新型冠状病毒信息简报

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上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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1. 2020 年 4 月 22 日疫情

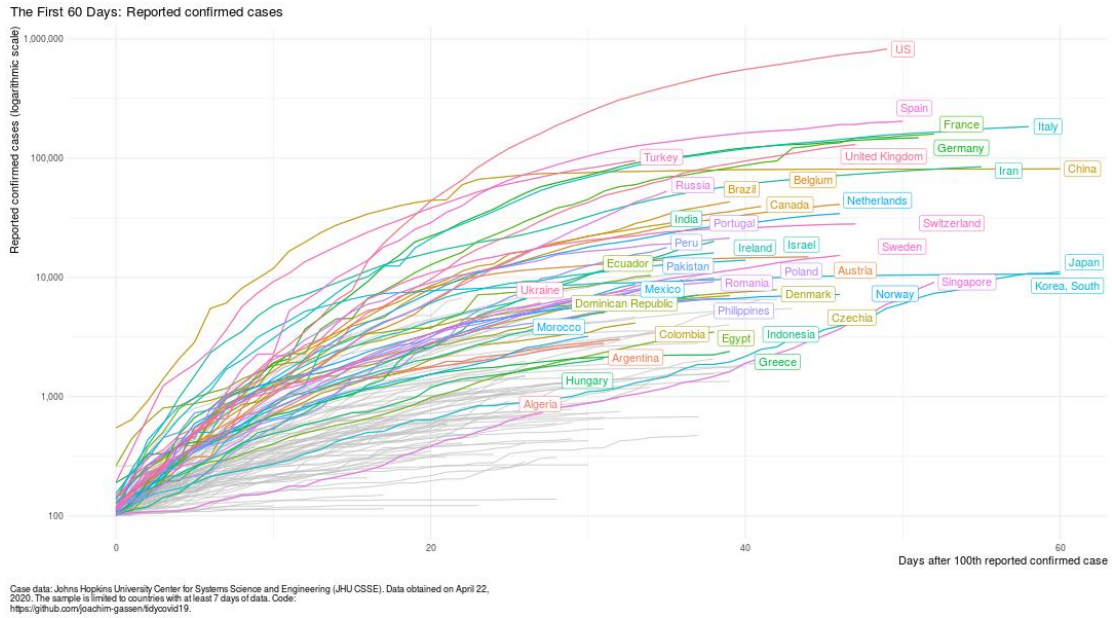
数据来源：WHO

发布时间：2020 年 4 月 22 日北京时间下午 4 点

链接：https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

根据 WHO 提供的数据，2020 年 4 月 22 日全球累计确诊新型冠状病毒病人 2471136 例，当日新增确诊 73920 例，累计死亡 169006 例，当日新增死亡 6058。

中国累计确诊 84287 例，累计死亡 4642 例，当日新增确诊 37 例，新增死亡 0 例。



重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止 4 月 22 日北京时间下午 4 点）

全国新型冠状病毒肺炎新增确诊病例分布图（4 月 22 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. SARS-CoV-2 病毒在通风不良的餐厅中可能会通过气溶胶传播的证据—计算机模拟复原

Evidence for probable aerosol transmission of SARS-CoV-2 in a poorly ventilated restaurant

来源：medRxiv
发布时间：2020-04-22
链接：https://www.medrxiv.org/content/10.1101/2020.04.16.20067728v1

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中文摘要：

背景：SARS-CoV-2 病毒能否通过气溶胶传播仍存在争议。作者对在中国广州 X 餐厅用餐后，相继确诊 COVID-19 的 3 个无关联家庭的情况进行了分析。评估了 SARS-CoV-2 病毒通过气溶胶传播的可能性，并研究了相关的环境条件。

方法：作者收集了流行病学数据，餐厅的监控录像和餐厅内患者的就坐位置，并使用温暖示踪气体代替疑似患者呼出的飞沫，测量气体的分布。通过计算机模拟，得到呼出的细小液滴的扩散情况。最后，作者将随后确诊的感染病例在室内的位置与计算机模拟的载有病毒的气溶胶示踪气体的传播轨迹进行了比较。室内通气率使用示踪气体衰减法测量。

结果：3 个家庭（A，B，C）的 10 名成员于除夕当天（2020 年 1 月 24 日）在 X 餐厅中临近的三张餐桌吃过午饭，随后均被确诊。其中或有人早已被感染 SARS-CoV-2，其他人可能在此时被感染。随后，B 家庭的三名成员和 C 家庭的两名成员被感染，而其余 15 桌的 68 位顾客和服务员均未被感染。此时的通气率为每人 0.75-1.04 L/s。除部分顾客背靠背入座外，没有发现密切接触或污染物接触。结果表明，呼出的载有病毒的气溶胶传播方式与被感染者的位置分布一致。

结论：由通风不良导致的 SARS-CoV-2 通过气溶胶传播，可能是 COVID-19 在社区的传播途径。

Abstract:

Background: The role of aerosols in the transmission of SARS-CoV-2 remains debated. We analyzed an outbreak involving three non-associated families in Restaurant X in Guangzhou, China, and assessed the possibility of aerosol transmission of SARS-CoV-2 and characterize the associated environmental conditions.

Methods: We collected epidemiological data, obtained a video record and a patron seating-arrangement from the restaurant, and measured the dispersion of a warm tracer gas as a surrogate for exhaled droplets from the suspected index patient. Computer simulations were performed to simulate the spread of fine exhaled droplets. We compared the in-room location of subsequently infected cases and spread of the simulated virus-laden aerosol tracer. The ventilation rate was measured using the tracer decay method.

Results: Three families (A, B, C), 10 members of which were subsequently found to have been infected with SARS-CoV-2 at this time, or previously, ate lunch at Restaurant X on Chinese New Year's Eve (January 24, 2020) at three neighboring tables. Subsequently, three members of family B and two members of family C

became infected with SARS-CoV-2, whereas none of the waiters or 68 patrons at the remaining 15 tables became infected. During this occasion, the ventilation rate was 0.75-1.04 L/s per person. No close contact or fomite contact was observed, aside from back-to-back sitting by some patrons. Our results show that the infection distribution is consistent with a spread pattern representative of exhaled virus-laden aerosols.

Conclusions: Aerosol transmission of SARS-CoV-2 due to poor ventilation may explain the community spread of COVID-19.

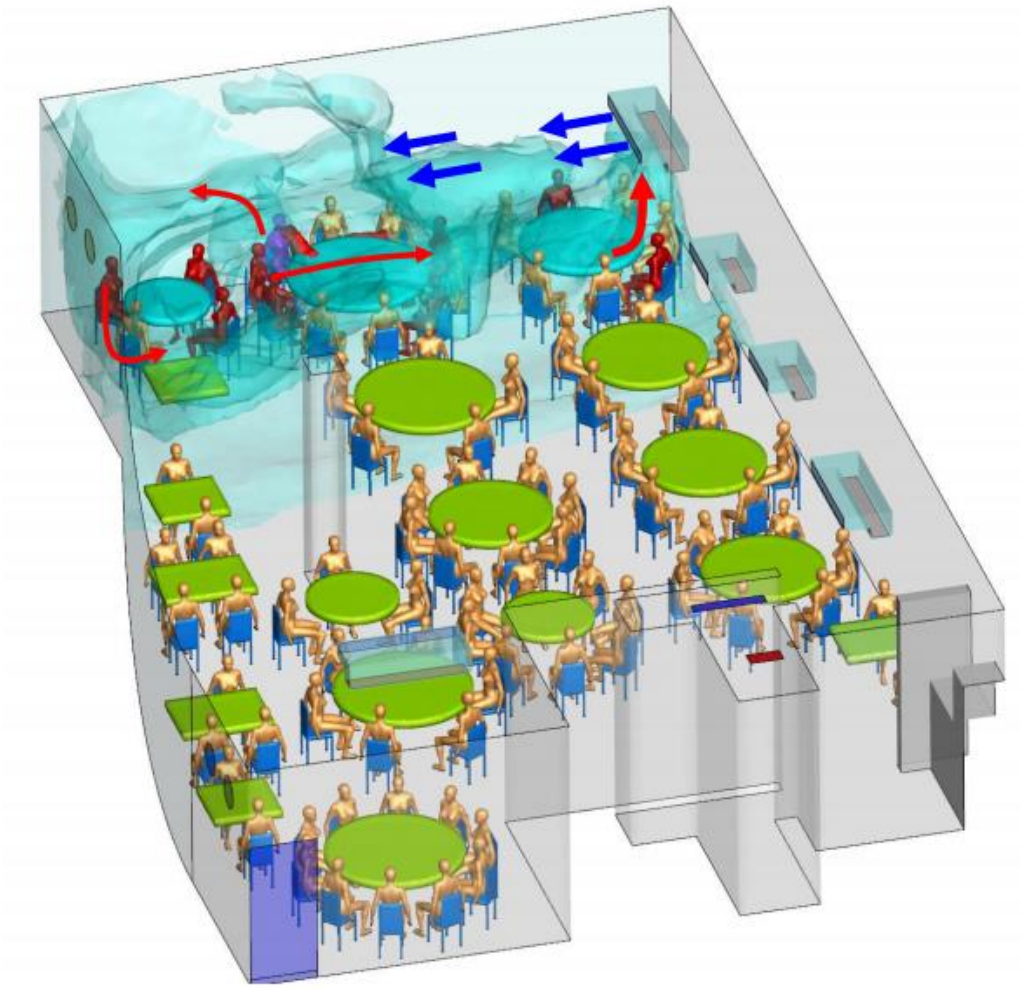

Figure 3. Simulated dispersion of fine droplets exhaled from index Patient A1 (magenta-blue), which are initially confined within the cloud envelope due to the zoned air-conditioning arrangement. The fine droplets eventually disperse into the other zones via air exchange and are eventually removed via the restroom exhaust fan. The ABC zone clearly has a higher concentration of fine droplets than the non-ABC zone. Other infected patients are shown in red and other non-infected in gold color. Only a single human body is used to represent all patrons.

3. 对于 COVID-19 患者的 SARS-CoV-2 检测，唾液比鼻咽拭子更灵敏

Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs

来源：medRxiv
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DOI：Preprint
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中文摘要：
快速、准确的 SARS-CoV-2 诊断检测对控制目前流行的 COVID-19 至关重要。目前诊断 COVID-19 的金标准是从鼻咽拭子中实时 RT-PCR 检测 SARS-CoV-2。然而，低敏感度、医护人员的暴露风险以及全球拭子和个人防护设备的短缺，需要验证新的诊断方法。唾液是 SARS-CoV-2 诊断的一个有前途的候选者，美国罗格斯大学(Rutgers University)开发的第一个基于唾液的新的 SARS-CoV-2 检测方法于 4 月 14 日获得 FDA 的紧急使用授权（4 月 15 日简报中有提到）。因为（1）唾液收集是几乎无创的，并且可以可靠地自己收集；（2）在此前的研究中，唾液在检测其他呼吸道病原体方面也表现出与鼻咽拭子相当的敏感性。为了验证唾液在 SARS-CoV-2 检测中的应用，作者对确诊的 COVID-19 患者的鼻咽和唾液样本以及 COVID-19 病房医护人员的自取样本进行了检测。比较鼻咽和唾液样本中 SARS-CoV-2 的检测结果，发现唾液在整个感染过程中具有更高的检测灵敏度和一致性。此外，自行采集的唾液样本的变异性较小。综上所述，这项研究结果表明，唾液是一种可行的、更敏感的鼻咽拭子替代品，可以在家自行采集样本，用于精确的大规模 SARS-CoV-2 检测。

Abstract:
Rapid and accurate SARS-CoV-2 diagnostic testing is essential for controlling the ongoing COVID-19 pandemic. The current gold standard for COVID-19 diagnosis is real-time RT-PCR detection of SARS-CoV-2 from nasopharyngeal swabs. Low sensitivity, exposure risks to healthcare workers, and global shortages of swabs and personal protective equipment, however, necessitate the validation of new diagnostic approaches. Saliva is a promising candidate for SARS-CoV-2 diagnostics because (1) collection is minimally invasive and can reliably be self-administered and (2) saliva has exhibited comparable sensitivity to nasopharyngeal swabs in detection of other respiratory pathogens, including endemic human coronaviruses, in previous studies. To validate the use of saliva for SARS-CoV-2 detection, we tested nasopharyngeal and saliva samples from confirmed COVID-19 patients and self-collected samples from healthcare workers on COVID-19 wards. When we compared SARS-CoV-2 detection from patient-matched nasopharyngeal and saliva samples, we found that saliva yielded greater detection sensitivity and consistency throughout the course of infection. Furthermore, we report less variability in self-sample collection of saliva. Taken together, our findings demonstrate that saliva is a viable and more sensitive alternative to nasopharyngeal swabs and could enable at-home self-administered sample collection for accurate large-scale SARS-CoV-2 testing.

4. 质谱法检测 COVID-19 患者漱口水中的 SARS-CoV-2 蛋白

Mass Spectrometric Identification of SARS-CoV-2 Proteins from Gargle Solution Samples of COVID-19 Patients

来源：bioRxiv

发布时间:2020-04-19

通讯作者：Andrea Sinz

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链接：https://www.biorxiv.org/content/10.1101/2020.04.18.047878v1

编译：朱微

中文摘要：

质谱检测可以为 COVID-19 疾病的诊断提供有用信息。本文作者发展了一种基于质谱的简单方法，来检测 COVID-19 患者漱口水中的 SARS-CoV-2 蛋白。操作流程包括：丙酮沉淀法从漱口水中提取 SARS-CoV-2 的相关蛋白、胰蛋白酶消化蛋白以及靶向质谱分析；这种方法可以检测到 SARS-CoV-2 核蛋白的特征肽段。基于这些结果，可以发展更快的质谱检测方法，从而作为 COVID-19 患者的检测工具。

Abstract

Mass spectrometry (MS) can deliver valuable diagnostic data that complements genomic information and allows us to increase our current knowledge of the COVID-19 disease caused by the SARS-CoV-2 virus. We developed a simple, MS-based method to specifically detect SARS-CoV-2 proteins from gargle solution samples of COVID-19 patients. Our protocol consists of an acetone precipitation and tryptic digestion of proteins contained within the gargle solution, followed by a targeted MS analysis. Our methodology identifies unique peptides originating from SARS-CoV-2 nucleoprotein. Building on these promising initial results, faster MS protocols can now be developed as routine diagnostic tools for COVID-19 patients.

5. COVID-19 患者及健康者血液中 SARS-CoV-2 S 蛋白反应性 CD4+ T 细胞相关研究

Presence of SARS-CoV-2 reactive T cells in COVID-19 patients and healthy donors

来源：medRxiv

发布时间：2020-04-17

链接：https://www.medrxiv.org/content/10.1101/2020.04.17.20061440v1

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DOI：Preprint

编译者：孔娟

中文摘要：

SARS-CoV-2 已经引起了一场迅速蔓延的大流行，目前针对 SARS-CoV-2 的宿主免疫反应在病毒清除中的作用及其在发病机制中的作用仍然未知，相关的细胞免疫应答尚未被深入研究。研究者检测了在 COVID-19 患者与 SARS-CoV-2 血清阴性健康献血者相比，SARS-CoV-2 的 S 蛋白反应性 T 细胞的存在、频率和表型特征。

文中研究者描述了一种能够直接检测和表征外周血中 SARS-CoV-2 的 S 蛋白反应性 CD4+T 细胞的分析方法。研究中纳入了 68 例健康者血清及 18 例患者血清，结果显示在 83%的 COVID-19 患者和 34%的 SARS-CoV-2 血清阴性健康者中存在 S 反应性 CD4+T 细胞。值得注意的是在 COVID-19 患者中,S-反应性 CD4+T 细胞对 S 蛋白的 N-末端和 C-末端均有结合，而健康者 S-反应性 CD4+T 细胞几乎只靶向 S 蛋白 C-末端。S 蛋白 C 端其特征有：a）与“普通感冒”冠状病毒的 S 糖蛋白具有较高的同源性；b)含有 S 的 S2 亚单位，其具有细胞质肽(CP)、融合肽(FP)和跨膜域(TM)，但不具有受体结合域(RBD)。进一步研究发现与健康者 CD4+T 细胞不同的是 S-反应性 CD4+T 细胞中具有 CD38 和 HLA-DR 高表达的特征，这表明它们在体内被激活。

本研究中对 SARS-CoV-2 反应性 T 细胞的相关研究，为大规模检测和表征 SARS-CoV-2 的潜在交叉反应性细胞免疫提供了重要工具。

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a rapidly unfolding pandemic, overwhelming health care systems worldwide1. Clinical manifestations of Corona-virus-disease 2019 (COVID-19) vary broadly, ranging from asymptomatic infection to acute respiratory failure and death2, yet the underlying physiological conditions and mechanisms for this high variability are still unknown. Also, the role of host immune responses in viral clearance and its involvement in pathogenesis remains unresolved. For SARS-CoV (2002/03), however, CD4+ T cell responses are generally associated with positive outcomes3,4, while cellular immune responses to SARS-CoV-2 have not yet been investigated. Here we describe an assay that allows direct detection and characterization of SARS-CoV-2 spike glycoprotein (S)-reactive CD4+ T cells in peripheral blood. We demonstrate the presence of S-reactive CD4+ T cells in 83% of COVID-19 patients, as well as in 34% of SARS-CoV-2 seronegative healthy donors, albeit at lower frequencies. Strikingly, in COVID-19 patients S-reactive CD4+ T cells equally targeted both N-terminal and C-terminal parts of S whereas in healthy donors S-reactive CD4+ T cells reacted almost exclusively to the C terminal part that is a) characterized by higher homology to spike glycoprotein of human endemic "common cold" coronaviruses, and b) contains the S2 subunit of S with the cytoplasmic peptide (CP), the fusion peptide (FP), and the transmembrane domain (TM) but not the receptor-binding domain (RBD). S-reactive CD4+ T cells from COVID-19 patients were further distinct to those from healthy donors as they co-expressed higher levels of CD38 and HLA-DR, indicating their recent in vivo activation. Our study is the first to directly measure SARS-CoV-2-reactive T cell responses providing critical tools for large scale testing, in depth epitope mapping and characterization of potential cross-reactive cellular immunity to SARS-CoV-2. The presence of pre-existing SARS-CoV-2-reactive T cells in healthy donors is of high interest but larger scale prospective cohort studies are needed to assess whether their presence is a correlate of protection or pathology. Results of such studies will be key for a mechanistic understanding of the SARS-CoV-2 pandemic, adaptation of containment methods and to support vaccine development.

6. 来自意大利北部的大量 COVID-19 病例的肺的尸检结果

Pulmonary post-mortem findings in a large series of COVID-19 cases from Northern Italy

来源：medRxiv

发布时间：2020-04-22

链接：https://www.medrxiv.org/content/10.1101/2020.04.19.20054262v1

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DOI：preprint

编译者：宋张悦

中文摘要：

重要性：对 COVID-19 患者肺组织的分析可能有助于理解这种危及生命的呼吸系统疾病的发病机制和临床结局。

目的：探讨重度 COVID-19 患者肺组织的组织学形态。

设计和参与者：本研究是基于 2 月至 3 月间，对意大利北部两所医院（Luigi Sacco 和 Papa Giovanni XXIII 医院）的 38 例 COVID-19 死亡患者的肺组织进行了系统分析。每个肺样本取 7 个组织块(范围 5-9)，肉眼选择最具代表性的区域。将组织固定在 10%福尔马林液中 48 小时。对样本进行苏木精-伊红（HE）染色、免疫组化检查炎性浸润和细胞成分。选择病例的其他样本固定在戊二醛中，电镜观察，并使用 EM-109 ZEISS 和 CCD-Megaview G2 (I-TEM 成像平台软件)进行检查。

结果：取样死亡病例中，男性 33 例，女性 5 例，平均年龄 69 岁(32-86 岁)，患者在亚加/重症监护病房的时间从 1 天到 23 天不等(6.87 天)，患者在出现症状到死亡的中位时间为 16.27 天(5-31 天)。发现弥漫性肺泡病（DAD）渗出期和增殖期特征有：毛细血管充血、肺细胞坏死、透明膜、间质水肿、肺细胞增生和反应性异型性、血小板纤维蛋白血栓。炎性浸润主要由肺泡腔内的巨噬细胞和间质内的淋巴细胞组成。电镜显示肺细胞胞质空泡内有病毒颗粒。

结论和意义：COVID-19 患者肺部病变的主要类型为弥漫性肺泡病（DAD），正如另外两种感染人类的冠状病毒 SARS-CoV 和 MERS-CoV 所描述的那样。肺透明膜的形成和肺细胞的不典型增生是常见的。相关的主要发现是血小板纤维蛋白血栓存在于小动脉血管中：这一重要的观察结果符合凝血障碍病的临床背景，凝血障碍病在这些患者中占主导地位，也是治疗的主要目标之一。

Abstract:

Importance. The analysis of lung tissues of patients with COVID-19 may help understand pathogenesis and clinical outcomes in this life-threatening respiratory illness. Objective. To determine the histological patterns in lung tissue of patients with severe COVID-19. Design and participants. Lungs tissues of 38 cases who died for COVID-19 in two hospital of Northern Italy were systematically analysed. Hematoxylin-eosin staining, immunohistochemistry for the inflammatory infiltrate and cellular components, electron microscopy were performed. Results. The features of the exudative and proliferative phases of Diffuse Alveolar Disease (DAD) were found: capillary congestion, necrosis of pneumocytes, hyaline membrane, interstitial oedema, pneumocyte hyperplasia and

reactive atypia, platelet-fibrin thrombi. The inflammatory infiltrate was composed by macrophages in alveolar lumens and lymphocytes mainly in the interstitium. Electron microscopy revealed viral particles within cytoplasmic vacuoles of pneumocytes. Conclusions and relevance. The predominant pattern of lung lesions in COVID-19 patients is DAD, as described for the other two coronavirus that infect humans, SARS-CoV and MERS-CoV. Hyaline membrane formation and pneumocyte atypical hyperplasia are frequently found. The main relevant finding is the presence of platelet-fibrin thrombi in small arterial vessels; this important observation fits into the clinical context of coagulopathy which dominates in these patients and which is one of the main targets of therapy.

7. 胆固醇代谢对 SARS-CoV-2 感染预后、进入和抗病毒治疗的影响

Cholesterol Metabolism--Impact for SARS-CoV-2 Infection Prognosis, Entry, and Antiviral Therapies

来源：medRxiv

发布时间：2020-04-16

链接：https://www.medrxiv.org/content/10.1101/2020.04.16.20068528v1

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DOI 或 PUBMED ID：Preprint

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中文摘要：

最近出现的致病性 SARS 冠状病毒 2（SARS-CoV-2）迅速传播，导致全球范围内的大流行。因此,迫切需要确定 SARS-CoV-2 感染的发病率和细胞协同受体的危险因素。在这项研究中，作者对 861 例 COVID-19 患者进行了回顾性研究，这些患者来自一个单一中心分为轻度、中度、重度或严重，发现 SARS-CoV-2 感染与临床显著降低胆固醇水平相关。TC(血清总胆固醇)和 HDL（高密度脂蛋白）水平与 SARS-CoV-2 感染严重程度呈负相关。此外，在重症患者中，血清 HDL 水平的显著升高与良好的预后相关。作者还发现一种临床认可的 HDLR 拮抗剂可以抑制 SARS-CoV-2 假病毒感染。值得注意的是，SARS-2-S 与胆固醇有关。这些研究结果不仅确定了 HDL 水平作为 SARS-CoV-2 感染的预后指标，而且还表明了抗病毒干预的潜在靶点。

Abstract:

The recently emerged pathogenic SARS-coronavirus 2 (SARS-CoV-2) has spread rapidly, leading to a global pandemic. Identification of risk factors for morbidity and cellular coreceptors for SARS-CoV-2 entry is thus urgently needed. In this study, we performed a retrospective study involving 861 patients with COVID-19 from a single-center classified as mild, moderate, severe or critical and found that SARS-CoV-2 infection was associated with clinically significant lower levels of cholesterol. The levels of both TC and HDL were inversely associated with the severity of SARS-CoV-2 infection. In addition, in patients with severe disease, a significant increase in the serum HDL level was correlated with good outcomes. We also showed that a clinically approved HDLR antagonist inhibited SARS-CoV-2 pseudovirus infection. Notably, SARS-2-S bound to

cholesterol. Our results not only identify the HDL level as a prognostic marker for SARS-CoV-2 infection but also indicate a potential target for antiviral intervention.

8. 数百人自愿感染冠状病毒

Hundreds of people volunteer to be infected with coronavirus

来源：nature

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第一作者：Ewen Callaway

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通讯作者单位：

DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

对一项有争议的“人类挑战”疫苗研究的支持与日俱增，但目前还没有试验计划。

通过将冠状病毒感染健康的年轻志愿者，加速冠状病毒疫苗研发的计划正在形成。据统计，这项有争议的方法已经吸引了近 1500 名潜在的志愿者参与，即人类挑战试验。

这项被称为“提前 1 天”的计划，与开发或资助冠状病毒疫苗的团体或公司无关。但联合创始人 Josh Morrison 表明，人类挑战试验得到广泛支持，这种试验有可能比标准试验更快地提供有效的冠状病毒疫苗。

经典的疫苗试验需要很长时间，因为成千上万的人接受疫苗或安慰剂，研究人员跟踪谁在日常生活中受到了感染。这项挑战性的研究在理论上可能要快得多：一个数量少得多的志愿者小组将接受候选疫苗，然后故意感染病毒，以判断免疫效果。

“我们希望招募尽可能多的人来做这件事，如果他们有可能参加挑战性试验，我们会对他们进行资格预审。” Morrison 说。新泽西州新不伦瑞克罗格斯大学的生物伦理学家 Nir Eyal 领导的一个研究小组在上个月的传染病杂志中提到，人类挑战试验可以安全、合乎道德地进行。这种做法也获得了一些政治支持。本周， 35 名美国国会议员呼吁卫生和公共服务部考虑冠状病毒疫苗的人体挑战试验。Wellcome 疫苗项目负责人，伦敦生物医学研究资助者 Charlie Weller 说，该慈善机构已经开始讨论冠状病毒疫苗人类挑战试验的伦理和后勤问题。但她同时提到，目前还不清楚这样的试验是否真的能加快疫苗的研发。研究人员首先需要确定如何使人类尽可能安全地接触病毒，并考虑如何甚至是否可以从伦理角度进行此类研究。“我认为这是有潜力的，” Weller 补充道，“但我们还有很多问题要解决，以了解它是否能在一定时间内发挥作用。”

Abstract:

Support grows for a controversial ‘human challenge’ vaccine study — but no trial is yet planned.

Momentum is building to speed the development of coronavirus vaccines by intentionally infecting healthy, young volunteers with the virus. A grass-roots effort has attracted nearly 1,500 potential volunteers for the controversial approach, known as a human-challenge trial.

The effort, called 1Day Sooner, is not affiliated with groups or companies developing or funding coronavirus vaccines. But co-founder Josh Morrison hopes to show that there is broad support for human-challenge trials, which have the potential to deliver an effective coronavirus vaccine more quickly than standard trials.

Typical vaccine trials take a long time because thousands of people receive either a vaccine or a placebo, and researchers track who becomes infected in the course of their daily lives. A challenge study could in theory be much faster: a much smaller group of volunteers would receive a candidate vaccine and then be intentionally infected with the virus, to judge the efficacy of the immunization.

“We want to recruit as many people as possible who want to do this, and pre-qualify them as likely to be able to participate in challenge trials should they occur,” says Morrison, who is also the executive director of organ-donation advocacy group Waitlist Zero. “At the same time, we feel that the public policy decisions around challenge trials will be better informed if they highlight the voice of people interested in participating in such trials.”

Morrison says that the people who have signed up to be part of a challenge trial tend to be young and live in urban areas, and are highly motivated to do something constructive to address the coronavirus pandemic. “Many note that they recognize the risk but believe the benefits of vaccine acceleration are so tremendous that it is worth it to them,” he says.

Challenge studies have been conducted before for diseases including influenza and malaria. A team led by bioethicist Nir Eyal at Rutgers University in New Brunswick, New Jersey, argued that a human challenge trial could be conducted safely and ethically, in a paper in The Journal of Infectious Diseases last month.

The approach is also gaining some political support. This week, 35 members of the US Congress, led by Bill Foster (Democrat, Illinois) and Donna Shalala (Democrat, Florida), called on Department of Health and Human Services director Alex Azar to consider human-challenge trials of coronavirus vaccines.

Charlie Weller, head of the vaccines programme at Wellcome, a biomedical-research funder in London, says the charity has begun discussing the ethics and logistics of a human-challenge trial for a coronavirus vaccine. But she says it is unclear whether such a trial could actually speed vaccine development. Researchers first need to determine how to expose humans to the virus as safely as possible, and to consider how and even whether such studies can be done ethically. “I think there’s potential,” Weller adds, “but we’ve got so many questions to work through to understand whether it can help in the timelines we have.”

9. 利用 IL-6 阻断治疗重症 COVID-19

Interleukin-6 blockade for severe COVID-19

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DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：
在 COVID-19 大流行和全球医疗设施日益紧张的背景下，迫切需要有效的治疗，以减少 ICU 病床的紧张。这篇文章利用 IL6 受体阻断剂托珠单抗治疗重症高炎性的 COVID-19 患者，并对临床经验进行了总结。实验组 30 名患者年龄小于 80 岁，入组条件：发病至少 5 天、重症（必须超过 6L/min 的氧气治疗）且迅速恶化（过去 12 小时内氧气流量增加超过 3L/min）的 COVID-19 相关肺炎患者。通过与未接受托珠单抗的对照组患者（使用逆概率处理加权法匹配年龄、性别和疾病严重程度）的比较，发现在这 30 位高度筛选的患者中，IL6 阻断可以抑制“细胞因子风暴”，减少 ICU 入院和机械通气的需要。尽管这项回顾性小样本研究存在缺陷，但相信这些初步发现支持了在对抗 COVID-19 诱导的炎症方面所做的努力，特别是在患者需要进入 ICU 之前。

Abstract:
In the context of COVID-19 pandemic and growing tensions worldwide regarding healthcare facilities, there is an urgent need for effective treatments likely to reduce the crunch of ICU beds. Following the assumption by Mehta and colleagues who exhorted physicians to screen patients with severe COVID-19 for hyperinflammation and investigate immunomodulatory drugs in this setting, we relate our short-term - yet promising - experience regarding IL6 blockade with tocilizumab in 30 selected patients of less than 80 years of age, >5 days of prior disease duration, severe (i.e. requiring strictly over 6L/min of oxygen therapy) rapidly deteriorating (i.e. increase by more than 3L/min of oxygen flow within the previous 12 hours) COVID-19-related pneumonia. By comparison with a control group of patients (matched for age, gender and disease severity using the inverse probability of treatment weighted methodology) that did not receive tocilizumab. We demonstrate that, in highly selected patients, IL6 blockade could curb the ″cytokine storm″, prevent ICU admission and the requirement for mechanical ventilation. Notwithstanding the shortcomings of this retrospective small sample-size study, we believe that these preliminary findings support the fostering of research efforts in the fight against COVID-19-induced inflammation, especially before patients require admission to the ICU.

10. 与年龄相关的 COVID－19 恒河猴模型

Age－related rhesus macaque models of COVID－19

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编译者：宋张悦
中文摘要：
背景：自 2019 年 12 月以来，由严重急性呼吸综合征冠状病毒（SARS-CoV-2）引起的 2019 年冠状病毒病(COVID－19)已成为国际关注的突发公共卫生大事件。由 SARS－CoV－2 引起的老年病例的高致死率需要用非人类灵长类动物模型来探索可能的与年龄相关的现象。
方法：选取 3 只 3-5 岁的幼年恒河猴和 2 只 15 岁的老年恒河猴在气管内感染 SARS-CoV-2，然后通过临床体征、病毒复制、胸透、组织病理学变化和免疫反应进行分析。本研究中使用的 SARS-CoV-2 病毒株（命名为：HB-01）由中国 CDC 的谭教授提供，它的完整基因组已经被放入 GISAID (BetaCoV/Wuhan/IVDC-HB-01/2020|EPI_ISL_402119)。
结果：在 SARS-CoV-2 接种后的 14 天内，老年猴的鼻咽拭子、肛门拭子和肺的病毒复制较幼年猴更为活跃。猴子出现了典型的间质性肺炎，表现为肺泡隔增厚，并伴有炎症和水肿，值得注意的是，老年猴表现出弥漫性严重间质性肺炎。病毒抗原主要在肺泡上皮细胞和巨噬细胞中进行检测。
结论：SARS-CoV-2 在老年猴中引起的间质性肺炎较幼年猴严重。感染 SARS-CoV-2 的恒河猴模型为深入了解致病机制提供了信息，并促进了 SARS-CoV-2 感染的疫苗和治疗方法的开发。
Abstract:
Background Since December 2019, an outbreak of the Corona Virus disease 2019 (COVID－19) caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) in Wuhan, China, has become a public health emergency of international concern. The high fatality of aged cases caused by SARS-CoV-2 was a need to explore the possible age－related phenomena with non－human primate models.
Methods Three 3－5 years old and two 15 years old rhesus macaques were intratracheally infected with SARS-CoV-2, and then analyzed by clinical signs, viral replication, chest X－ray, histopathological changes and immune response.
Results Viral replication of nasopharyngeal swabs, anal swabs and lung in old monkeys was more active than that in young monkeys for 14 days after SARS-CoV-2 challenge. Monkeys developed typical interstitial pneumonia characterized by thickened alveolar septum accompanied with inflammation and edema, notably, old monkeys exhibited diffuse severe interstitial pneumonia. Viral antigens were detected mainly in alveolar epithelial cells and macrophages.
Conclusion SARS-CoV-2 caused more severe interstitial pneumonia in old monkeys than that in young monkeys. Rhesus macaque models infected with SARS-CoV-2 provided insight into the pathogenic mechanism and facilitated the development of vaccines and therapeutics against SARS-CoV-2 infection.

11. 非人灵长类单细胞图谱揭示 COVID-19 的新致病机制

Single-cell atlas of a non-human primate reveals new pathogenic mechanisms of COVID-19

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DOI：
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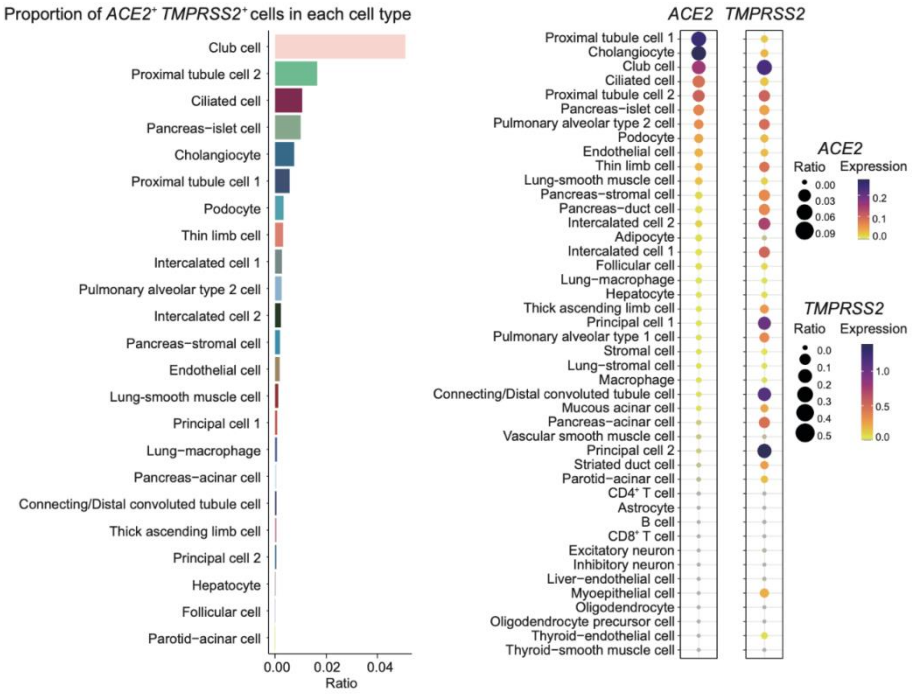
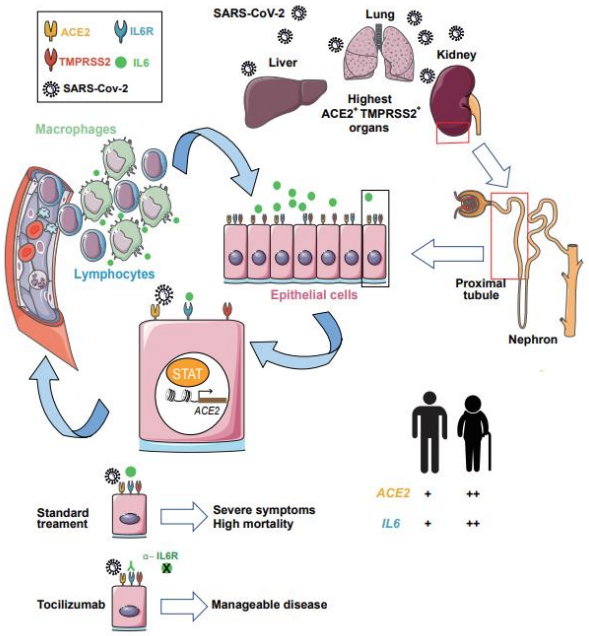
中文摘要：
抗击 COVID-19 是全世界的首要任务。了解 SARS-CoV-2 病毒靶向的细胞类型、是否存在种间差异以及细胞状态的变化如何影响病毒进入是加速开发治疗和预防方法的基础。该研究应用华大智造自主研发的 DNBelab C4 便携式单细胞系统，在单细胞水平上分析了一只食蟹猴（6 岁，雌性）9 种组织的转录组，组织包括肺，肾脏，肝，胰腺，大脑，主动脉，甲状腺，腮腺和血液，鉴定出食蟹猴的 44 种主要细胞类型。SARS-CoV-2 受体 ACE2 和辅助蛋白酶 TMRPSS2 在不同细胞亚型中的分布显示，在肺、肾、甲状腺和肝脏中表现出明显的异质性。通过对 ACE2 和 TMPRSS2 的共表达分析以及后续的分析，发现肺部的一种上皮细胞 club cell 是 ACE2 和 TMPRSS2 双阳性细胞比例最高的细胞类型（图一），提示这种肺部上皮细胞类型极易受到新冠病毒的侵入。共表达分析表明，IDO2 和 ANPEP 等免疫调节蛋白是导致免疫细胞衰竭的潜在 SARS-CoV-2 靶点。此外，肾脏的单细胞染色质可及性(scATAC-seq)分析揭发现 ACE2 转录起始位点附近富集干扰素响应顺式元件（IRF1）以及 STAT 转录因子的结合位点，这可以将 ACE2 的表达与一些患者的严重免疫反应联系起来。特别是发现临床上炎症因子风暴的核心炎症因子 IL-6 受体 IL-6R 与 ACE2 在组织中具有共表达的规律，提示 IL6 与 ACE2 的正反馈调节作用可能是临床上炎症因子风暴的重要原因（图二）。该研究工作构成的独特资源，可以用来了解两个系统发育相近物种的 SARS-CoV-2 病理生理学，这可能会指导人类有效治疗的发展。

要点
1. 使用 9 种猴组织的单细胞转录组图谱来研究 COVID-19。
2. 肺、肾、肝上皮细胞 ACE2+及 TMPRSS2+是 SARS-CoV-2 的靶细胞。
3. ACE2 相关性分析显示 IDO2 和 ANPEP 是潜在的治疗靶点。
4. 揭示了 IL6、STAT 转录因子与促进 SARS-CoV-2 进入之间的联系。

部分文字来自微信公众号文章：https://mp.weixin.qq.com/s/y0k8ynVpcXcLCS1x7OBlVQ



图一 新冠病毒受体表达的组织分布



图二 新冠病毒感染启动 IL-6 免疫信号通路机制

Abstract:
Stopping COVID-19 is a priority worldwide. Understanding which cell types are targeted by SARS-CoV-2 virus, whether interspecies differences exist, and how variations in cell state influence viral entry is fundamental for accelerating therapeutic and preventative approaches. In this endeavor, we profiled the transcriptome at single-cell resolution of nine tissues from a Macaca fascicularis monkey. The distribution of SARS-CoV-2 facilitators, ACE2 and

TMRPSS2, in different cell subtypes showed substantial heterogeneity across lung, kidney, thyroid and liver. Co-expression analysis identified immunomodulatory proteins such as IDO2 and ANPEP as potential SARS-CoV-2 targets responsible for immune cell exhaustion. Furthermore, single-cell chromatin accessibility analysis of the kidney unveiled a plausible link between IL6-mediated innate immune responses aiming to protect tissue and enhanced ACE2 expression that could promote viral entry. Our work constitutes a unique resource for understanding SARS-CoV-2 pathophysiology in two phylogenetically close species, which might guide in the development of effective treatments in humans.

Bullet points
We used a single-cell transcriptome atlas of 9 monkey tissues to study COVID-19.
ACE2+TMPRSS2+ epithelial cells of lung, kidney and liver are targets for SARS-CoV-2.
ACE2 correlation analysis shows IDO2 and ANPEP as potential therapeutic opportunities.
We unveil a link between IL6, STAT transcription factors and boosted SARS-CoV-2 entry.

12. 单细胞图谱整合分析，揭示了年龄，性别、吸烟史对介导 SARS-CoV-2 病毒进入宿主的介质基因的细胞类型特异性表达的影响，强调了可能的感染目标细胞中的炎症过程

Integrated analyses of single-cell atlases reveal age, gender, and smoking status associations with cell type-specific expression of mediators of SARS-CoV-2 viral entry and highlights inflammatory programs in putative target cells

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通讯作者单位：The NHLBI LungMAP Consortium, and The Human Cell Atlas Lung Biological Network
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编译者：宋珂
中文摘要：由 SARS-CoV-2 引起的 COVID-19 疫情严重威胁了全球的公共健康，迫切地需要科研人员研究清楚介导病毒感染和繁殖的分子机制，以及组织病理学特征。在之前的研究中发现，分布于细胞膜表面的血管紧张素转化酶 2（ACE2）和相关的蛋白酶，跨膜丝氨酸蛋白酶 2（TMPRSS2）和组织蛋白酶 L（CTSL），是 SARS-CoV2 侵入细胞的介质。本文中，作者对 107

个样品进行单细胞测序和单核 RNA 测序数据进行了综合分析，研究了 ACE2，TMPRSS2 和 CTSL 的细胞类型特异性的 RNA 表达，包括 22 个肺和呼吸道数据集（16 个未发表），以及 85 个其他不同器官的数据集。作者将呼吸道上皮细胞中，存在 ACE2 和辅助蛋白酶联合表达的特定细胞类别定义为病毒在鼻、呼吸道和肺泡中感染的假定目标。在其他器官的细胞中也发现了存在 ACE2 和蛋白酶共表达的细胞，其中一些与 COVID-19 传播或病理学相关。包括，肠道小肠上皮细胞，角膜上皮细胞，心肌细胞，心脏周细胞，嗅觉性半球状细胞和肾上皮细胞。作者首次对 scRNA-seq 的数据进行了 meta 分析，样本来自 164 名捐献者，包括鼻，呼吸道和肺实质样本 282 份，实际对 1176683 个细胞的进行了测序。这些捐献者涵盖胎儿，儿童，成人和老年人。针对每种特定的细胞类型，对 ACE2，TMPRSS2 和 CTSL 表达水平的提高与年龄增加，性别和吸烟史进行了相关性分析。从流行病学的角度分析，这些特征都与 COVID-19 易感性和结果有关联。值得注意的是，现有的分析中，有少数幼儿样本的 ACE2 表达特别低。进一步的分析揭示了 ACE2+和 TMPRSS2+细胞在鼻，肺和肠组织中，表现出的相同的基因表达程序。包括可能介导病毒进入，维持关键免疫功能和介导上皮-巨噬细胞交互作用的基因。其中包括 IL6，其受体和共受体，IL1R，TNF 响应通路和补体基因。在小鼠的肺和呼吸道中，发现了相同特异性的细胞类型，吸烟的影响也相同。作者的分析表明，介导 SARS-CoV-2 病毒侵入细胞的介质在不同细胞类型上的特异性表达差异可能是造成 COVID-19 流行病学和临床病程差异的原因，并提出了与疾病易感性和发病机制相关的分子通路假设。

Abstract: The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, creates an urgent need for identifying molecular mechanisms that mediate viral entry, propagation, and tissue pathology. Cell membrane bound angiotensin-converting enzyme 2 (ACE2) and associated proteases, transmembrane protease serine 2 (TMPRSS2) and Cathepsin L (CTSL), were previously identified as mediators of SARS-CoV2 cellular entry. Here, we assess the cell type-specific RNA expression of ACE2, TMPRSS2, and CTSL through an integrated analysis of 107 single-cell and single-nucleus RNA-Seq studies, including 22 lung and airways datasets (16 unpublished), and 85 datasets from other diverse organs. Joint expression of ACE2 and the accessory proteases identifies specific subsets of respiratory epithelial cells as putative targets of viral infection in the nasal passages, airways, and alveoli. Cells that co-express ACE2 and proteases are also identified in cells from other organs, some of which have been associated with COVID-19 transmission or pathology, including gut enterocytes, corneal epithelial cells, cardiomyocytes, heart pericytes, olfactory sustentacular cells, and renal epithelial cells. Performing the first meta-analyses of scRNA-seq studies, we analyzed 1,176,683 cells from 282 nasal, airway, and lung parenchyma samples from 164 donors spanning fetal, childhood, adult, and elderly age groups, associate increased levels of ACE2, TMPRSS2, and CTSL in specific cell types with increasing age, male gender, and smoking, all of which are epidemiologically linked to COVID-19 susceptibility and outcomes. Notably, there was a particularly low expression of ACE2 in the few young pediatric samples in the analysis. Further analysis reveals a gene expression program shared by ACE2+TMPRSS2+ cells in nasal, lung and gut tissues, including genes that may mediate viral entry, subtend key immune functions, and mediate epithelial-macrophage cross-talk. Amongst these are IL6, its receptor and co-receptor, IL1R, TNF response pathways,

and complement genes. Cell type specificity in the lung and airways and smoking effects were conserved in mice. Our analyses suggest that differences in the cell type-specific expression of mediators of SARS-CoV-2 viral entry may be responsible for aspects of COVID-19 epidemiology and clinical course, and point to putative molecular pathways involved in disease susceptibility and pathogenesis.

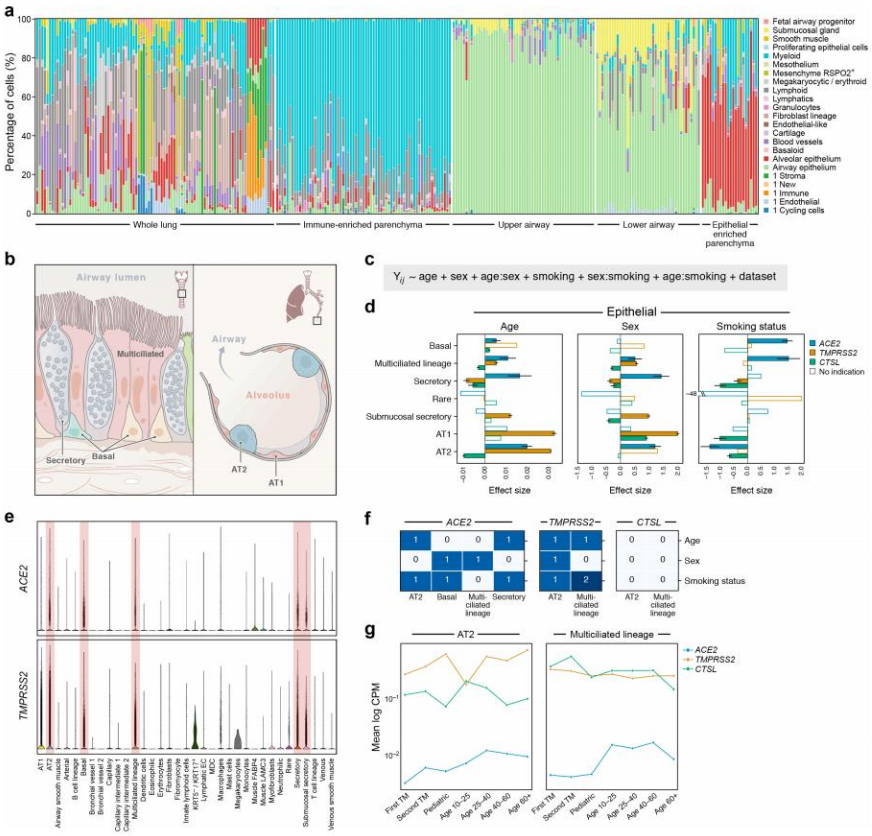

Figure 3. *ACE2*, *TMPRSS2*, and *CTSL* expression in AT2 cells increases with age and smoking status, and in men

(a) Samples in the aggregated lung and airway dataset partition to several classes by their cell composition. Percentage of cells (y axis) by level 2 cell annotations (Annotations with a preceding "1" indicate coarse annotations) across samples (x axis). The 282 samples are ordered by sample composition clusters. (b) Schematic of key lung and airway cell types highlighted in the study. (c) Statistical model. Model fitted to the data to assess sex, age, and smoking status associations with expression of the three genes. denotes gene counts and *nUMI* denotes the total UMI counts per cell. (d) Age, sex, and smoking status associations with expression of *ACE2* (blue), *TMPRSS2* (orange), and *CTSL* (green) in epithelial cells. Effect size (x axis) of the association, in log fold change (sex, smoking status) or slope of log expression with age. Colored bars: associations with an FDR-corrected p-value<0.05, where pseudo-bulk analysis shows a consistent effect direction. Error bars: standard errors around coefficient estimates. (e) Distribution of *ACE2* and *TMPRSS2* expression across level 3 lung cell types. Red shading indicates the main cell types that express *ACE2* and *TMPRSS2*. (f) Hold out analysis shows the robustness of associations to holding out a dataset. The values show the number of held-out datasets that result in loss of association between a given covariate (rows) and *ACE2*, *TMPRSS2*, *or CTSL* expression in a given cell type (columns). Robust trends are determined by significant effects that are robust to holding out any dataset (0 values). (g) Low expression in pediatric samples. Mean expression level (log CPM, y axis) of *ACE2* (blue), *TMPRSS2* (orange), and *CTSL* (green) across age bins (x axis) in AT2 (left) and ciliated (right) cells. Pediatric samples: 0-10 years. Samples from past or current smokers were removed from this plot to avoid smoking confounders. Error bars are omitted due to y-axis limitations. They are typically 10-fold the mean value (Supplementary Table 5). Multiciliated and AT2 cells are shown as these cell types are present in fetal data, and show significant age associations with *ACE2* expression.

13. SARS-CoV-2 的受体 ACE2 在人气道上皮细胞中被干扰素刺激表达

SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues

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中文摘要：

Abstract:
There is pressing urgency to understand the pathogenesis of the severe acute respiratory syndrome coronavirus clade 2 (SARS-CoV-2) which causes the disease COVID-19. SARS-CoV2 spike (S)-protein binds ACE2, and in concert with host proteases, principally TMPRSS2, promotes cellular entry. The cell subsets targeted by SARS-CoV-2 in host tissues, and the factors that regulate ACE2 expression, remain unknown. Here, we leverage human, non-human primate, and mouse single-cell RNA-sequencing (scRNA-seq) datasets across health and disease to uncover putative targets of SARS-CoV-2 amongst tissue-resident cell subsets. We identify ACE2 and TMPRSS2 co-expressing cells within lung type II pneumocytes, ileal absorptive enterocytes, and nasal goblet secretory cells. Strikingly, we discover that ACE2 is a human interferonstimulated gene (ISG) in vitro using airway epithelial cells, and extend our findings to in vivo viral infections. Our data suggest that SARS-CoV-2 could exploit species-specific interferon-driven upregulation of ACE2, a tissue-protective mediator during lung injury, to enhance infection.

目前我们仍然急需了解 SARS-CoV-2 导致 COVID-19 的致病机理。SARS-CoV-2 的棘突 S 蛋白和宿主细胞的 ACE2 集合，协同宿主的蛋白酶，主要是 TMPRSS2，促进病毒进入宿主细胞。SARS-CoV-2 靶向宿主组织的哪些细胞，以及哪些因素会调控 ACE2 的表达，目前还未知（注：对于靶向细胞，目前稍有所知）。研究者们用人、非人类灵长类以及小鼠的单细胞测序数据集包括一些疾病状态样品的数据集合来发现 SARS-CoV-2 在组织里的靶细胞。研究者们在 II 型肺细胞、吸收性肠细胞以及鼻内酒杯状分泌细胞里面有 ACE2 和 TMPRSS2 的共表达。非常让人吃惊的是，研究者们发现 ACE2 在体外实验的人气道上皮细胞可以被干扰素刺激表达（是一个 ISG 基因，干扰素刺激的基因，Figure 5），这个现象在体内病毒感染中也存在。公开数据集也支持这个发现。作者在小鼠体外和体内实验中，都不能观察到这个现象。该研究的数据提示 SARS-CoV-2 可能利用干扰素通路来上调 ACE2 来增强感染力。
编者注：该研究中用到的体内外模型都没有涉及到 SARS-CoV-2 的直接感染，只是以往流感病毒或者干扰素的直接处理，需要更多的验证。前面两篇相关的文章中（1，2），我们讲到在体外、离体以及体内实验中，被 SARS-CoV-2 感染的组织细胞的转录变化中缺失了干扰素本身的表达上调，但是 ISG 基因却仍然有表达上调，说明要么存在一个干扰素瞬态上调，要

么干扰素本身的表达被抑制，ISG 通路对应的转录因子比如 STAT1 仍然受到病毒的调控。另外，目前干扰素被应多国用于临床预防或者治疗 COVID-19，干扰素在 SARS-CoV-2 的致病机理中可能起到复杂且重要的作用，需要进一步通过临床样本检测以及体外实验中进行进一步研究。

同期 cell 的 Imbalanced host response to SARS-CoV-2 drives development of COVID-19 https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00985.pdf，我们之前报道了预印本的内容，见 4 月 20 日简报第 10 条。

2，Comparative replication and immune activation profiles of SARS-CoV-2 and SARS-CoV in human lungs: an ex vivo study with implications for the pathogenesis of COVID-19 ，https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa410/5818134?searchresult=1#，见 4 月 21 日简报第 5 条

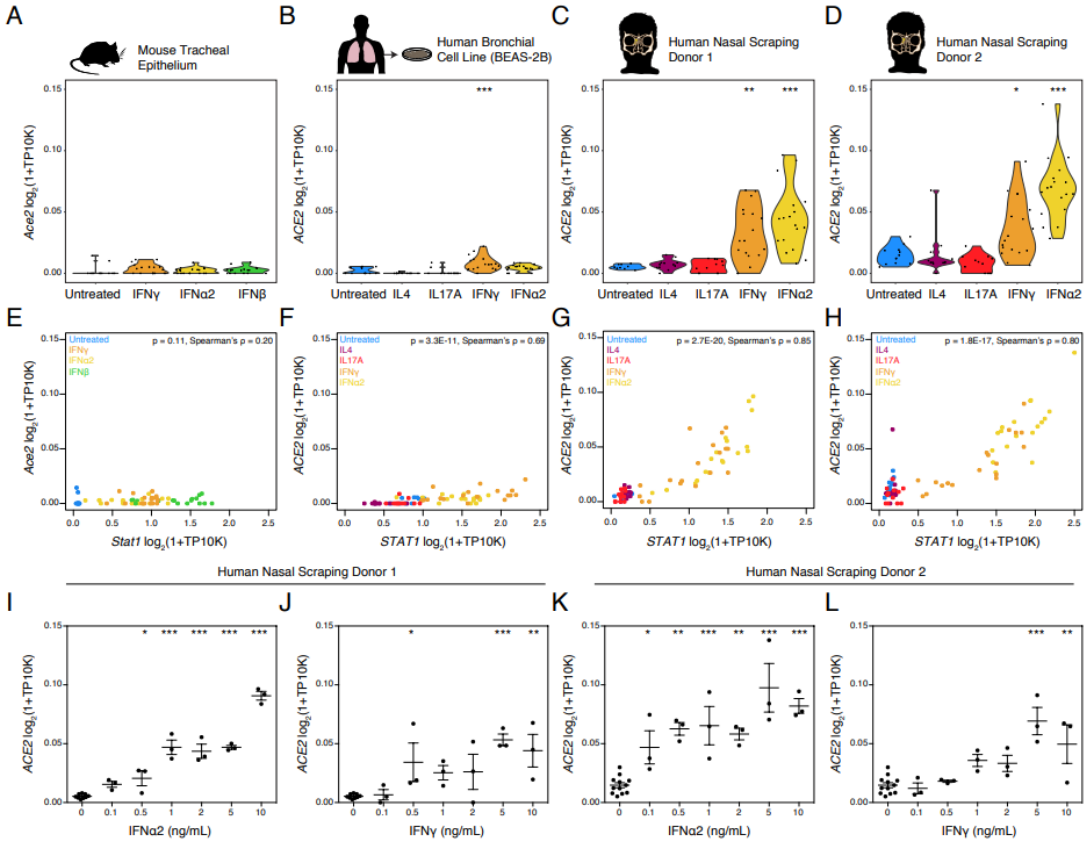

Figure 5. ACE2 is an Interferon-Stimulated gene in Primary Human Barrier Tissue Epithelial Cells A-D. Basal epithelial cells from distinct sources were cultured to confluence and treated with increasing doses (0.1 to 10 ng/mL) of IFNα2, IFNγ, IL-4, IL-17A, and/or IFNβ for 12 hours and bulk RNA-seq analysis was performed. Expression of ACE2 (human) or Ace2 (mouse) by cell type and stimulation condition. A. Primary mouse basal cells from tracheal epithelia, B. BEAS-2B Human Bronchial Cell Line, C. Primary human basal cells from nasal scraping, Donor 1, D. Primary human basal cells from nasal scraping, Donor 2. TP10K: transcripts per 10,000 reads. *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, Bonferronicorrected t-test compared

to Untreated condition. E.-H. Co-expression of STAT1/Stat1 and ACE2/Ace2 by cell type. E. Primary mouse basal cells from tracheal epithelia, F. BEAS-2B Human Bronchial Cell Line, G. Primary human basal cells from nasal scraping, Donor 1, H. Primary human basal cells from nasal scraping, Donor 2. TP10K: transcripts per 10,000 reads. Statistical significance assessed by Spearman's rank correlation. I.-L. Expression of ACE2 in primary human basal cells from nasal scrapings across a range of concentrations of IFNγ or IFNα2. I. IFNα2 dose response in Donor 1, $p < 0.001$ by oneway ANOVA. J. IFNγ dose response in Donor 1, $p < 0.01$ by one-way ANOVA. K. IFNα2 dose response in Donor 2, $p < 0.001$ by one-way ANOVA. L. IFNγ dose response in Donor 2, $p < 0.001$ by one-way ANOVA. TP10K: transcripts per 10,000 reads. *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, Bonferroni-corrected post-hoc testing compared to 0 ng/mL condition.

14. 关于人体细胞图谱（HCA）项目

https://chanzuckerberg.com/science/programs-resources/humancellatlas/

人体细胞图谱（HCA）是一项由扎克伯格基因会支持的全球性的由科学家领头的合作。该合作项目旨在对健康人体的细胞进行绘制和刻画包括：细胞类型，数量，位置，关系和分子成分的图谱和特征。这个项目一旦完成，它将成为科学家们的一个重要基本资源。借助于这个资源，科学家们可以更好地了解健康细胞的工作方式以及各种疾病的细胞水平机制。
扎克伯格基金会通过各种机制为 HCA 提供支持，包括帮助建立数据协调平台，支持计算工具以及拨款。该项目是支持单细胞生物学的一个组成部分，以帮助阐明支持所有疾病的细胞机制。
目前，项目产生的数据目录在以下网站可以看到：https://data.humancellatlas.org/
HCA 的项目按照人体组织分成子项目，每个子项目由多个团队合作完成。

15. D3Targets-2019-nCoV，一个用于预测药物靶点和基于 COVID-19 的多靶点和多位点的虚拟筛选的网络服务器

D3Targets-2019-nCoV a webserver for predicting drug targets and for multi-target and multi-site based virtual screening against COVID-19
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https://www.sciencedirect.com/science/article/pii/S2211383520305499?via%3Dihub=
第一作者：Yulong Shi, Xinben Zhang, Kaijie Mu, Cheng Peng
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通讯作者单位：中国科学院上海药物研究所药物研发中心受体研究重点实验室；中国科学院大学药学院
编译者：张怡
中文摘要：
迫切需要一种高效药物来治疗 COVID-19。为此，作者开发了一种基于分子对接的网络服务器，即 D3Targets-2019-nCoV，具有两种功能，一是通过观察临床或体外/体内研究，预测药物或活性化合物的药物靶点，二是通过对接识别潜在药物靶点的先导化合物。该服务器有其

独特的特点，(1)尽可能多的包含了从病毒感染到复制和释放整个过程中涉及的潜在靶蛋白及其不同构象;(2)蛋白结构上所有体积大于 200 Å3 的潜在配体结合位点进行对接;(3)标注出某些构象或结合位点之间的相关信息;(4)易于更新，对公众可自由访问(https://www.d3pharma.com/d3target-2019-ncov/index.php)。目前，服务器包含 42 个蛋白[20 个与严重急性呼吸综合征相关的冠状病毒 2 (SARS-CoV-2)编码蛋白和 22 个参与病毒感染、复制和释放的人类蛋白]，共 69 个不同的构象/结构和 557 个潜在的配体结合口袋。通过 6 个示例，作者证明了服务器对于药物化学家、药理学家和临床医生有效地发现或开发针对 SARS-CoV-2 的有效药物来治愈 COVID-19 应该是有用的。

Abstract

A highly effective medicine is urgently required to cure coronavirus disease 2019 (COVID-19). For the purpose, we developed a molecular docking based webserver, namely D3Targets-2019-nCoV, with two functions, one is for predicting drug targets for drugs or active compounds observed from clinic or in vitro/in vivo studies, the other is for identifying lead compounds against potential drug targets via docking. This server has its unique features, (1) the potential target proteins and their different conformations involving in the whole process from virus infection to replication and release were included as many as possible; (2) all the potential ligand-binding sites with volume larger than 200 Å3 on a protein structure were identified for docking; (3) correlation information among some conformations or binding sites was annotated; (4) it is easily to be updated, and is accessible freely to public (https://www.d3pharma.com/D3Targets-2019-nCoV/index.php). Currently, the webserver contains 42 proteins [20 severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) encoded proteins and 22 human proteins involved in virus infection, replication and release] with 69 different conformations/structures and 557 potential ligand-binding pockets in total. With 6 examples, we demonstrated that the webserver should be useful to medicinal chemists, pharmacologists and clinicians for efficiently discovering or developing effective drugs against the SARS-CoV-2 to cure COVID-19.