

广州发现 1 例新冠无症状感染者
新华社公众号相关链接：https://mp.weixin.qq.com/s/rTMlBz7pd701zrTouZ-Nww
广州花都区发生一例和境外人员隔离酒店关联的酒店工作人员例行检测新冠病毒阳性。

2. 甲型流感病毒的合并感染增强了 SARS-CoV-2 的传染性

Co-infection of influenza A virus enhances SARS-CoV-2 infectivity
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发布时间：2020-10-14
链接：https://www.biorxiv.org/content/10.1101/2020.10.14.335893v1
第一作者：Lei Bai, Yongliang Zhao, Jiazhen Dong, Simeng Liang, Ming Guo
通讯作者：蓝柯、徐可
通讯作者单位：武汉大学，生命科学学院，病毒学国家重点实验室
DOI 或 PUBMED ID：Preprint
编译者：宋张悦
中文摘要：
即将到来的北半球流感季节与当前 COVID-19 大流行相结合，可能对公共卫生构成潜在的严

重威胁。然而，对于甲型流感病毒(IAV)和 SARS-CoV-2 合并感染的后果知之甚少。通过实验将 IAV 与伪病毒或 SARS-CoV-2 活病毒共感染，我们发现 IAV 预感染显著促进了 SARS-CoV-2 在广泛细胞类型中的感染性。有趣的是，这种增强 SARS-CoV-2 的传染性只在与 IAV 共感染的情况下出现，而与其他几种病毒包括仙台病毒、人鼻病毒、人副流感病毒、人呼吸道合胞病毒或人肠道病毒 71 中没有出现。IAV 感染而不是干扰素信号诱导了 ACE2 的表达升高，这是增强 SARS-CoV-2 感染的必要条件。值得注意的是，我们进一步证实，IAV 预感染确实导致了 hace2 转基因小鼠 SARS-CoV-2 病毒载量的增加和更严重的肺损伤。本研究表明，IAV 的合并感染加重了 SARS-CoV-2 感染，加重了病情严重程度，因此，预防流感季和 COVID-19 大流行的并发具有重要意义。

Abstract

The upcoming flu season in the northern hemisphere merging with the current COVID-19 pandemic may raise a potentially severe threat to public health. However, little is known about the consequences of the co-infection of influenza A virus (IAV) and SARS-CoV-2. Through experimental co-infection of IAV with either pseudotyped or SARS-CoV-2 live virus, we found that IAV pre-infection significantly promoted the infectivity of SARS-CoV-2 in a broad range of cell types. Intriguingly, such enhancement of SARS-CoV-2 infectivity was only seen under co-infection with IAV but not with several other viruses including Sendai virus, human rhinovirus, human parainfluenza virus, human respiratory syncytial virus, or human enterovirus 71. IAV infection rather than interferon signaling induced elevated expression of ACE2 essential for such enhancement of SARS-CoV-2 infectivity. Remarkably, we further confirmed that the pre-infection of IAV indeed resulted in an increased SARS-CoV-2 viral load and more severe lung damage in hACE2-transgenic mice. This study illustrates that the co-infection of IAV aggravates SARS-CoV-2 infection and disease severity, which in turn suggests that preventing the convergence of flu season and COVID-19 pandemic would be of great significance.

3. 在 COVID-19 小鼠模型中，甲型流感病毒继发感染 SARS-CoV-2 病毒可导致危重症和脑炎

Sequential infection with influenza A virus followed by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leads to more severe disease and encephalitis in a mouse model of COVID-19

来源：bioRxiv

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第一作者：Jordan J. Clark, Rebekah Penrice-Randal

通讯作者：James P. Stewart

通讯作者单位：Department of Infection Biology & Microbiomes, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, UK

DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

COVID-19 是人类感染 SARS-CoV-2 引起的一系列临床症状。SARS-CoV-2 是近期出现的一种

冠状病毒，迅速引发了一场大流行。这种病毒的第二波与季节性呼吸道病毒，特别是流感病毒合并，可能是一个全球卫生问题。为了研究这一点，在上皮细胞角蛋白-18 基因启动子(K18-hACE2)的驱动下，表达人类 ACE2 受体的转基因小鼠首先感染了甲型流感病毒 IAV，紧接着感染了 SARS-CoV-2。与仅感染 IAV 或 SARS-CoV-2 的 K18-hACE2 小鼠比较了宿主反应和病毒生物学效应。与对照组小鼠相比，感染每种病毒的小鼠产生一种疾病表型。虽然，SARS-CoV-2 RNA 合成在继发性感染小鼠中明显减少，但与单独感染或对照小鼠相比，这些小鼠体重下降更快，肺损伤更严重，先天反应延长。继发性感染还加重了与 SARS-CoV-2 相关的肺外表现。其中包括更严重的脑炎。综上所述，数据表明，“双重感染”是有害的，应采取缓解措施，作为应对 COVID-19 大流行的综合公共卫生对策的一部分。

Abstract

COVID-19 is a spectrum of clinical symptoms in humans caused by infection with SARS-CoV-2, a recently emerged coronavirus that has rapidly caused a pandemic. Coalescence of a second wave of this virus with seasonal respiratory viruses, particularly influenza virus is a possible global health concern. To investigate this, transgenic mice expressing the human ACE2 receptor driven by the epithelial cell cytokeratin-18 gene promoter (K18-hACE2) were first infected with IAV followed by SARS-CoV-2. The host response and effect on virus biology was compared to K18-hACE2 mice infected with IAV or SARS-CoV-2 only. Infection of mice with each individual virus resulted in a disease phenotype compared to control mice. Although, SARS-CoV-2 RNA synthesis appeared significantly reduced in the sequentially infected mice, these mice had a more rapid weight loss, more severe lung damage and a prolongation of the innate response compared to singly infected or control mice. The sequential infection also exacerbated the extrapulmonary manifestations associated with SARS-CoV-2. This included a more severe encephalitis. Taken together, the data suggest that the concept of “twinfection” is deleterious and mitigation steps should be instituted as part of a comprehensive public health response to the COVID-19 pandemic.

4. COVID-19 的较轻病程与季节性人类冠状病毒 OC43 和 HKU1（HCoV OC43，HCoV HKU1）抗体水平升高有关

Less severe course of COVID-19 is associated with elevated levels of antibodies against seasonal human coronaviruses OC43 and HKU1 (HCoV OC43, HCoV HKU1)

来源：medRxiv

发布时间：2020-10-14

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第一作者：Martin Dugas

通讯作者：Joachim Kühn

通讯作者单位：德国明斯特大学医院

DOI 或 PUBMED ID：https://doi.org/10.1101/2020.10.12.20211599

编译者：刘焕珍

中文摘要：

我们进行了一项观察研究，以评估先前感染季节性冠状病毒对 COVID-19 严重程度的影响。60 例确诊为 COVID-19 感染的患者（年龄 30-82 岁；男性 52 例，女性 8 例）：危重病住院患者 19 例，重症或中度疾病患者 16 例，门诊患者 25 例（年龄和性别与住院患者匹配）。与其

他 COVID-19 患者相比，危重病患者初次就诊时 HCoV OC43-（p=0.016）和 HCoV HKU1 特异性抗体（p=0.023）水平显著降低。我们的研究结果表明，以前感染季节性冠状病毒可能会预防严重的疾病进程。这一发现应在其他环境中得到验证，并有助于在感染前确定有危险的人。

Abstract:
The clinical course of COVID-19 is very heterogeneous: Most infected individuals can be managed in an outpatient setting, but a substantial proportion of patients requires intensive care, resulting in a high rate of fatalities. Recently, an association between contact to small children and mild course of COVID-19 was reported. We performed an observational study to assess the impact of previous infections with seasonal coronaviruses on COVID-19 severity. 60 patients with confirmed COVID-19 infections were included (age 30 - 82 years; 52 males, 8 females): 19 inpatients with critical disease, 16 inpatients with severe or moderate disease and 25 outpatients (age and gender matched to inpatients). Patients with critical disease had significantly lower levels of HCoV OC43- (p=0.016) and HCoV HKU1-specific (p=0.023) antibodies at the first encounter compared to other COVID-19 patients. Our results indicate that previous infections with seasonal coronaviruses might protect against a severe course of disease. This finding should be validated in other settings and could contribute to identify persons at risk before an infection.

5. 新晋诺奖得主团队开发简易新冠病毒检测，无需 PCR 扩增，手机定量检测病毒水平

发布时间：2020.10.13
文章链接：https://mp.weixin.qq.com/s/8nRL_mgiwf_UKnHyCTks2Q
编译者：张怡
中文摘要：
今年诺贝尔化学奖得主之一 Jennifer Doudna 博士率领的团队和她的合作伙伴在预印本网站 medRxiv 上发布了一篇论文，基于 CRISPR-Cas13a 技术开发了一种新型新冠病毒检测，作者还通过使用多个靶向不同病毒序列的 crRNA 能够提高检测灵敏度。这款检测与众不同之处在于它不需要对病毒 RNA 使用 RT-PCR 进行扩增，可以直接定量检测样本中的病毒 RNA 水平。研究人员还开发了一款基于智能手机相机的检测系统，让医务人员不需要复杂的仪器，就可以在实验室以外的环境中读出检测结果。
参考资料：Fozouni et al., Direct detection of SARS-CoV-2 using CRISPR-Cas13a and a mobile phone. medRxiv, doi: https://doi.org/10.1101/2020.09.28.20201947

6. SARS-CoV-2 感染 COVID-19 患者脑星形胶质细胞并损害神经元活力

SARS-CoV-2 infects brain astrocytes of COVID-19 patients and impairs neuronal viability
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第一作者：Fernanda Crunfli、Victor Corasolla Carregari、Flavio Protasio Veras、Pedro Henrique Vendramini
通讯作者：Clarissa Lin Yasuda、Marcelo A. Mori、Thiago Mattar Cunha、Daniel

Martins-de-Souza
通讯作者单位：巴西圣保罗坎皮纳斯大学、圣保罗大学里贝雷托医学院
DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：
COVID-19 患者可能表现出神经精神和/或神经症状。研究人员发现 28-56%的 SARS-CoV-2 感染者表现出焦虑和认知障碍，这些症状轻微或没有呼吸道症状，并且与大脑皮质厚度改变有关。通过一个独立的队列研究，我们发现 19%死于 COVID-19 的个体存在脑损伤的组织病理学征象。所有受累脑组织均显示 SARS-CoV-2 感染灶，尤其是星形胶质细胞。神经干细胞源性星形胶质细胞的感染改变了能量代谢，改变了关键蛋白和代谢物，用于为神经元提供能量和神经递质的生物发生，并引发了一种降低神经元活力的分泌表型。这些数据支持 SARS-CoV-2 到达大脑、感染星形胶质细胞并引发神经病理性改变的模型，这些改变导致了 COVID-19 患者大脑结构和功能的改变。
Abstract:
COVID-19 patients may exhibit neuropsychiatric and/or neurological symptoms. We found that anxiety and cognitive impairment are manifested by 28-56% of SARS-CoV-2-infected individuals with mild or no respiratory symptoms and are associated with altered cerebral cortical thickness. Using an independent cohort, we found histopathological signs of brain damage in 19% of individuals who died of COVID-19. All of the affected brain tissues exhibited foci of SARS-CoV-2 infection, particularly in astrocytes. Infection of neural stem cell-derived astrocytes changed energy metabolism, altered key proteins and metabolites used to fuel neurons and for biogenesis of neurotransmitters, and elicited a secretory phenotype that reduces neuronal viability. Our data support the model where SARS-CoV-2 reaches the brain, infects astrocytes and triggers neuropathological changes that contribute to the structural and functional alterations in the brain of COVID-19 patients.

7. 识别 ACE2 的 IgM 自身抗体与严重 COVID-19 相关

IgM autoantibodies recognizing ACE2 are associated with severe COVID-19
来源：medRxiv
发布时间：2020-10-15
链接：https://www.medrxiv.org/content/10.1101/2020.10.13.20211664v1
第一作者：Livia Casciola-Rosen
通讯作者：Antony Rosen
通讯作者单位：Johns Hopkins University School of Medicine, Baltimore, Maryland
DOI 或 PUBMED ID：
编译者：张鹏伟
中文摘要：
严重 COVID-19 的 ACE2 自身抗体具有 T 细胞非依赖性免疫反应的特点，可能介导血管损伤。
ACE2 autoantibodies in severe COVID-19 have features of a T-independent immune response, and may mediate vascular damage.

8. 轻度/无症状 SARS-CoV-2 感染的医护人员在第一波感染后表现出 T 细胞反应和中和抗体

Healthcare workers with mild / asymptomatic SARS-CoV-2 infection show T cell responses and neutralising antibodies after the first wave

来源：medrxiv

发布时间：2020-10-14

链接：https://www.medrxiv.org/content/10.1101/2020.10.13.20211763v1

第一作者：Catherine J. Reynolds, Leo Swadling, Joseph M. Gibbons, Corinna Pade

通讯作者：Rosemary J. Boyton1,1,15

通讯作者单位：1 Department of Infectious Disease, Imperial College London, London, UK

15 Lung Division, Royal Brompton & Harefiled NHS Foundation Trust, London, UK

DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

对 SARS-CoV-2 的适应性免疫研究包括研究致死、严重和轻症病例的特征。了解轻度或无症状感染的人群的免疫力持续多久是至关重要的。在大流行的早期阶段接触和感染 SARS-CoV-2 的医护人员（Healthcare worker，HCW）是研究这个问题的宝贵资源。UK COVIDsortium 是一个纵向的，伦敦医院的 HCW 队列，从英国封禁时开始跟踪；每周的 PCR、血清学和症状日志可以捕捉到发病前后的无症状感染，因此可以跟踪免疫持续时间。该研究对英国禁闭后 16-18 周的 136 例 HCW 进行了横断面病例对照亚研究，其中 76 例有实验室证实的 SARS-CoV-2 轻度或无症状感染。在第一波感染后 90%的感染 HCW 样本中存在中和抗体（nAb）；在 16-18 周时，66%的 HCW 中检测到可能与功能保护相关的滴度。在无症状感染的 HCW 中，T 细胞反应往往低于那些报告病例定义的 COVID-19 症状的患者，而 nAb 滴度与症状无关。T 细胞和抗体反应不一致。缺乏 nAb 的 HCW 也表现出无法检测到的对应刺突蛋白质的 T 细胞，但有其他特异性的 T 细胞。该研究结果表明，大多数轻度或无症状 SARS-CoV-2 感染的 HCW 在轻度或无症状的 SARS-CoV-2 感染后至少 4 个月内携带 nAb，并伴有多种特异性 T 细胞应答。

Abstract

Studies of adaptive immunity to SARS-CoV-2 include characterisation of lethal, severe and mild cases. Understanding how long immunity lasts in people who have had mild or asymptomatic infection is crucial. Healthcare worker (HCW) cohorts exposed to and infected by SARS-CoV-2 during the early stages of the pandemic are an invaluable resource to study this question. The UK COVIDsortium is a longitudinal, London hospital HCW cohort, followed from the time of UK lockdown; weekly PCR, serology and symptom diaries allowed capture of asymptomatic infection around the time of onset, so duration of immunity could be tracked. Here, we conduct a cross-sectional, case-control, sub-study of 136 HCW at 16-18 weeks after UK lockdown, with 76 having had laboratory-confirmed SARS-CoV-2 mild or asymptomatic infection. Neutralising antibodies (nAb) were present in 90% of infected HCW sampled after the first wave; titres, likely to correlate with functional protection, were present in 66% at 16-18 weeks. T cell responses tended to be lower in asymptomatic infected HCW than those reporting case-definition symptoms of COVID-19, while nAb titres were maintained irrespective of symptoms. T cell and antibody responses were discordant. HCW lacking nAb also

showed undetectable T cells to Spike protein but had T cells of other specificities. Our findings suggest that the majority of HCW with mild or asymptomatic SARS-CoV-2 infection carry nAb complemented by multi-specific T cell responses for at least 4 months after mild or asymptomatic SARS-CoV-2 infection.

9. SARS-CoV-2 病毒感染会损害呼吸道运动纤毛并削弱黏膜纤毛清除功能

SARS-CoV-2 infection damages airway motile cilia and impairs mucociliary clearance

来源：bioRxiv

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第一作者：Rémy Robinot, Mathieu Hubert

通讯作者：Vincent Michel[11], Olivier Schwartz[1], Lisa A. Chakrabarti[1]

通讯作者单位：

1 Virus & Immunity Unit, Department of Virology, Institut Pasteur, Paris, France; CNRS UMR 3569, Paris, France

11 Institut de l'Audition, Institut Pasteur, INSERM, Paris, France

DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

了解 SARS-CoV-2 病毒如何在呼吸道内传播，对于明确影响 COVID-19 严重性的参数非常重要。本文中，作者在重组的人支气管上皮模型中验证了 SARS-CoV-2 感染对其功能和结构影响。尽管 SARS-CoV-2 病毒颗粒穿越上皮的能力仍然受到了限制，但病毒的复制造成了上皮屏障功能的短暂下降，并破坏了上皮细胞间的紧密连接。而且，SARS-CoV-2 的复制导致纤毛层的快速丧失。在超微结构水平上的特征表现为轴丝的缺失和剩余基座结构的取向错误。通过黏膜纤毛清除功能试验的测量，发现运动纤毛功能受到损害。只有在纤毛损伤开始后，上皮细胞的防御机制，包括基底细胞的活动能力和干扰素-lambda 的诱导，才得到增强。对 SARS-CoV-2 感染的叙利亚仓鼠的分析进一步证明了活体内运动纤毛的损伤。本文的研究明确了纤毛损伤是一种可能促进 SARS-CoV-2 传播到更深的肺实质的致病机理。

Abstract

Understanding how SARS-CoV-2 spreads within the respiratory tract is important to define the parameters controlling the severity of COVID-19. We examined the functional and structural consequences of SARS-CoV-2 infection in a reconstituted human bronchial epithelium model. SARS-CoV-2 replication caused a transient decrease in epithelial barrier function and disruption of tight junctions, though viral particle crossing remained limited. Rather, SARS-CoV-2 replication led to a rapid loss of the ciliary layer, characterized at the ultrastructural level by axoneme loss and misorientation of remaining basal bodies. The motile cilia function was compromised, as measured in a mucociliary clearance assay. Epithelial defense mechanisms, including basal cell mobilization and interferon-lambda induction, ramped up only after the initiation of cilia damage. Analysis of SARS-CoV-2 infection in Syrian hamsters further demonstrated the loss of motile cilia in vivo. This study identifies

cilia damage as a pathogenic mechanism that could facilitate SARS-CoV-2 spread to the deeper lung parenchyma.

10. SARS-CoV-2 灭活疫苗安全性和免疫原性的深入研究

An in-depth investigation of the safety and immunogenicity of an inactivated SARS-CoV-2 vaccine

来源：medRxiv

发布时间：2020-10-06

链接：https://www.medrxiv.org/content/10.1101/2020.09.27.20189548v1

第一作者：Jing Pu

通讯作者：Qihan Li

通讯作者单位：云南省重症传染病疫苗研究开发重点实验室

DOI 或 PUBMED ID：

编译者：张鹏伟

中文摘要：

背景：需要对 SARS-CoV-2 灭活疫苗的安全性和免疫原性进行深入研究。

方法：在一项包括 192 名 18-59 岁健康成年人的随机、双盲、安慰剂对照试验中，两次肌肉注射三种不同剂量（5OEU、1OOEU 和 15OEU）的 SARS-CoV-2 灭活疫苗或安慰剂，注射间隔为 2 周或 4 周。在 28 天内评价疫苗的安全性和免疫原性。

发现：在这项研究中，191 名被分配到三个剂量组或安慰剂组的受试者完成了 28 天的试验。28 天内共有 44 例不良反应，以注射部位轻度疼痛、发红或轻度疲劳为主，免疫组血清中 48 种细胞因子未见异常变化。从 1:32 稀释至 1:4096 的血清样本与病毒孵育后，对人类自然杀伤细胞、巨噬细胞或树突状细胞没有显示抗体依赖性增强效应（ADEs）。第 14 天血清转化率分别达到 92%、100%和 96%，几何平均滴度（GMTs）分别为 18.0、54.5 和 37.1；第 28 天，0、14 和 0、28 个程序的血清转化率分别为 10.6、15.4 和 19.6，血清转化率分别达到 80%、96%和 92%。血清转化与抗 S 蛋白、N 蛋白和病毒离子的 ELISA 抗体同步上调和细胞毒性 T 淋巴细胞（CTL）反应有关。转录组分析形成了疫苗诱导的免疫反应的遗传多样性。

解释：在 18-59 岁的人群中，这种 SARS-CoV-2 灭活疫苗是安全和免疫原性的。

Abstract:

BACKGROUND In-depth investigations of the safety and immunogenicity of inactivated SARS-CoV-2 vaccines are needed.

METHOD In a phase I randomized, double-blinded, and placebo-controlled trial involving 192 healthy adults 18-59 years of age, two injections of three different doses (50 EU, 100 EU and 150 EU) of an inactivated SARS-CoV-2 vaccine or the placebo were administered intramuscularly with a 2- or 4-week interval between the injections. The safety and immunogenicity of the vaccine were evaluated within 28 days.

FINDING In this study, 191 subjects assigned to three doses groups or the placebo group completed the 28-day trial. There were 44 adverse reactions within the 28 days, most commonly mild pain and redness at the injection site or slight fatigue, and no abnormal variations were observed in 48 cytokines in the serum samples of immunized subjects. The serum samples diluted from 1:32 to 1:4096 and incubated with the virus did not show antibody-dependent enhancement effects (ADEs) with regard to human natural killer cells, macrophages or dendritic cells. At day 14,

the seroconversion rates had reached 92%, 100% and 96% with geometric mean titers (GMTs) of 18.0, 54.5 and 37.1, and at day 28, the seroconversion rates had reached 80%, 96% and 92% with GMTs of 10.6, 15.4 and 19.6in 0, 14 and 0, 28 procedures, respectively. Seroconversion was associated with the synchronous upregulation of ELISA antibodies against the S protein, N protein and virion and a cytotoxic T lymphocyte (CTL) response. Transcriptome analysis shaped the genetic diversity of immune response induced by the vaccine.
INTERPRETATION In a population aged 18-59 years, this inactivated SARS-CoV-2 vaccine was safe and immunogenic.

11. 100 年历史的苏拉明治疗 COVID-19 的结构基础

Structural basis for repurposing a 100-years-old drug suramin for treating COVID-19
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文章链接：https://www.biorxiv.org/content/10.1101/2020.10.06.328336v1
第一作者：Wanchao Yin, Xiaodong Luan, Zhihai Li, Leike Zhang, Ziwei Zhou,
通讯作者：H. Eric Xu
通讯作者单位：中国科学院上海药物研究所受体研究重点实验室，中国科学院大学
doi: https://doi.org/10.1101/2020.10.06.328336
编译者：张怡
中文摘要：
作者报道了苏拉明的发现，这是一种有 100 年历史的药物，通过阻断 RNA 与酶的结合，作为 SARS-CoV-2 RNA 依赖的 RNA 聚合酶(RdRp)的有效抑制剂。在生化检测中，苏拉明及其衍生物的效力比目前批准的用于 COVID-19 的核苷酸药物 remdesivir 至少高出 20 倍。2.6 Å 冷冻电镜结构的病毒 RdRp 绑定到苏拉明显示苏拉明的两个结合位点,与一个结合位点直接阻断 RNA 模板链的结合，另一个结合位点与 RdRp 催化活性位点附近的 RNA 引物链发生碰撞,因此抑制病毒 RNA 复制。此外，苏拉明能有效抑制 Vero E6 细胞的 SARS-CoV-2 复制。这些结果提供了首个 SARS-CoV-2 RdRp 非核苷酸抑制剂的结构机制，并为重新利用苏拉明治疗 COVID-19 提供了理论依据。
Abstract
Here we report the discovery of suramin, a 100-year-old drug, as a potent inhibitor of the SARS-CoV-2 RNA dependent RNA polymerase (RdRp) through blocking the binding of RNA to the enzyme. In biochemical assays, suramin and its derivatives are at least 20-fold more potent than remdesivir, the currently approved nucleotide drug for COVID-19. The 2.6 Å cryo-EM structure of the viral RdRp bound to suramin reveals two binding sites of suramin, with one site directly blocking the binding of the RNA template strand and the other site clash with the RNA primer strand near the RdRp catalytic active site, therefore inhibiting the viral RNA replication. Furthermore, suramin potently inhibits SARS-CoV-2 duplication in Vero E6 cells. These results provide a structural mechanism for the first non-nucleotide inhibitor of the SARS-CoV-2 RdRp and a rationale for repurposing suramin for treating COVID-19.

12. 礼来新冠中和抗体一项 III 期临床遭 FDA 叫停；Moderna 公司在加拿大递交新冠疫苗滚动申请

发布时间：2020.10.14

文章链接：https://mp.weixin.qq.com/s/kO39R0ha5jwg7eSbkzprHA

编译者：张怡

中文摘要：

在强生因一例受试者出现不明原因疾病而暂停其新冠肺炎候选疫苗 JNJ-78436735 临床试验后。10 月 13 日，礼来新冠中和抗体 LY-CoV555 也因安全性问题遭到 FDA 叫停临床试验。礼来目前正在推进 2 款新冠中和抗体，其中，LY-CoV555 由礼来与 AbCellera 公司合作开发，LY-CoV016 则从君实生物引进。此外，Moderna 公司在同日宣布向加拿大卫生部递交其新冠疫苗 mRNA-1273 滚动申请。此次申请是基于 mRNA-1273 的临床前研究和一项针对健康成人（18-55 岁）和（56-70 岁和 71+岁）的 I 期临床中期分析结果，后者研究结果已发表于 NEJM。

13. SARS-CoV-2 特异性 B 细胞克隆的扩增和抗 SARS-CoV-2 抗体的趋同性研究

Human B Cell Clonal Expansion and Convergent Antibody Responses to SARS-CoV-2

来源：Cell host & Microbe

发布时间： 2020-10-07

链接：https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30503-5

第一作者：Sandra C.A. Nielsen

通讯作者：Catherine A. Blish

通讯作者单位：Department of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, CA 94305, USA

DOI 或 PUBMED ID：https://doi.org/10.1016/j.chom.2020.09.002

编译者：孔娟

摘要：

B 细胞对抗体的产生和对抗病毒的保护性免疫至关重要。文中研究发现 COVID-19 患者表现出 B 细胞的早期募集，该 B 细胞表达有限的 IGHV 基因。研究者通过人类 IGH 病毒全序列测定法鉴定了 SARS-CoV-2 特异性 B 细胞克隆。研究发现在感染的最初几周，此类 B 细胞发展为具有高度多克隆反应的 B 细胞，具有更广泛的 IGHV 基因的表达和更强的向有限体细胞突变的 IgG 和 IgA 亚类的类别转换的能力。新冠肺炎患者之间共享趋同的病毒特异性抗体序列，更加突出显示了人类抗病毒的天然免疫反应。值得注意的是，先前报道的对 COVID-19 患者中 B 细胞克隆类型的测序结果提示针对 SARS-CoV-2 受体结合结构域可能存在交叉反应的抗体。这些发现从分子层面为人类 B 细胞对 SARS-2 和 SARS-CoV 反应的共同特征提供了一定的见解。

Abstract:

B cells are critical for the production of antibodies and protective immunity to viruses. Here we show that patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who develop coronavirus disease 2019 (COVID-19) display early recruitment of B cells expressing a limited subset of IGHV genes, progressing to a highly polyclonal response of B cells with broader IGHV gene usage and extensive class switching to IgG and IgA subclasses with limited somatic hypermutation in the initial weeks of infection. We identify convergence of antibody sequences across SARS-CoV-2-infected patients, highlighting stereotyped naive responses to this virus. Notably, sequence-based

detection in COVID-19 patients of convergent B cell clonotypes previously reported in SARS-CoV infection predicts the presence of SARS-CoV/SARS-CoV-2 cross-reactive antibody titers specific for the receptor-binding domain. These findings offer molecular insights into shared features of human B cell responses to SARSCoV-2 and SARS-CoV.

14. SARS-CoV-2 和泛冠状病毒宿主因子网络的基因组水平上的鉴定

Genome-scale identification of SARS-CoV-2 and pan-coronavirus host factor networks

来源：biorxiv

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第一作者：William M. Schneider

通讯作者：Charles M. Rice 1, John T. Poirier 3

通讯作者单位：1 Laboratory of Virology and Infectious Disease, The Rockefeller University, New York, NY 10065, USA

3 Laura and Isaac Perlmutter Cancer Center, New York University Langone Health, New York, NY 10016 USA

DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

COVID-19 大流行已经夺去了全世界 100 多万人的生命。病原体 SARS-CoV-2 是冠状病毒科的一员，冠状病毒是能引起不同严重程度呼吸道感染的病毒。SARS-CoV-2 和其他冠状病毒在其生命周期中所选择的细胞宿主因子和途径仍不明确。为了绘制一份广泛的 SARS-CoV-2 和三种季节性冠状病毒（HCoV-OC43、HCoV-NL63 和 HCoV-229E）感染所需的宿主因子，该研究进行了基因组规模的 CRISPR 基因敲除筛查。这些筛选揭示了具有泛冠状病毒和病毒特异功能作用的多种宿主因子和途径，包括对糖胺聚糖生物合成、SREBP 信号和糖基磷脂酰肌醇生物合成的主要依赖性，以及对一些目前了解不多的蛋白质。确定了 SARS-CoV-2 和所有其他冠状病毒感染包含 VTT 结构域的蛋白 TMEM41B 的绝对需要量。该人类冠状病毒科宿主因子图谱是一个丰富的资源，为急性 COVID-19 和潜在的未来冠状病毒爆发事件开发新的治疗策略。

Abstract

The COVID-19 pandemic has claimed the lives of more than one million people worldwide. The causative agent, SARS-CoV-2, is a member of the Coronaviridae family, which are viruses that cause respiratory infections of varying severity. The cellular host factors and pathways co-opted by SARS-CoV-2 and other coronaviruses in the execution of their life cycles remain ill-defined. To develop an extensive compendium of host factors required for infection by SARS-CoV-2 and three seasonal coronaviruses (HCoV-OC43, HCoV-NL63, and HCoV-229E), we performed parallel genome-scale CRISPR knockout screens. These screens uncovered multiple host factors and pathways with pan-coronavirus and virus-specific functional roles, including major dependency on glycosaminoglycan biosynthesis, SREBP signaling, and glycosylphosphatidylinositol biosynthesis, as well as an unexpected requirement for several poorly characterized proteins. We identified

an absolute requirement for the VTT-domain containing protein TMEM41B for infection by SARS-CoV-2 and all other coronaviruses. This human Coronaviridae host factor compendium represents a rich resource to develop new therapeutic strategies for acute COVID-19 and potential future coronavirus spillover events.

15. SARS-CoV-2 病毒的 NSP1 蛋白充当了核糖体的守门人，能够关闭宿主的翻译进程并促进病毒自身的翻译

The viral protein NSP1 acts as a ribosome gatekeeper for shutting down host translation and fostering SARS-CoV-2 translation

来源：bioRxiv

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第一作者：Antonin TIDU

通讯作者：Franck MARTIN

通讯作者单位：Institut de Biologie Moléculaire et Cellulaire, “Architecture et Réactivité de l’ARN” CNRS UPR9002, Université de Strasbourg, 3, allée Roetgen, F-67084 Strasbourg (France)

DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

SARS-CoV-2 冠状病毒导致了 Covid-19 疫情的大流行。在感染的早期阶段，病毒的单链正向 RNA 基因组被翻译成非结构蛋白（NSP）。其中，NSP1 作为病毒感染过程中产生的首批蛋白质之一，能够与宿主核糖体结合并阻断 mRNA 进入通道，抑制了细胞内的翻译进程。尽管核糖体结合了 NSP1，但病毒的翻译却未受影响。不过，所谓的病毒对 NSP1 抑制的逃逸现象的分子机制仍尚不明确。本文中，作者首先证明了在 NSP1 存在的条件下，病毒的翻译仍能够进行。病毒的逃逸 NSP1 的翻译抑制作用是通过 SARS-CoV-2 病毒 5’UTR 中的顺式作用 RNA 的发夹结构 SL1 的介导的。将 SL1 移植转移到报告转录本上也可以实现这种逃逸作用。病毒的翻译仅需要利用 SL1 的顶端部分。作者发现，在病毒翻译过程中 NSP1 仍然结合在核糖体上。作者推测，在 NSP1 保持与核糖体结合的同时，NSP1 和 SL1 之间的相互作用释放了 mRNA 调节通道。因此，NSP1 充当了核糖体守门人的角色，能够关闭宿主的翻译或促进 SARS-CoV-2 的翻译，具体的功能取决于 5’UTR SL1 发夹是否存在。在感染过程的后期，SL1 也存在，并且对亚基因 RNA 的翻译是不可或缺的。综上，以 SL1 为靶点的治疗策略，在 SARS-CoV-2 病毒感染的早期和晚期都可能会影响病毒的翻译。因此，SL1 可能是 SARS-CoV-2 病毒的真正“致命弱点”。

Abstract

SARS-CoV-2 coronavirus is responsible for Covid-19 pandemic. In the early phase of infection, the single-strand positive RNA genome is translated into non-structural proteins (NSP). One of the first proteins produced during viral infection, NSP1, binds to the host ribosome and blocks the mRNA entry channel. This triggers translation inhibition of cellular translation. In spite of the presence of NSP1 on the ribosome, viral translation proceeds however. The molecular mechanism of the so-called viral evasion to NSP1 inhibition remains elusive. Here, we confirm that viral translation is maintained in the presence of NSP1. The evasion to NSP1-inhibition is mediated by the cis-acting RNA hairpin

SL1 in the 5′ UTR of SARS-CoV-2. NSP1-evasion can be transferred on a reporter transcript by SL1 transplantation. The apical part of SL1 is only required for viral translation. We show that NSP1 remains bound on the ribosome during viral translation. We suggest that the interaction between NSP1 and SL1 frees the mRNA accommodation channel while maintaining NSP1 bound to the ribosome. Thus, NSP1 acts as a ribosome gatekeeper, shutting down host translation or fostering SARS-CoV-2 translation depending on the presence of the SL1 5′ UTR hairpin. SL1 is also present and necessary for translation of sub-genomic RNAs in the late phase of the infectious program. Consequently, therapeutic strategies targeting SL1 should affect viral translation at early and late stages of infection. Therefore, SL1 might be seen as a genuine 'Achille heel' of the virus.

16. COVID-19 严重程度的大规模多组学分析

Large-scale Multi-omic Analysis of COVID-19 Severity

来源：Cell

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第一作者：Katherine A. Overmyera, Evgenia Shishkovaa, Ian J. Millera, Joseph Balnis

通讯作者：Joshua J. Coon1, Ariel Jaitovich4

通讯作者单位：1 National Center for Quantitative Biology of Complex Systems, Madison, WI 53562, USA; 4 Division of Pulmonary and Critical Care Medicine, Albany Medical Center, Albany, NY 12208, USA

DOI 或 PUBMED ID：https://doi.org/10.1016/j.cels.2020.10.003

编译者：宋张悦

中文摘要：

我们对来自 COVID-19 阳性和阴性患者的 128 份血液样本进行了 RNA-Seq 和高分辨率质谱分析，这些患者具有不同的疾病严重程度和预后。在一个 curated relational database 数据库中，定量的转录本、蛋白质、代谢物和脂质与临床结局相关联，可以特异性地进行系统分析，并支持分子和患者预后的交叉相关性分析。我们绘制了 219 个对 COVID-19 状态和严重程度具有重要意义的分子特征，其中许多与补体激活、脂质转运异常和中性粒细胞激活有关。我们确定了一系列的协变分子，例如，蛋白胶溶蛋白和代谢物柠檬酸盐或血浆白蛋白和载脂蛋白，提供病理生理学的见解和治疗建议。观察到的血小板功能失调、凝血、急性期反应和内皮病变进一步阐明了 COVID-19 独特的表型。我们提供了一个基于网络的工具(covid-omics.app)，可以对我们的概要进行交互式探索，并通过机器学习方法说明了它在预测 COVID-19 严重程度方面的效用。

Abstract

Highlights

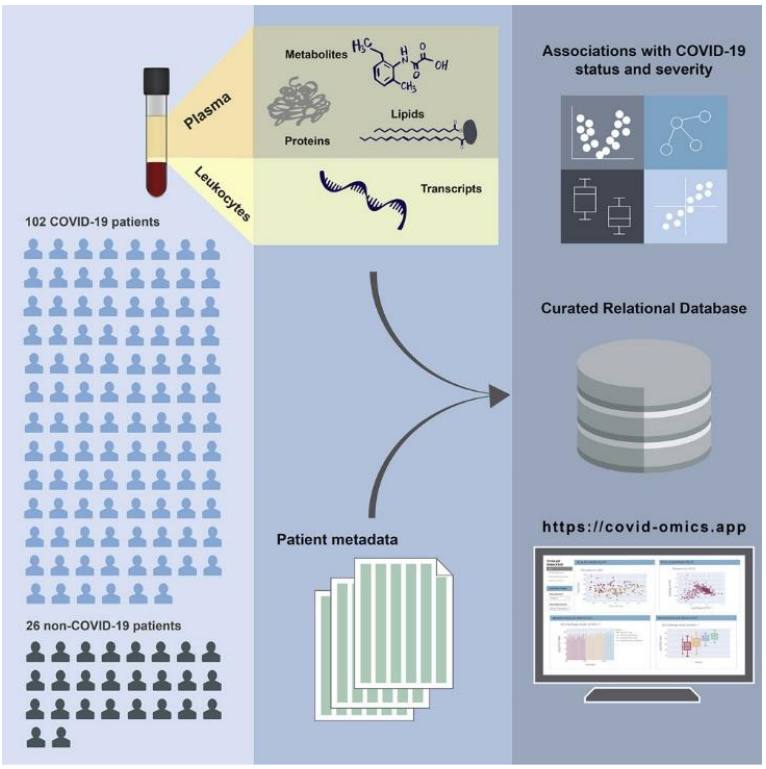
- We surveyed biomolecules in 102 COVID-19 and 26 non-COVID-19 patient blood samples
- We found 219 biomolecules strongly associated with COVID-19 status and severity
- We observed pronounced dysregulation of lipid transport and neutrophil degranulation

- Our resource of measurements and patient data is located at https://covid-omics.app

Summary

We performed RNA-Seq and high-resolution mass spectrometry on 128 blood samples from COVID-19 positive and negative patients with diverse disease severities and outcomes. Quantified transcripts, proteins, metabolites, and lipids were associated with clinical outcomes in a curated relational database, uniquely enabling systems analysis and cross-ome correlations to molecules and patient prognoses. We mapped 219 molecular features with high significance to COVID-19 status and severity, many involved in complement activation, dysregulated lipid transport, and neutrophil activation. We identified sets of covarying molecules, e.g., protein gelsolin and metabolite citrate or plasmalogens and apolipoproteins, offering pathophysiological insights and therapeutic suggestions. The observed dysregulation of platelet function, blood coagulation, acute phase response, and endotheliopathy further illuminated the unique COVID-19 phenotype. We present a web-based tool (covid-omics.app) enabling interactive exploration of our compendium and illustrate its utility through a machine learning approach for prediction of COVID-19 severity.

Graphical Abstract



17. 肾脏损伤分子-1 是 SARS-CoV-2 的潜在受体

Kidney injury molecule-1 is a potential receptor for SARS-CoV-2

来源：bioRxiv

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第一作者：Chen Yang

通讯作者：Kun Huang
通讯作者单位：华中科技大学
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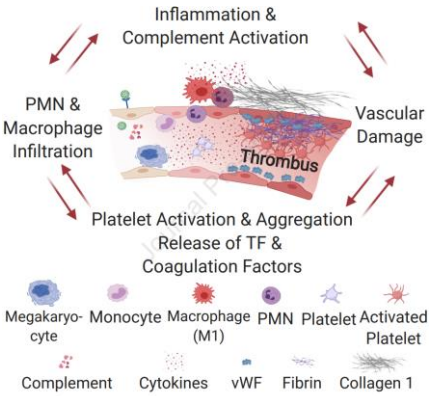
编译者：刘焕珍
中文摘要：
肾损伤分子-1（KIM1）是一种跨膜蛋白，在肾损伤后急剧上调。SARS-CoV-2-RBD 结合 KIM1 IgV 的亲和力高于 SARS-CoV-RBD 和 MERS-COV-RBD。KIM1 可能介导和加剧 SARS-CoV-2 感染。
Abstract:
Kidney injury molecule-1 (KIM1) is a transmembrane protein that drastically upregulated after renal injury. SARS-CoV-2-RBD binds KIM1 Ig V with a higher affinity than that of SARS-CoV-RBD and MERS-COV-RBD。KIM1 may mediate and exacerbate SARS-CoV-2 infection。

18. 感染 SARS-CoV-2 的恒河猴的血管疾病和血栓形成

Vascular Disease and Thrombosis in SARS-CoV-2 Infected Rhesus Macaques
来源：Cell
发布时间：2020-10-9
链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31311-8
第一作者：Malika Aid
通讯作者：Dan H. Barouch
通讯作者单位：Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center, Boston, MA02215, USA.
DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2020.10.005
编译者：宋张悦
中文摘要：
新冠肺炎大流行在世界范围内造成了广泛的发病率和死亡率。人类 SARS-CoV-2 发病机制的临床特征包括炎症和血栓形成，但这些过程背后的机制细节仍有待确定。在这项研究中，我们证实了感染 SARS-CoV-2 的人类和恒河猴的肺组织病理切片中的内皮破裂和血管血栓形成。为了确定与恒河猴 SARS-CoV-2 发病机制相关的关键分子通路，我们对支气管肺泡灌洗液(BAL)和外周血进行了转录组分析，并对血清进行了蛋白质组学分析。我们观察到在肺巨噬细胞浸润、巨噬细胞上调、补充、血小板活化、血栓形成和促炎分子标记物，包括 C 反应蛋白、MX1, IL-6, IL-1, IL-8, TNFα 和 NF-κB。这些结果提示了一个模型，其中炎症和血栓通路之间的关键相互作用导致了 SARS-CoV-2 诱导的血管疾病。我们的研究结果提示了 COVID-19 的潜在治疗靶点。



Abstract
The COVID-19 pandemic has led to extensive morbidity and mortality throughout the world. Clinical features that drive SARS-CoV-2 pathogenesis in humans include inflammation and thrombosis, but the mechanistic details underlying these processes remain to be determined. In this study, we demonstrate endothelial disruption and vascular thrombosis in histopathologic sections of lungs from both humans and rhesus macaques infected with SARS-CoV-2. To define key molecular pathways associated with SARS-CoV-2 pathogenesis in macaques, we performed transcriptomic analyses of bronchoalveolar lavage (BAL) and peripheral blood and proteomic analyses of serum. We observed macrophage infiltrates in lung and upregulation of macrophage, complement, platelet activation, thrombosis, and proinflammatory markers, including C-reactive protein, MX1, IL-6, IL-1, IL-8, TNFα, and NF-κB. These results suggest a model in which critical interactions between inflammatory and thrombosis pathways lead to SARS-CoV-2 induced vascular disease. Our findings suggest potential therapeutic targets for COVID-19.

19. COVID-19 宿主遗传学倡议

The covid-19 host genetics initiative

链接：https://www.covid19hg.org/

COVID-19 宿主遗传学倡议是一个自下而上的项目，主要有三个目标：

1)提供一个促进共享 COVID-19 宿主相关遗传研究资源的环境（比如实验方案，问卷）

2)组织跨研究的分析行动鉴定决定 COVID-19 易感性和症状严重层度的宿主遗传因子

3)提供一个可以共享这些合作结果以及个体水平数据的平台，以期惠于更广的科学团体

Overview

The COVID-19 pandemic is a global crisis creating severe disruptions across the economy and health system. Insights into how to better understand and treat COVID-19 are desperately needed. Given the importance and urgency in obtaining these insights, it is critical for the scientific community to come together around this shared purpose.

The COVID-19 host genetics initiative brings together the human genetics community to generate, share, and analyze data to learn the genetic determinants of COVID-19 susceptibility, severity, and outcomes. Such discoveries could help to generate hypotheses for drug repurposing, identify individuals at unusually high or low risk, and contribute to global knowledge of the biology of SARS-CoV-2 infection and disease.

Nothing is written in stone other than we must all act together and with no personal gain or ownership of results – just rapid and immediate dissemination of the maximum possible data and information that can be responsibly released.

Aims

The COVID-19 host genetics initiative is a bottom-up collaborative effort that has three main goals:

Provide an environment to foster the sharing of resources to facilitate COVID-19 host genetics research (e.g. protocols, questionnaires).

Organize analytical activities across studies to identify genetic determinants

of COVID-19 susceptibility and severity.
Provide a platform to share the results from such activities, as well as the individual-level data where possible, to benefit the broader scientific community.

20. 新冠肺炎后的持续性症状:对 114 名长期新冠患者的定性研究和服务质量的标准草案

Persistent symptoms after Covid-19: qualitative study of 114 long Covid patients and draft quality criteria for services
来源：medRxiv
发布时间： 2020-10-14
链接：https://www.medrxiv.org/content/10.1101/2020.10.13.20211854v1
第一作者：Emma Ladds
通讯作者：Trisha Greenhalgh
通讯作者单位：Nuffield Department of Primary Care Health Sciences, University of Oxford
DOI 或 PUBMED ID：preprint
编译者：孔娟
摘要：
背景:大约 10%的新冠肺炎病患者经历 3-4 周以上的症状。患者称之为“长 Covid”。研究者试图记录这些病人的生活经历,他们获得和接受医疗保健的情况,以及他们改善服务的想法。
方法：研究者进行了 55 次个人采访和 8 个焦点小组(n = 59)，这些人是从英国的长期 Covid 患者支持小组、社交媒体和滚雪球招募的。我们将一些焦点小组限制在卫生专业人员，因为他们已经自我组织成在线社区。参与者被邀请讲述他们的个人故事和评论他人的故事。使用 NVIVO 对数据进行录音、转录、匿名和编码。分析纳入了疾病、治疗、同伴支持、临床关系、获得护理和服务重新设计的社会学理论。
结果：样本为 70%的女性，年龄在 27-73 岁之间，包括英国白人（74%），亚洲人（11%），其他白人（7%），黑人（4%）和混合（4%）。 27 名医生和 23 名其他卫生专业人员。 10%已住院。分析显示这是一种令人困惑的疾病,具有多种多样且经常复发的症状且预后不确定。严重的失落感和耻辱感；难以访问和进行导向服务；具有被难以认真对待和诊断的困难；脱节和孤立的护理（包括无法获得专业服务）；服务标准的差异（例如看病，调查和转诊患者的标准不一致）;治疗关系的质量参差不齐（一些参与者感到很好的支持，而另一些参与者则感到“烦恼”）；以及可能的严重事件（例如，无法访问服务而导致的恶化）。参与者的情感接触点经验有助于改善服务。
结论：长期提供 Covid 服务的质量原则应包括确保获得护理，减轻疾病负担，承担临床责任和提供护理的连续性，多学科康复，循证调查和管理以及知识库和临床服务的进一步发展。
结论:长期 Covid 服务的质量原则应包括确保获得护理、减轻疾病负担、承担临床责任和提供护理连续性、多学科康复、循证调查和管理以及进一步发展知识库和临床服务。
Abstract
Background： Approximately 10% of patients with Covid-19 experience symptoms beyond 3-4 weeks. Patients call this “long Covid”. We sought to document the lived experience of such patients, their accounts of accessing and receiving healthcare, and their ideas for improving services.
Method： We held 55 individual interviews and 8 focus groups (n = 59) with people recruited from UK-based long Covid patient support groups, social media and snowballing. We restricted some focus groups to health professionals since

they had already self-organised into online communities. Participants were invited to tell their personal stories and comment on others' stories. Data were audiotaped, transcribed, anonymised and coded using NVIVO. Analysis incorporated sociological theories of illness, healing, peer support, the clinical relationship, access to care, and service redesign.
Results: The sample was 70% female, aged 27-73 years, and comprised White British (74%), Asian (11%), White Other (7%), Black (4%), and Mixed (4%). 27 were doctors and 23 other health professionals. 10% had been hospitalised. Analysis revealed a confusing illness with many, varied and often relapsing-remitting symptoms and uncertain prognosis; a heavy sense of loss and stigma; difficulty accessing and navigating services; difficulty being taken seriously and achieving a diagnosis; disjointed and siloed care (including inability to access specialist services); variation in standards (e.g. inconsistent criteria for seeing, investigating and referring patients); variable quality of the therapeutic relationship (some participants felt well supported while others felt "fobbed off"); and possible critical events (e.g. deterioration after being unable to access services). Emotional touch points in participants' experiences informed ideas for improving services.
Conclusion: Quality principles for a long Covid service should include ensuring access to care, reducing burden of illness, taking clinical responsibility and providing continuity of care, multidisciplinary rehabilitation, evidence-based investigation and management, and further development of the knowledge base and clinical services.

21. 中国正式加入 COVAX：发言人

China officially joins COVAX: spokesperson
来源：新华网
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链接：http://www.xinhuanet.com/english/2020-10/09/c_139427617.htm
第一作者：huaxia 编辑
通讯作者：huaxia
通讯作者单位：新华网
DOI 或 PUBMED ID：
编译者：张丽双
中文摘要：
10 月 8 日，中国与全球疫苗免疫联盟签署协议，正式加入"新冠疫苗实施计划"（COVAX）。这是中国秉持人类卫生健康共同体理念、履行自身承诺推动疫苗成为全球公共产品的一个重要举措。
目前，COVID-19 大流行仍然对各国人民的安全和健康构成严重威胁。中国继续致力于确保发展中国家平等获得适当、安全和有效的疫苗。
外交部发言人华春莹表示："尽管中国多支疫苗研发处于国际领先水平并具备充足的生产能力，但中国还是决定加入该计划，目的就是以实际行动确保疫苗的公平分配，特别是向发展中国家，并希望有能力的国家也加入并支持 COVAX。"中国还将通过 COVAX 网络加强与相关国家的疫苗合作。

华春莹说，中国将继续与 COVAX 合作伙伴一道，为全球抗击疫情的斗争贡献自己的一份力量，以保障全人类的安全和健康。

Abstract:

BEIJING, Oct. 9 (Xinhua) -- China Thursday signed an agreement with Gavi, the Vaccine Alliance, officially joining COVAX, Foreign Ministry spokesperson Hua Chunying said Friday.

This is an important step China has taken to uphold the concept of a shared community of health for all and to honor its commitment of turning COVID-19 vaccines into a global public good, Hua said in a statement released on the Foreign Ministry's website.

Currently, the COVID-19 pandemic still poses a severe threat to the safety and health of people in all countries. China continues to focus on ensuring that developing countries have equal access to appropriate, safe and effective vaccines.

"To that end, we have solemnly pledged to make vaccines developed and deployed by China a global public good, which will be provided to developing countries as a priority," Hua said.

China has maintained close communication with COVAX with a positive attitude towards joining it, Hua said, noting that even when China is leading the world with several vaccines in advanced stages of R&D and with ample production capacity, it still decided to join COVAX.

"We are taking this concrete step to ensure equitable distribution of vaccines, especially to developing countries, and hope more capable countries will also join and support COVAX. China will also strengthen vaccine cooperation with relevant countries through the COVAX network," said the spokesperson.

China will continue to work together with COVAX partners and contribute its share to the global fight against the pandemic to safeguard all human beings' safety and health, Hua said.