新型冠状病毒信息简报

第 73 期（2020 年 9 月 19-25 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

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内容介绍

1. 2020 年 9 月 24 日疫情

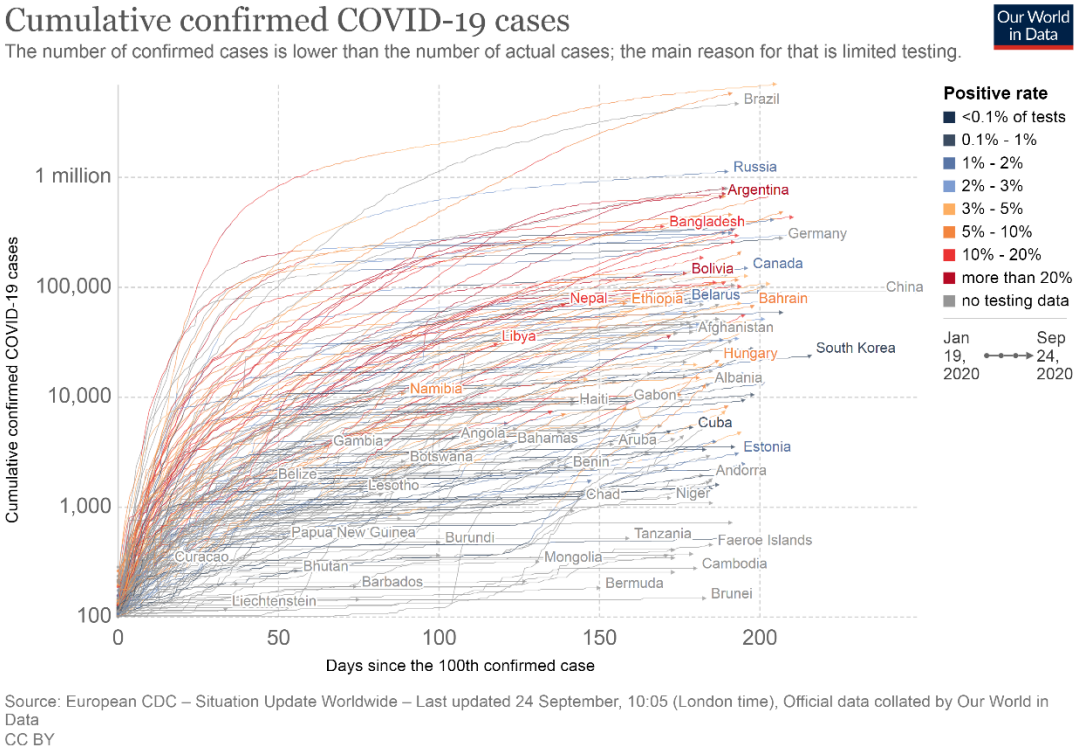
数据来源：WHO

发布时间：2020 年 9 月 24 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 9 月 24 日全球累计确诊新型冠状病毒病人 **31,798,308** 例，当日新增确诊 **298,085** 例，累计死亡 **973,653** 例，当日新增死亡 **5,918**。

中国累计确诊 90,918 例，累计死亡 4,745 例，当日新增确诊 10 例，新增死亡 1 例。



Source: European CDC – Situation Update Worldwide – Last updated 24 September, 10:05 (London time), Official data collated by Our World in Data
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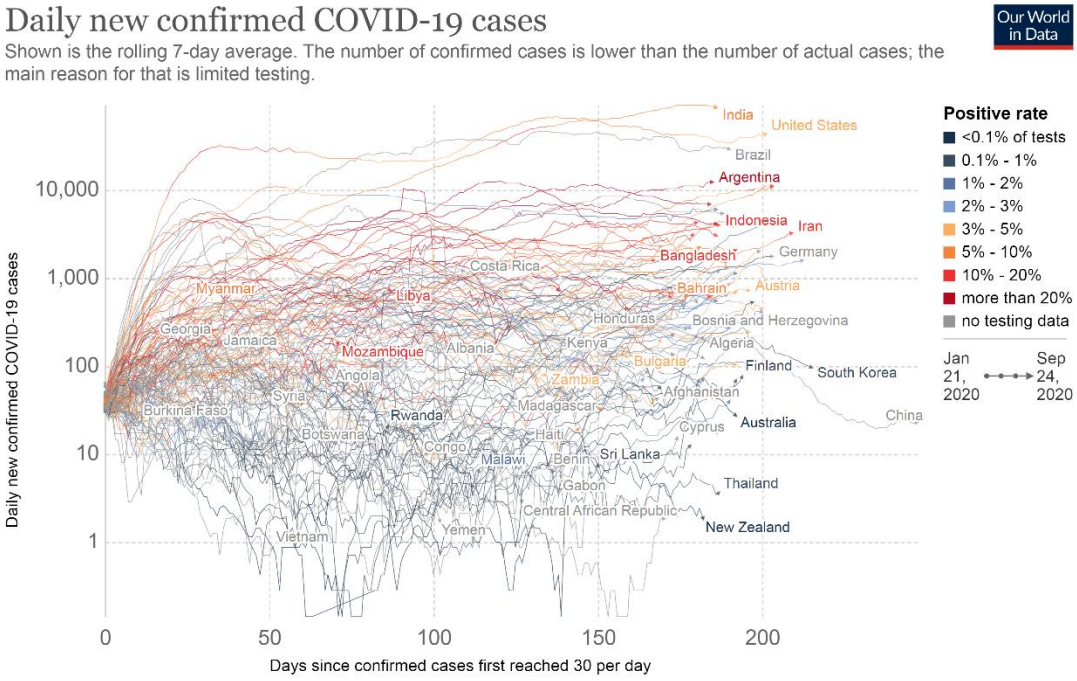
重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



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（9 月 24 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 青岛发现 2 例无症状感染者均为装卸工人

来源：人民网

发布时间：2020-09-25

链接：http://ln.people.com.cn/n2/2020/0925/c378326-34317615.html
人民网北京 9 月 25 日电 据青岛市卫健委官方网站消息，2020 年 9 月 24 日，在对青岛港大港公司“应检尽检”人员定期例行检测中，先后发现 2 名装卸工人感染新型冠状病毒，属无症状感染者。

3. 接下来 5 年里 SARS-CoV-2 的动力学和免疫的生活史、疫苗接种的关系

Immune life history, vaccination, and the dynamics of SARS-CoV-2 over the next 5 years
来源：science
发布时间：2020-09-21
第一作者：Chadi M. Saad-Roy
通讯作者：Bryan T. Grenfell2
通讯作者单位：Princeton University
链接：https://science.sciencemag.org/content/early/2020/09/18/science.abd7343
编译：蒋立春
中文摘要：
未来 Covid-19 的疫情发展情况取决于人群中针对 SARS-CoV2 的适应性免疫。但是我们还不是很确定自然感染 SARS-CoV-2 或者接种 SARS-CoV-2 疫苗引发的免疫反应的特征。
作者用简单的流行病学模型对未来 Covid-19 疫情的程度和时间线进行了估计。在该模型中，作者探索了适应性免疫反应对 SARS-CoV-2 保护作用效果和时长，以及适应性免疫与疫苗和非药物干涉的相互作用下，未来 Covid-19 疫情的广泛程度和时间。通过模型模拟，作者们发现对 SARS-CoV-2 初次感染以及可能的疫苗的免疫反应差异可以对免疫图谱以及重症负担造成重大影响，疫情可能在持续到近乎清除的范围内变动。作者们发现阐述了未来 Covid-19 疫情的动力学非常复杂，强调了除了对活跃感染病人的免疫反应之外的免疫反应进行研究外，才能更好地预测 SARS-CoV-2 感染的免疫图谱。

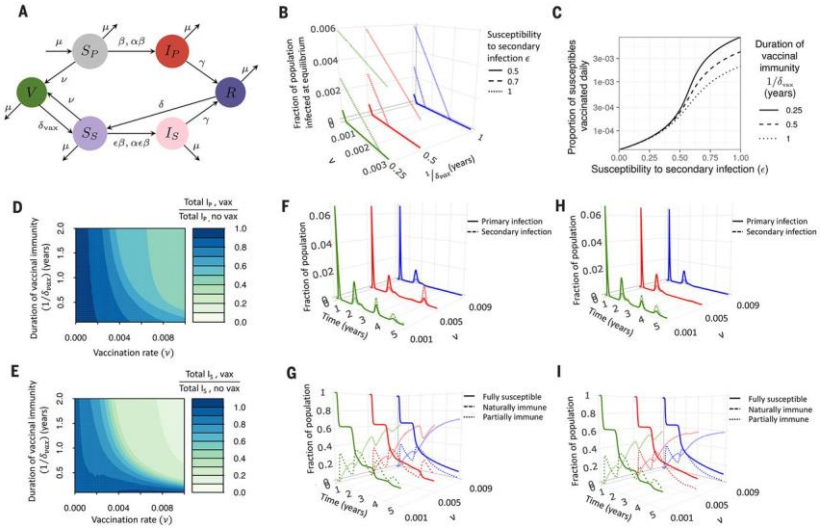


Fig. 3 Impact of vaccination and vaccinal immunity on disease dynamics. (A) Modified model flowchart that incorporates a vaccinated class V(37). (B) Total infected fraction of the population at equilibrium as a function of the vaccination rate ν for different values of the duration of vaccinal immunity ($1/\delta_{vax}$ = 0.25 years: green lines, $1/\delta_{vax}$ = 0.5 years: red lines, and

1/δvax = 1 year: blue lines) and the susceptibility to secondary infection (ε = 0.5: solid lines, ε = 0.7: dashed lines, and ε = 1: dotted lines). (C) Daily proportion of susceptibles who must be vaccinated in order to achieve a disease-free state at equilibrium as a function of ε for different values of the duration of vaccinal immunity (1/δvax = 0.25 years: solid line, 1/δvax = 0.5 years: dashed line, and 1/δvax = 1 year: dotted line). In (B) and (C) the relative transmissibility of secondary infections and duration of natural immunity are taken to be α = 1 and 1/δ = 1 year, respectively, and the transmission rate is derived from the mean value of seasonal NYC-based weekly reproduction numbers ([Math Processing Error]$\bar{R}_0$ = 1.75) (37) (fig. S2C). (D and E) The ratio of the total number of primary (D) and secondary (E) infections with vaccination versus without during years 1.5-5 (i.e., after the introduction of the vaccine) are plotted as a function of the weekly vaccination rate ν and the duration of vaccinal immunity 1/δvax. (F to I) Time series of the various immune classes plotted for different values of the vaccination rate ν. The top row ((F) and (H)) contains the time series of primary (IP, solid lines) and secondary (IS, dashed lines) infections, while the bottom row ((G) and (I)) contains the time series of the fully susceptible (SP, solid lines), naturally immune (R, dashed lines), and partially immune (SS, dotted lines) subpopulations. The duration of vaccinal immunity is taken to be 1/δvax = 0.5 years (shorter than natural immunity) in (F) and (G), and 1/δvax = 1 year (equal to natural immunity) in (H) and (I). In (D) to (I), the relative susceptibility to secondary infection, relative transmissibility of secondary infections, and duration of natural immunity are taken to be ε = 0.7, α = 1, and 1/δ = 1 year, respectively. Vaccination is introduced 1.5 years after the onset of the epidemic (i.e., during the 79th week) following a 40 week period of social distancing during which the force of infection was reduced to 60% of its original value during weeks 16 to 55 (i.e., the scenario described in Fig. 2B of the main text), and a seasonal transmission rate derived from the climate of NYC with no lag is assumed.

Abstract:

The future trajectory of the Covid-19 pandemic hinges on the dynamics of adaptive immunity against SARS-CoV2; however, salient features of the immune response elicited by natural infection or vaccination are still uncertain.

We use simple epidemiological models to explore estimates for the magnitude and timing of future Covid-19 cases given different protective efficacy and duration of the adaptive immune response to SARS-CoV-2, as well as its interaction with vaccines and nonpharmaceutical interventions. We find that variations in the immune response to primary SARS-CoV-2 infections and a potential vaccine can lead to dramatically different immune landscapes and burdens of critically severe cases, ranging from sustained epidemics to near elimination. Our findings illustrate likely complexities in future Covid-19 dynamics, and highlight the importance of immunological characterization beyond the measurement of active infections for adequately projecting the immune landscape generated by SARS-CoV-2 infections.

4. 英国猫的呼吸道疾病与 SARS-CoV-2 的人-猫传播有关

Respiratory disease in cats associated with human-to-cat transmission of SARS-CoV-2 in the UK

来源：biorxiv

发布时间：2020-09-23

链接：https://www.biorxiv.org/content/10.1101/2020.09.23.309948v1

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DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

通过免疫荧光、原位杂交、逆转录酶定量 PCR 和病毒基因组测序，发现来自英国不同 COVID-19 感染家庭的两只猫感染了来自人类的 SARS-CoV-2。猫 1 死后采集的肺组织显示出与病毒性肺炎一致的病理和组织学特征，且 SARS-CoV-2 抗原和 RNA 检测呈阳性。从患有鼻炎和结膜炎的猫 2 的口咽拭子中检测到 SARS-CoV-2 RNA。对来自猫 2 的病毒高通量测序表明，与最相近的英国人 SARS-CoV-2 序列相比，病毒基因组包含 5 个单核苷酸多态性（SNP），与最初的 Wuhan-Hu-1 参考基因组相比，包含 8 个 SNP。对猫 2 的病毒基因组和来自世界各地的其他 9 个猫源性 SARS-CoV-2 序列的分析表明，没有共同的猫特异性突变。这些发现表明，SARS-CoV-2 在英国的人-猫传播发生在 COVID-19 大流行期间，受感染的猫会患上轻微或严重的呼吸道疾病。鉴于这种新型冠状病毒的多功能性，对人与猫、猫与猫、猫与人之间的传播进行监测是非常重要的。

Abstract:

Two cats from different COVID-19-infected households in the UK were found to be infected with SARS-CoV-2 from humans, demonstrated by immunofluorescence, in situ hybridisation, reverse transcriptase quantitative PCR and viral genome sequencing. Lung tissue collected post-mortem from cat 1 displayed pathological and histological findings consistent with viral pneumonia and tested positive for SARS-CoV-2 antigens and RNA. SARS-CoV-2 RNA was detected in an oropharyngeal swab collected from cat 2 that presented with rhinitis and conjunctivitis. High throughput sequencing of the virus from cat 2 revealed that the feline viral genome contained five single nucleotide polymorphisms (SNPs) compared to the nearest UK human SARS-CoV-2 sequence, and this human virus contained eight SNPs compared to the original Wuhan-Hu-1 reference. An analysis of the viral genome of cat 2 together with nine other feline-derived SARS-CoV-2 sequences from around the world revealed no shared cat-specific mutations. These findings indicate that human-to-cat transmission of SARS-CoV-2 occurred during the COVID-19 pandemic in the UK, with the infected cats developing mild or severe respiratory disease. Given the versatility of the new coronavirus, it will be important to monitor for human-to-cat, cat-to-cat and cat-to-human transmission.

5. 钙保护素升高和异常髓样细胞亚群使 COVID-19 重症区别于轻症

Elevated Calprotectin and Abnormal Myeloid Cell Subsets Discriminate Severe from Mild COVID-19
来源：cell
发布时间：2020-09-17
链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7405878/#abs0015title
第一作者：Aymeric Silvin
通讯作者：Florent Ginhoux
通讯作者单位：Singapore Immunology Network (SIgN), Agency for Science, Technology and Research
DOI 或 PUBMED ID：10.1016/j.cell.2020.08.002
编译者：孔娟
中文摘要：
众所周知，在 COVID-19 中 SARS-CoV-2 引起血液髓样细胞失调。先天髓样反应是否因疾病严重程度而异，以及先天免疫标记物是否能区分高危患者这些研究尚不清楚。研究者对新冠肺炎患者外周血细胞进行了多维流式细胞术和单细胞 RNA 测序，并检测到非经典型的 CD14LowCD16High 的单核细胞的消失、HLA-DRLow 经典单核细胞(人类白细胞抗原-DR 同型)的积聚，以及重症病例中大量钙卫蛋白(S100A8/S100A9)的释放。检测结果发现具有免疫抑制特征的未成熟的 CD10Low CD101- CXCR4+/-中性粒细胞在血液和肺中积累，提示急性骨髓的生成。最后，研究者表明通过检测病人钙卫蛋白血浆水平和利用常规流式细胞术检测非经典型单核细胞频率的降低可能成为鉴别会发展为严重新冠肺炎病的患者的一种方案。
Abstract：
Blood myeloid cells are known to be dysregulated in coronavirus disease 2019 (COVID-19), caused by SARSCoV-2. It is unknown whether the innate myeloid response differs with disease severity and whether markers of innate immunity discriminate high-risk patients. Thus, we performed high-dimensional flow cytometry and single-cell RNA sequencing of COVID-19 patient peripheral blood cells and detected disappearance of non-classical CD14LowCD16High monocytes, accumulation of HLA-DRLow classical monocytes (Human Leukocyte Antigen – DR isotype), and release of massive amounts of calprotectin (S100A8/S100A9) in severe cases. Immature CD10LowCD101CXCR4+/-neutrophils with an immunosuppressive profile accumulated in the blood and lungs, suggesting emergency myelopoiesis. Finally, we show that calprotectin plasma level and a routine flow cytometry assay detecting decreased frequencies of non-classical monocytes could discriminate patients who develop a severe form of COVID-19, suggesting a predictive value that deserves prospective evaluation.

6. 先前存在的 T 细胞记忆为老年人患 COVID-19 重症的危险因素

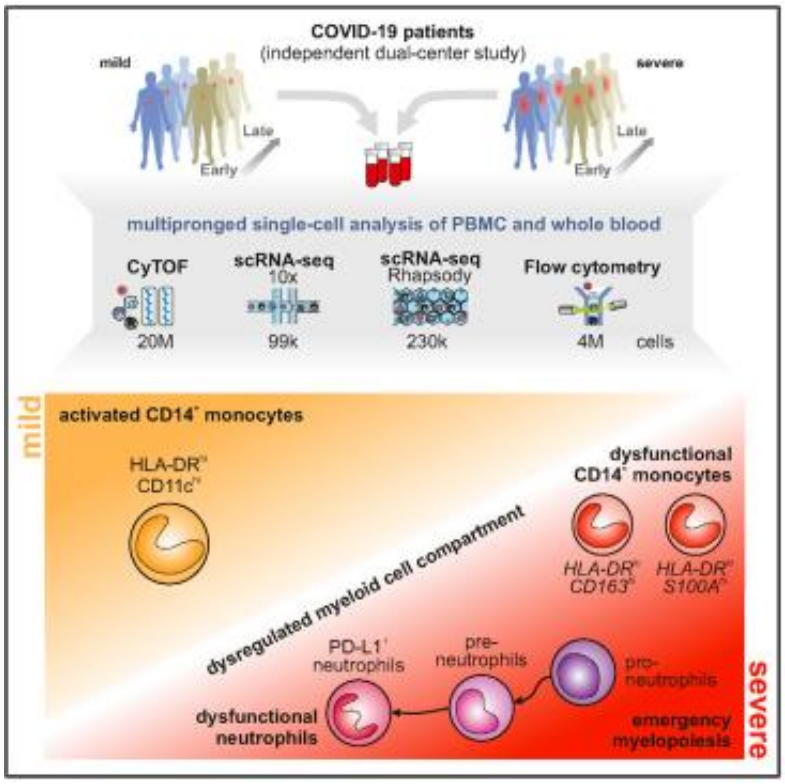
Pre-existing T cell memory as a risk factor for severe 1 COVID-19 in the elderly
来源：medRxiv
发布时间：2020-09-18
链接：https://www.medrxiv.org/content/10.1101/2020.09.15.20188896v1
第一作者：Petra Bacher
通讯作者：Petra Bacher
通讯作者单位：Christian-Albrechts Universität zu Kiel & Universitätsklinik

Schleswig-Holstein Institute of Immunology & Insitute of Clinical Molecular Biology Arnold-Heller-Str. 3, 24105 Kiel, Germany
DOI 或 PUBMED ID：
编译者：雷颖
中文摘要：
COVID-19 表现出较高的临床变异性，但决定疾病严重程度的参数尚不清楚。先前存在的 T 细胞记忆被认为是一种保护机制，但缺乏确凿的证据。文中作者证明，所有未暴露的个体都携带 SARS-CoV-2 特异性记忆 T 细胞，与普通感冒冠状病毒和其他无关病毒有边缘的交叉反应。它们表现出低的功能亲和力和广泛的蛋白质目标特异性，它们的频率与反映个体免疫年龄的 CD4 记忆室的总体大小相关。COVID-19 患者明显增加了 SARS-CoV-2 特异性炎症 T 细胞反应，这些反应与严重程度相关。 然而，严重的 COVID-19 患者表现出较低的 TCR 功能亲和力和较少的克隆扩增。数据表明，预先存在的低亲和力 T 细胞记忆对新抗原如 SARS-CoV-2 的 T 细胞反应质量产生负面影响，这可能会导致不适当的免疫反应，尤其是在老年人中。作者提出免疫年龄是发展成重症 COVID-19 的独立危险因素。
Abstract
Coronavirus disease 2019 (COVID-19) displays high clinical variability but the parameters that determine disease severity are still unclear. Pre-existing T cell memory has been hypothesized as a protective mechanism but conclusive evidence is lacking. Here we demonstrate that all unexposed individuals harbor SARS-CoV-2-specific memory T cells with marginal cross-reactivity to common cold corona and other unrelated viruses. They display low functional avidity and broad protein target specificities and their frequencies correlate with the overall size of the CD4+ memory compartment reflecting the immunological age of an individual. COVID-19 patients have strongly increased SARS-CoV-2-specific inflammatory T cell responses that are correlated with severity. Strikingly however, patients with severe COVID-19 displayed lower TCR functional avidity and less clonal expansion. Our data suggest that a low avidity pre-existing T cell memory negatively impacts on the T cell response quality against neoantigens such as SARS-CoV-2, which may predispose to develop inappropriate immune reactions especially in the elderly. We propose the immunological age as an independent risk factor to develop severe COVID-19.

7. 严重的 COVID-19 表现为一个失调的髓样细胞室

Severe COVID-19 Is Marked by a Dysregulated Myeloid Cell Compartment
来源：cell
发布时间：2020-09-17
链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7405822/
第一作者：Jonas Schulte-Schrepping
通讯作者：Jonas Schulte-Schrepping
通讯作者单位： Life and Medical Sciences (LIMES) Institute, University of Bonn, Germany
DOI 或 PUBMED ID：10.1016/j.cell.2020.08.001
编译者：张鹏伟
中文摘要：

2019 年冠状病毒病（COVID-19）是一种轻至中度呼吸道感染，但有一部分患者会发展为严重疾病和呼吸衰竭。轻度保护性免疫的机制以及与中性粒细胞计数增加和免疫反应失调相关的严重 COVID-19 的发病机制仍不清楚。在一项双中心、两个队列研究中，我们结合了单细胞 RNA 测序和全血和外周血单个核细胞的单细胞蛋白质组学，以确定轻度和重度 COVID-19（109 个个体的 242 个样本）的免疫细胞组成和活化随时间的变化。在轻度 COVID-19 中，具有干扰素刺激的基因特征的 HLA-DRhiCD11chi 炎性单核细胞升高。严重的 COVID-19 以中性粒细胞前体的出现为标志，可作为紧急骨髓生成，功能异常的成熟中性粒细胞和 HLA-DRlo 单核细胞的证据。我们的研究提供了对 SARS-CoV-2 感染的全身免疫反应的详细见解，并揭示了与严重 COVID-19 相关的髓样细胞区室的深刻变化。



Abstract:

Coronavirus disease 2019 (COVID-19) is a mild to moderate respiratory tract infection, however, a subset of patients progress to severe disease and respiratory failure. The mechanism of protective immunity in mild forms and the pathogenesis of severe COVID-19 associated with increased neutrophil counts and dysregulated immune responses remain unclear. In a dual-center, two-cohort study, we combined single-cell RNA-sequencing and single-cell proteomics of whole-blood and peripheral-blood mononuclear cells to determine changes in immune cell composition and activation in mild versus severe COVID-19 (242 samples from 109 individuals) over time. HLA-DRhiCD11chi inflammatory monocytes with an interferon-stimulated gene signature were elevated in mild COVID-19. Severe COVID-19 was marked by occurrence of neutrophil precursors, as evidence of emergency myelopoiesis, dysfunctional mature neutrophils, and *HLA-DRlo* monocytes. Our study provides detailed insights into the systemic immune response to SARS-CoV-2 infection and reveals profound alterations in the myeloid cell compartment associated with severe COVID-19.

8. COVID-19 的亚基疫苗候选——S 三聚体的冷冻电镜结构

Cryo-EM structure of S-Trimer, a subunit vaccine candidate for COVID-19

来源：bioRxiv

发布时间：2020-09-21

链接：https://www.biorxiv.org/content/10.1101/2020.09.21.306357v1

第一作者：Jiahao Ma, Danmei Su

通讯作者：梁朋，郑三多

通讯作者单位：三叶草生物制药公司，NIBS

DOI 或 PUBMED ID：preprint

编译者：雷颖

中文摘要：

SARS-CoV-2 在出现不到一年的时间里，已在全世界感染了 2200 万人，死亡人数接近 100 万。疫苗接种仍然是最终结束这一流行病的最佳希望。文中作者利用 Trimer-Tag 技术生产了野生型（WT）和弗林蛋白酶切位点突变（MT）的 S 三聚体，用于 COVID-19 疫苗研究。分别在 3.2A 和 2.6A 测定的 WT 和 MT 的 S 三聚体的 Cryo-EM 结构表明，这两种抗原都采用紧密封闭的构象，其结构与先前解构的全长 WT 的 S 蛋白基本相同。这些结果验证了 Trimer-Tag 作为亚稳态 WT 的 S 三聚体生产的平台技术，也是 COVID-19 亚单位疫苗的候选技术。

Abstract

Less than a year after its emergence, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 22 million people worldwide with a death toll approaching 1 million. Vaccination remains the best hope to ultimately put this pandemic to an end. Here, using Trimer-Tag technology, we produced both wild-type (WT) and furin site mutant (MT) S-Trimers for COVID-19 vaccine studies. Cryo-EM structures of the WT and MT S-Trimers, determined at 3.2 Å and 2.6 Å respectively, revealed that both antigens adopt a tightly closed conformation and their structures are essentially identical to that of the previously solved full-length WT S protein in detergent. These results validate Trimer-Tag as a platform technology in production of metastable WT S-Trimer as a candidate for COVID-19 subunit vaccine.

9. 研发中的 SARS-CoV-2 疫苗

SARS-CoV-2 vaccines in development

来源：Nature

发布时间：2020-09-23

链接：https://www.nature.com/articles/s41586-020-2798-3

作者：Florian Krammer

作者单位：Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

DOI 或 PUBMED ID：https://doi.org/10.1038/s41586-020-2798-3

编译者：雷颖

中文摘要：

SARS-CoV-2 于 2019 年底在中国出现，引起 COVID-19 大流行。为了减轻病毒对公众健康、经济和社会的影响，迫切需要一种疫苗。SARS-CoV-2 疫苗的研制始于 2020 年 1 月初，当时该病毒序列已获得，并以创纪录的速度进行，一项临床一期试验已于 2020 年 3 月开始，目

前有 180 多种疫苗处于不同的研制阶段。几个疫苗候选者的临床一期/二期试验数据已经获得，许多已经进入临床三期试验。到目前为止，现有的数据表明，有效和安全的疫苗可能会在几个月内而不是几年内获得。

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in late 2019 in China and caused a coronavirus disease 2019 (COVID-19) pandemic. To mitigate the public health, economic and societal impacts of the virus, a vaccine is urgently needed. The development of SARS-CoV-2 vaccines was initiated in early January 2020 when the sequence of the virus became available and moved at record speed with one Phase I trial already starting in March 2020 and currently more than 180 vaccines in various stages of development. Phase I/II trial data is already available for several vaccine candidates and many have moved into Phase III trials. The data available so far suggests that effective and safe vaccines might become available within months rather than years.

10. 罗氏发布 III 期 EMPACTA 临床研究进展，IL-6 抑制剂雅美罗®(托珠单抗)改善重症 COVID-19 患者的临床疗效

Genentech finds right endpoint to show IL-6 benefit in COVID-19

来源：Biocentury

发布时间：2020-09-19

链接：

https://www.biocentury.com/article/630509?editionId=ckf90mvnk0kd00133pf5qn058&editionType=weekly

作者：STEPHEN HANSEN,编辑

DOI 或 PUBMED ID：

编译者：孔娟

中文摘要：

晚期新冠肺炎病患者表现出细胞因子风暴类似于接受 CAR T 疗法的癌症患者所经历的症状，在 CAR-T 疗法中 IL-6 抑制剂被证明是有效的。2020 年 9 月 18 日，罗氏集团宣布，III 期 EMPACTA 临床研究达到主要终点。该研究结果显示，新冠肺炎患者在标准治疗基础上联合雅美罗®(托珠单抗)，患者的机械通气或死亡进展比安慰剂加标准护理减少了 44%（p 值 = 0.0348）。截至第 28 天，雅美罗®(托珠单抗)组患者进展至行机械通气或死亡的累积比例为 12.2%，而安慰剂组为 19.3%。EMPACTA 研究中未发现雅美罗® (托珠单抗)新的安全性信号。EMPACTA 研究的另一个特点是以人群多样性为核心，入组的 389 名患者中，85%来自种族或少数民族群体，其中大多数是拉丁裔，同时也有相当比例的美国原住民和黑人群体。这项研究在美国、南非、肯尼亚、巴西、墨西哥和秘鲁进行。罗氏表示，计划与 FDA 和其他监管机构分享数据，以评估下一步措施。

Abstract：

The Genentech Inc. unit of Roche (SIX:ROG; OTCQX:RHHBY) said Friday that the Phase III EMPACTA trial of Actemra tocilizumab met the primary endpoint by showing a 44% reduction in progression to mechanical ventilation or death vs. placebo plus standard of care in patients with COVID-19 associated pneumonia (p=0.0348). But three prior Phase III trials of IL-6 inhibitors had all failed to demonstrate a clinical benefit. Each of these studies had similar primary

endpoints that looked for improvements in clinical status based on a seven-category ordinal scale. In late July, Genentech said that Actemra missed the primary endpoint of an improvement in clinical status vs. placebo in the Phase III COVACTA trial. Similarly, Kevzara sarilumab from partners Regeneron Pharmaceuticals Inc. (NASDAQ:REGN) and Sanofi (Euronext:SAN; NASDAQ:SNY) missed the primary endpoint in two Phase III trials assessing clinical improvement on a seven-category ordinal scale. One of the Kevzara trials enrolled patients who were already on mechanical ventilation (see "First Phase III Data for an IL-6 mAb in COVID-19 Disappoint"). In EMPACTA, Actemra repeated that result once more, failing to show improvement on the seven-category scheme as a secondary endpoint. It also failed to demonstrate benefit on two other secondary endpoints, mortality and time to hospital discharge. Where Actemra succeeded was reducing the need for mechanical ventilation, which alone can be a meaningful outcome for hospitalized patients. The EMPACTA study is also set apart by the fact that was the first Phase III trial for COVID-19 to target enrollment of racial and ethnic minorities, which have been disproportionately affected by the pandemic. Genentech said 85% of the study's 389 patients were from racial or ethnic minority groups, with the majority Hispanic. The study was conducted in the U.S., South Africa, Kenya, Brazil, Mexico and Peru (see Back to School 2020: "Biopharmas Must Address the Reality of Racial Disparities"). Roche said it plans to share the data with FDA and other regulators to assess the next steps. Actemra is also being tested in the Phase III REMDACTA trial in combination with Veklury remdesivir vs. Veklury alone. The primary endpoint is an improvement in clinical status as assessed by a seven-category ordinal scale. The fraction of patients who require mechanical ventilation and the number of ventilator-free days are secondary endpoints.

11. Baricitinib 治疗可解决 SARS-CoV-2 感染的恒河猴的下呼吸道炎症和中性粒细胞募集

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

来源：bioRxiv

发布时间：2020-09-16

链接：https://www.biorxiv.org/content/10.1101/2020.09.16.300277v1

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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.09.16.300277

编译者：刘焕珍

中文摘要：

SARS-CoV-2 诱导的高细胞血症和全身性炎症与疾病严重程度有关。Baricitinib 是一种临床批准的 JAK1/2 抑制剂，，具有很强的抗炎作用，目前正在 COVID -19 人类临床试验中进行研究。最近的报道表明，baricitinib 可能在限制病毒内吞作用方面也具有抗病毒活性。在这里，我们研究了 baricitinib 在 SARS-CoV-2 感染恒河猴的猕猴模型中的免疫和病毒学功效。使用 Baricitinib 不会减少从鼻和咽拭子、支气管肺泡灌洗液和组织中排出的病毒。两组之

间的 I 型 IFN 抗病毒反应和 SARS-CoV-2 特异性 T 细胞反应仍然相似。然而，重要的是，用 Baricitinib 治疗的动物显示出较低的免疫激活，减少了中性粒细胞向肺的浸润，降低了 NETosis 活性。此外，用 baricitinib 治疗的动物对引起炎症和嗜中性白细胞募集的细胞因子和趋化因子的肺泡巨噬细胞衍生的产生具有快速且显着的抑制作用。这些数据支持使用 Baricitinib 作为由 SARS-CoV-2 感染引起的严重炎症的一线治疗的有益作用，并阐明了其潜在的免疫学机制。

Abstract:
Effective therapeutics aimed at mitigating COVID-19 symptoms are urgently needed. SARS-CoV-2 induced hypercytokinemia and systemic inflammation are associated with disease severity. Baricitinib, a clinically approved JAK1/2 inhibitor with potent anti-inflammatory properties is currently being investigated in COVID-19 human clinical trials. Recent reports suggest that baricitinib may also have antiviral activity in limiting viral endocytosis. Here, we investigated the immunologic and virologic efficacy of baricitinib in a rhesus macaque model of SARS-CoV-2 infection. Viral shedding measured from nasal and throat swabs, bronchoalveolar lavages and tissues was not reduced with baricitinib. Type I IFN antiviral responses and SARS-CoV-2 specific T cell responses remained similar between the two groups. Importantly, however, animals treated with baricitinib showed reduced immune activation, decreased infiltration of neutrophils into the lung, reduced NETosis activity, and more limited lung pathology. Moreover, baricitinib treated animals had a rapid and remarkably potent suppression of alveolar macrophage derived production of cytokines and chemokines responsible for inflammation and neutrophil recruitment. These data support a beneficial role for, and elucidate the immunological mechanisms underlying, the use of baricitinib as a frontline treatment for severe inflammation induced by SARS-CoV-2 infection.

12. 随着冠状病毒疫苗试验的重新开始，科学家们松了一口气-但质疑缺乏透明度

Scientists relieved as coronavirus vaccine trial restarts — but question lack of transparency

来源：Nature 新闻稿

发布时间：2020-09-14

链接：https://www.nature.com/articles/d41586-020-02633-6

第一作者：David Cyranoski、Smriti Mallapaty

通讯作者：David Cyranoski、Smriti Mallapaty

通讯作者单位：Nature

DOI 或 PUBMED ID：10.1038/d41586-020-02633-6

编译者：张丽双

中文摘要：

短暂停顿后，英国已重启对牛津和阿斯利康的 AZD1222 疫苗试验，但有关事件的关键细节尚未公布。牛津大学表示，到目前为止，全球已有 18,000 人接种了该疫苗。于 6 月开始在英国进行的 III 期疗效试验旨在招募 10,000 人，而在巴西进行的 III 期试验则希望招募 5,000 名参与者。美国的试验于 8 月开始，旨在招募 30,000 名参与者。南非的 I / II 期安全性和有效性试验希望招募 2,000 名志愿者。

牛津大学和制药公司阿斯利康（AstraZeneca）于 9 月 6 日暂停了其候选疫苗的全球试验，因为参加该英国试验的人出现了不良反应。科学家们说，在大型试验中，停顿并不罕见，而且有望迅速恢复测试。“就像其他知道疫苗重要性的人一样，我很高兴试验能够继续进行，”世界卫生组织严重急性呼吸综合征的研究和流行病学部门负责人，退休的流感研究员克劳斯·斯托尔说。但是一些科学家批评试验赞助商没有发布更多有关暂停原因及其决策的信息。牛津大学和阿斯利康大学尚未公布导致试验中止的不良反应的详细信息，以及如何做出恢复英国研究的决定。巴西监管机构宣布，该疫苗的试验将于周一重新开始，但尚不清楚何时在南非和美国进行类似试验。

Abstract:
So far, some 18,000 people globally have received the vaccine, according to the University of Oxford. Phase III efficacy trials in the United Kingdom, which began in June, aim to recruit 10,000 people, and a phase III trial in Brazil hopes to recruit 5,000 participants. The US trial, which started in August, is aiming to recruit 30,000 participants. A phase I/II safety and efficacy trial in South Africa wants to recruit 2,000 volunteers.

13. 强生公司开始对 Janssen 的 COVID-19 疫苗候选进行关键的全球 3 期临床试验

Johnson & Johnson Initiates Pivotal Global Phase 3 Clinical Trial of Janssen’s COVID-19 Vaccine Candidate

来源：强生公司新闻稿

发布时间：2020-09-23

链接：https://www.jnj.com/johnson-johnson-initiates-pivotal-global-phase-3-clinical-trial-of-janssens-covid-19-vaccine-candidate

第一作者：Chris DelOrefice

通讯作者：Jake Sargent

通讯作者单位：强生

编译者：张丽双

中文摘要：
9 月 23 日周三，美国强生公司宣布其研发的新冠疫苗进入 3 期临床测试阶段，Janssen COVID-19 候选疫苗利用了该公司的 AdVac®技术平台制备的腺病毒载体疫苗，该平台还用于开发和制造 Janssen 的欧洲委员会批准的埃博拉疫苗，并构建其寨卡、RSV 和 HIV 候选疫苗。目前，强生计划招募 6 万人进行 3 期临床测试，测试将在全美 215 个地点以及南美地区的阿根廷、巴西、智利、秘鲁等地开放。并预计第一批 COVID-19 疫苗将在 2021 年初获得紧急使用授权，如果被证明是安全有效的。

Abstract:
The Phase 3 ENSEMBLE study is a randomized, double-blind, placebo-controlled clinical trial designed to evaluate the safety and efficacy of a single vaccine dose versus placebo in up to 60,000 adults 18 years old and older, including significant representation from those that are over age 60. The trial will include those both with and without comorbidities associated with an increased risk for progression to severe COVID-19, and will aim to enroll participants in Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa and the United States. In order to evaluate the effectiveness of Janssen’s COVID-19 vaccine, countries and clinical trial sites which have a high incidence of COVID-19 and

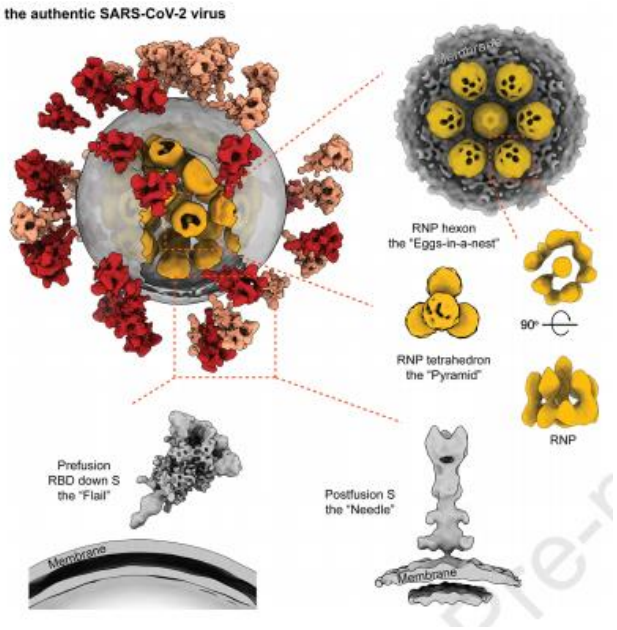
the ability to achieve a rapid initiation will be activated.
With Janssen's AdVac® technology, the vaccine, if successful, is estimated at launch to remain stable for two years at -20 ° C and at least three months at 2-8° C. This makes the vaccine candidate compatible with standard vaccine distribution channels and would not require new infrastructure to get it to the people who need it.

14. SARS-CoV-2 病毒的分子架构

Molecular architecture of the SARS-CoV-2 virus
来源：Cell
发布时间：2020-09-03
链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31159-4
第一作者：Hangping Yao, Yutong Song, Yong Chen, Nanping Wu, Jialu Xu
通讯作者：Sai Li
通讯作者单位：Tsinghua University,China
DOI 或 PUBMED ID：10.1016/j.cell.2020.09.018
编译者：宋珂
中文摘要：

导致 COVID-19 疫情的 SARS-CoV-2 是一种包膜病毒。尽管针对 SARS-CoV-2 病毒中各种蛋白的结构解析工作取得了很多新的进展，但完整病毒的详细架构仍有待研究。本文中，作者利用冷冻电子断层扫描（cryo-ET）和局部断层扫描图像平均（STA）技术，解析出了真实的 SARS-CoV-2 病毒中分子的组装形式。确定了 S 蛋白处于融合前以及融合后构象的天然结构，其平均分辨率为 8.7-11 Å。作者进一步通过质谱技术分析了天然 Spike 蛋白的 N 糖基化位点的多糖的组分。结果显示，天然多糖与重组糖蛋白多糖的整体加工状态高度相似。作者还解析了核糖核蛋白（RNP）以及 RNP 高度有序的聚集体的天然构象。总体而言，这些特征非常详细地描绘出了 SARS-CoV-2 病毒的架构，并阐明了该病毒如何在直径约 80 nm 的膜内空间中堆积了约 30 kb 长的单链 RNA。

结构数据：EMD-30426, EMD-30427, EMD-34028, EMD-34029, EMD-30430



Abstract:
SARS-CoV-2 is an enveloped virus responsible for the COVID-19 pandemic. Despite recent advances in the structural elucidation of SARS-CoV-2 proteins, detailed architecture of the intact virus remains to be unveiled. Here we report the molecular assembly of the authentic SARS-CoV-2 virus using cryo-electron tomography (cryo-ET) and subtomogram averaging (STA). Native structures of the S proteins in both pre- and postfusion conformations were determined to average resolutions of 8.7-11 Å. Compositions of the N-linked glycans from the native spikes were analyzed by mass-spectrometry, which revealed highly similar overall processing states of the native glycans to that of the recombinant glycoprotein glycans. The native conformation of the ribonucleoproteins (RNP) and its higher-order assemblies were revealed. Overall, these characterizations have revealed the architecture of the SARS-CoV-2 virus in exceptional detail, and shed lights on how the virus packs its ~30 kb long single-segmented RNA in the ~80 nm diameter lumen.

15. 蝙蝠和穿山甲中冠状病毒的 Spike 糖基化蛋白的结构为研究 SARS-CoV-2 进化提供了信息

Bat and pangolin coronavirus spike glycoprotein structures provide insights into SARS-CoV-2 evolution

来源：bioRxiv
发布时间：2020-09-22
链接：https://www.biorxiv.org/content/10.1101/2020.09.21.307439v1
第一作者：Shuyuan Zhang, Shuyuan Qiao, Jinfang Yu
通讯作者：Xinquan Wang
通讯作者单位：Tsinghua University, China
DOI 或 PUBMED ID：
编译者：宋珂
中文摘要：

冠状病毒的 Spike 糖基化蛋白负责识别宿主细胞受体，并能够介导病毒和宿主细胞膜融合，是病毒在跨物种传播和感染过程中最关键的蛋白。本文中，作者利用 cryo-EM 技术解析了与 SARS-CoV-2 密切相关的蝙蝠（RaTG13）和穿山甲（PCoV_GX）冠状病毒的 Spike 蛋白结构。在这两种 Spike 蛋白的三聚体中，三个 Spike 单体的受体结合结构域（RBD）均处于“向下”的构象，表明它们更倾向于处于这种未被受体结合激活的状态。然而，作者发现 PCoV_GX（而不是 RaTG13）的 Spike 蛋白在结合人源 ACE2 受体时，与 SARS-CoV-2 的 Spike 蛋白比较相似，并可以介导假病毒侵入细胞。通过结构和序列对比，作者确定了 RBD 中造成 RaTG13 和 PCoV_GX/SARS-CoV-2 Spike 蛋白的活性差异的关键残基，并预测 Spike 糖基化蛋白中的 N 糖基化位点的多糖充当了控制 RBD 构象的开关。现有的结果表明，SARS-CoV-2 病毒为了获得高效率的感染能力，需要沿着拥有更强的 RBD-ACE2 结合能力，以及高效的 RBD 构象采样能力的方向进化。

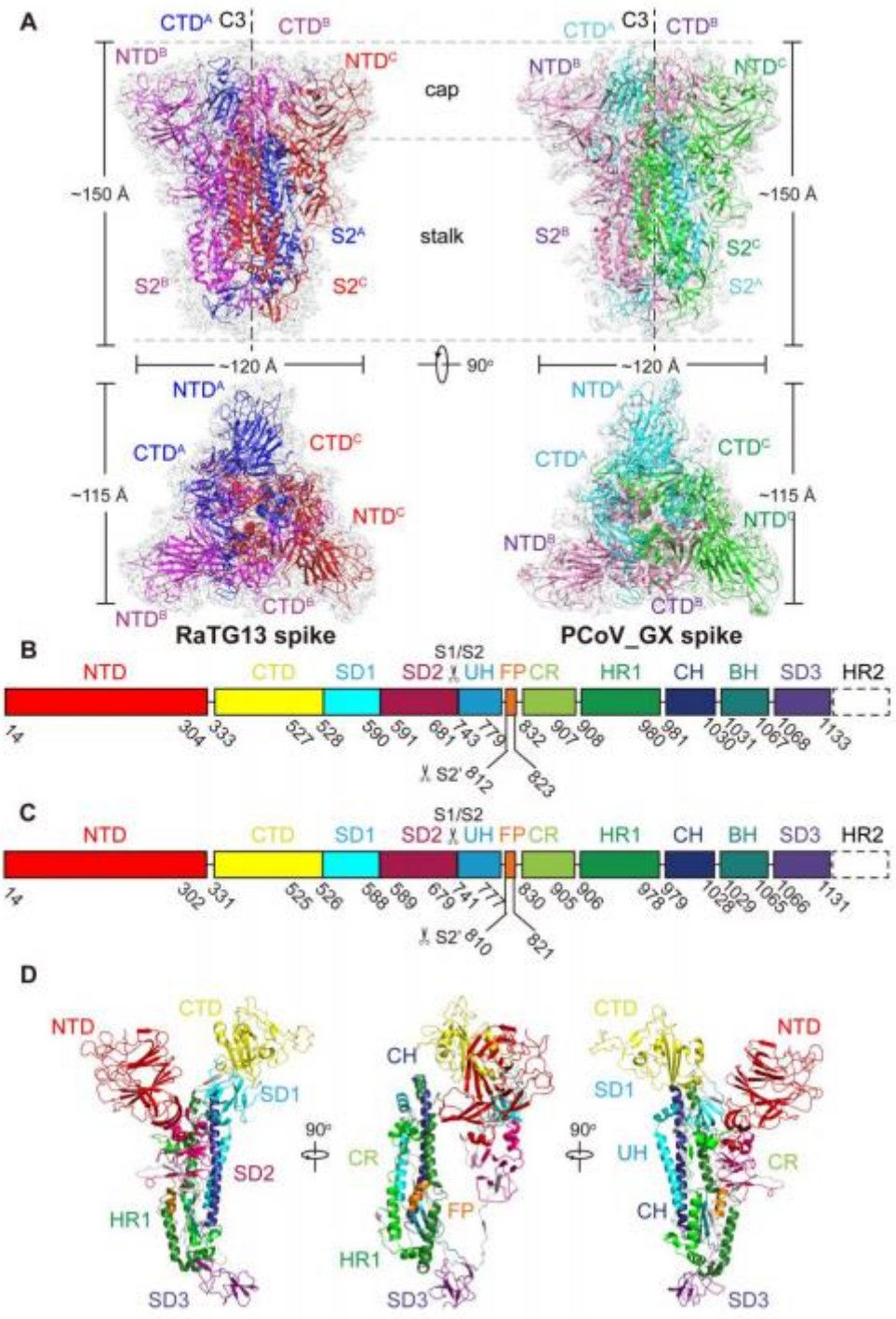


Fig.1 Over all str uctur es of the RaTG13 and PCoV_GX spike glycopr oteins. (A) Overall structures of RaTG13 and PCoV_GX spike glycoproteins shown in side view (upper panel) and top view (lower panel). Three monomers of the RaTG13 spike are colored magenta, red, and blue, respectively; three monomers of the PCoV_GX spike are colored hot pink, green and cyan, respectively. The cryo-EM maps are shown as a semitransparent surface. The trigonal axes are shown as black dashed lines. Visible segments of each monomer are labeled accordingly. The cap and stalk parts are partitioned by gray dashed lines. **(B)** Schematic representation of the RaTG13 spike monomer structural domains. The domains of RaTG13 are shown as boxes with the width related to the length of the amino acid sequence. The start and end amino acids of each segment are labeled. The position of the S1/S2 and S2’ cleavage

sites are indicated by scissors. NTD, N-terminal domain; CTD, C-terminal domain; SD1, subdomain 1; SD2, subdomain 2; UH, upstream helix; FP, fusion peptide; CR, connecting region; HR1, heptad repeat 1; CH, central helix; BH, β-hairpin; SD3, subdomain 3. **(C)** Schematic representation of the PCoV_GX spike monomer structural domains. The abbreviations of elements are the same as in **B. (D)** Cartoon diagrams depicting three orientations of the spike monomer colored as in **B** and **C**. As the RaTG13 and PCoV_GX spike monomers have extremely similar structures, thus only the RaTG13 spike monomer was used to show the detailed architecture.

Abstract:
In recognizing the host cellular receptor and mediating fusion of virus and cell membranes, the spike (S) glycoprotein of coronaviruses is the most critical viral protein for cross-species transmission and infection. Here we determined the cryo-EM structures of the spikes from bat (RaTG13) and pangolin (PCoV_GX) coronaviruses, which are closely related to SARS-CoV-2. All three receptor-binding domains (RBDs) of these two spike trimers are in the "down" conformation, indicating they are more prone to adopt this receptor-binding inactive state. However, we found that the PCoV_GX, but not the RaTG13, spike is comparable to the SARS-CoV-2 spike in binding the human ACE2 receptor and supporting pseudovirus cell entry. Through structure and sequence comparisons, we identified critical residues in the RBD that underlie the different activities of the RaTG13 and PCoV_GX/SARS-CoV-2 spikes and propose that N-linked glycans serve as conformational control elements of the RBD. These results collectively indicate that strong RBD-ACE2 binding and efficient RBD conformational sampling are required for the evolution of SARS-CoV-2 to gain highly efficient infection.

16. 锁定结构的 SARS-CoV-2 刺突蛋白的自由脂肪酸结合口袋

Free fatty acid binding pocket in the locked structure of SARS-CoV-2 spike protein

来源：science

发布时间：2020-09-21

第一作者：Christine Toelzer

通讯作者：Christiane Schaffitzel

通讯作者单位：University of Bristol, UK

链接：https://science.sciencemag.org/content/early/202/09/18/science.abd3255

编译：蒋立春

中文摘要：
作者们解析的 SARS-CoV-2 刺突蛋白的 2.85Å 的冷冻电镜结构揭示刺突蛋白的受体结合区域（RBDs）在三个结合口袋和人体必需的自由脂肪酸亚油酸紧密结合。这种口袋也存在于高致病性的冠状病毒 SARS-CoV 和 MERS-CoV。亚油酸稳定了锁住的 S 刺突蛋白的构象，在体外可以降低其和 ACE2 的结合。在人的细胞实验中，添加亚油酸可以和瑞德西韦起到协同抑制 SARS-CoV-2 的复制。该研究中的结构研究表明了亚油酸和刺突 S 蛋白的直接联系，干预亚油酸和 SARS-CoV-2 的结合可以作为抑制病毒的策略。

Abstract:
COVID-19, caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-

2), represents a global crisis. Key to SARS-CoV-2 therapeutic development is unraveling the mechanisms driving high infectivity, broad tissue tropism and severe pathology. Our 2.85 Å cryo-EM structure of SARS-CoV-2 spike (S) glycoprotein reveals that the receptor binding domains (RBDs) tightly bind the essential free fatty acid (FFA) linoleic acid (LA) in three composite binding pockets. The pocket also appears to be present in the highly pathogenic coronaviruses SARS-CoV and MERS-CoV. LA binding stabilizes a locked S conformation giving rise to reduced ACE2 interaction in vitro. In human cells, LA supplementation synergizes with the COVID-19 drug remdesivir, suppressing SARS-CoV-2 replication. Our structure directly links LA and S, setting the stage for intervention strategies targeting LA binding by SARS-CoV-2.

17. 人类常见的遗传变异影响体外对 SARS-CoV-2 感染的易感性

Common genetic variation in humans impacts in vitro susceptibility to SARS-CoV-2 infection

来源：bioRxiv

发布时间：2020-09-21

链接：https://www.biorxiv.org/content/10.1101/2020.09.20.300574v2

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通讯作者：Schahram Akbarian, Kristen J. Brennand

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DOI 或 PUBMED ID：

编译者：宋张悦

中文摘要：

世界正处于新型高传染性 SARS-CoV-2 引起的持续大流行之中。在受影响的组织以及对 SARS-CoV-2 反应的严重程度中，存在着显著的个体间差异。目前尚不清楚为什么有些健康的人会出现严重的 SARS-CoV-2 临床并发症，而有些人却没有。我们推测，除了病毒载量和宿主抗体库，宿主的遗传变异也影响感染的脆弱性。在此我们应用基于人诱导多能干细胞(hiPSC)的模型和 CRISPR-engineering 来探索 SARS-CoV-2 的宿主遗传学。我们证明了**一个单核苷酸多态性(rs4702)，在人群中普遍存在，位于蛋白酶 FURIN 的 3'UTR，影响 SARS-CoV-2 体外肺泡和神经元感染。**因此，我们提供了一个理论验证的发现，常见的遗传变异可以影响病毒感染，因此可能导致 SARS-CoV-2 的临床异质性。正在进行的基因研究将有助于更好地识别高危人群，预测临床并发症，并促进可能治疗疾病的药物的发现。

Supplemental Table 1. Excess of nominally significant GWAS variants within the SARS-CoV-2 host gene cis-regions when comparing individuals with COVID-19 to the general population.

Gene	Study name	Phenotype	Case number	Control number	N SNPs in cis-region (+/- 1e06)	N nominal (p<0.05)	% reaching nominal significance	binomial p value
ACE2	COVID19_HGI_ANA_B2	hospitalized covid vs. population	3199	897488	4839	480	9.919405	3.28E-44
ACE2	COVID19_HGI_ANA_C2	covid vs. population	6696	1073072	5281	497	9.411096	1.02E-39
CD147	COVID19_HGI_ANA_D1	predicted covid from self-reported symptoms vs. predicted or self-reported non-covid	1865	29174	6456	584	9.045849	2.54E-41
FURIN	COVID19_HGI_ANA_B2	hospitalized covid vs. population	3199	897488	11556	869	7.519903	3.57E-31
TMPRSS2	COVID19_HGI_ANA_B2	hospitalized covid vs. population	3199	897488	14047	919	6.542322	1.00E-15
TMPRSS2	COVID19_HGI_ANA_C1	covid vs. lab/self-reported negative	3523	36634	20141	1104	5.481356	0.00201
FURIN	COVID19_HGI_ANA_C1	covid vs. lab/self-reported negative	3523	36634	17346	921	5.309581	6.00E-02
TMPRSS2	COVID19_HGI_ANA_C2	covid vs. population	6696	1073072		21814	4.776749	
TMPRSS2	COVID19_HGI_ANA_D1	predicted covid from self-reported symptoms vs. predicted or self-reported non-covid	1865	29174		12030	4.763092	
CD147	COVID19_HGI_ANA_C2	covid vs. population	6696	1073072		14419	4.722935	
CD147	COVID19_HGI_ANA_B2	hospitalized covid vs. population	3199	897488		9554	4.406531	
CD147	COVID19_HGI_ANA_B2	hospitalized covid vs. population	3199	897488		9554	4.406531	
CD147	COVID19_HGI_ANA_C1	covid vs. lab/self-reported negative	3523	36634		13358	3.960174	
FURIN	COVID19_HGI_ANA_C2	covid vs. population	6696	1073072		19136	3.88796	
ACE2	COVID19_HGI_ANA_D1	predicted covid from self-reported symptoms vs. predicted or self-reported non-covid	1865	29174		532	3.383459	
ACE2	COVID19_HGI_ANA_C1	covid vs. lab/self-reported negative	3523	36634		4098	3.29429	
FURIN	COVID19_HGI_ANA_D1	predicted covid from self-reported symptoms vs. predicted or self-reported non-covid	1865	29174		9432	3.042833	

Abstract
The world is in the midst of an ongoing pandemic caused by the novel and highly contagious SARS-CoV-2. There is marked inter-individual variability in the tissues affected as well as the severity of response to SARS-CoV-2. It is unclear why some otherwise healthy individuals experience profound clinical complications to SARS-CoV-2 and others do not. We hypothesize that, in addition to viral load and host antibody repertoire, host genetic variants also impact vulnerability to infection. Here we apply human induced pluripotent stem cell (hiPSC)-based models and CRISPR-engineering to explore the host genetics of SARS-CoV-2. We demonstrate that a single nucleotide polymorphism (rs4702), common in the population at large, and located in the 3'UTR of the protease FURIN, impacts alveolar and neuron infection by SARS-CoV-2 in vitro. Thus, we provide a proof-of-principle finding that common genetic variation can impact viral infection, and so potentially contribute to clinical heterogeneity in SARS-CoV-2. Ongoing genetic studies will help to better identify high-risk individuals, predict clinical complications, and facilitate the discovery of drugs that might treat disease.

18. 利用环状聚合酶延伸反应建立 SARS-CoV-2 的反向遗传学体系

Establishment of a reverse genetics system for SARS-CoV-2 using circular polymerase extension reaction

来源：bioRxiv

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链接：https://www.biorxiv.org/content/10.1101/2020.09.23.309849v1

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DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

SARS-CoV-2 已被确认为 COVID-19 的病原体。虽然急需开发特异性治疗方法和疫苗，但缺乏方便的诱变方法限制了 SARS-CoV-2 的功能分析。在本研究中，我们建立了一种基于 PCR 的无需依赖细菌的方法来产生 SARS-CoV-2 感染性克隆。通过环状聚合酶延伸反应（CPER）组装 10 个 SARS-CoV-2 cDNA 片段，并将得到的环状基因组转染到易感细胞中，可获得高滴度、高精度的重组 SARS-CoV-2（如下图 1 所示）。值得注意的是，报告病毒和突变病毒的感染性克隆的构建可以通过两个简单的步骤完成：通过 PCR 将报告基因或突变导入所需的 DNA 片段（约 5000 个碱基对），然后通过 CPER 组装 DNA 片段。我们希望我们的反向遗传学系统将有助于进一步了解 SARS-CoV-2。

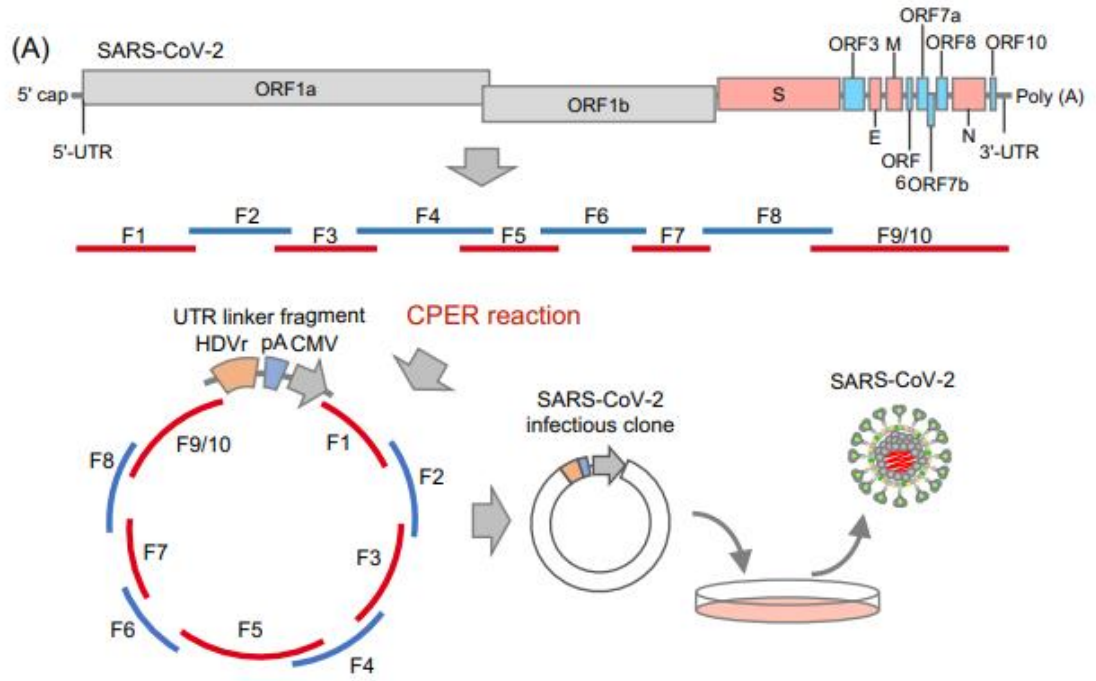

Figure 1. Establishment of CPER-based reverse genetics for SARS-CoV-2. (A) Schematic representation of a CPER approach for the generation of recombinant SARS-CoV-2. A total of 9 fragments (F1to F8, and F9/10) covering the full-length of the SARS-CoV-2 genome were amplified, then assembled with a UTR linker fragment including the HDVr, the BGH polyA signal and the CMV promoter by CPER. The resulting CPER products were transfected into the susceptible cells.

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been identified as the causative agent of coronavirus disease 2019 (COVID-19). While the development of specific treatments and a vaccine is urgently needed, functional analyses of SARS-CoV-2 have been limited by the lack of convenient mutagenesis methods. In this study, we established a PCR-based, bacterium-free method to generate SARS-CoV-2 infectious clones. Recombinant SARS-CoV-2 could be rescued at high titer with high accuracy after assembling 10 SARS-CoV-2 cDNA fragments by circular polymerase extension reaction (CPER) and transfection of the resulting circular genome into susceptible cells. Notably, the construction of infectious clones for reporter viruses and mutant viruses could be completed in two simple steps: introduction of reporter genes or mutations into the desirable DNA fragments (~5,000 base pairs) by PCR and assembly of the DNA fragments by CPER. We hope that our reverse genetics system will contribute to the further understanding of SARS-CoV-2.

19. 基础 T 细胞免疫表型预测 SARS-CoV 感染的病毒学和疾病控制

Baseline T cell immune phenotypes predict virologic and disease control upon SARS-CoV infection

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中文摘要：
在这里，我们利用来自感染 SARS-CoV 的合作杂交（CC）的遗传多样性小鼠的筛选数据来确定循环基线 T 细胞特征是否与病毒控制的缺乏和感染后的严重疾病有关。SARS-CoV 感染 CC 小鼠可导致多种病毒载量轨迹和疾病转归。此外，肺部病毒的早期控制与跨菌株感染前活化的 CD4 和 CD8 T 细胞以及调节性 T 细胞的数量增加有关。T 细胞在 TNFa 上表达 IFNg 和 IL17 的基本倾向也与早期病毒控制有关。总的来说，基线时循环 T 细胞的失调、促炎性信号与感染后的严重疾病相关。虽然未来需要对感染 SARS-CoV-2 之前的人体样本进行研究，但我们对 SARS-CoV 感染小鼠的研究证明了循环 T 细胞信号可以预测 SARS-CoV 感染后的临床和病毒学结果。在人类中识别基本免疫预测因子可使识别感染后出现严重临床和病毒性后果的最高风险的个人，因此，这些人可能从现有的临床干预措施中获益最大，以限制感染和疾病。总结　我们使用小鼠适应型 SARS-CoV 协同交叉感染的不同基因小鼠的筛选，结合综合感染前免疫表型，确定 SARS-CoV 感染后严重病毒学和临床结局的基线循环免疫相关因素。

Abstract:
The COVID-19 pandemic has revealed that infection with SARS-CoV-2 can result in a wide range of clinical outcomes in humans, from asymptomatic or mild disease to severe disease that can require mechanical ventilation. An incomplete understanding of immune correlates of protection represents a major barrier to the design of vaccines and therapeutic approaches to prevent infection or limit disease. This deficit is largely due to the lack of prospectively collected, pre-infection samples from indiviuals that go on to become infected with SARS-CoV-2. Here, we utilized data from a screen of genetically diverse mice from the Collaborative Cross (CC) infected with SARS-CoV to determine whether circulating baseline T cell signatures are associated with a lack of viral control and severe disease upon infection. SARS-CoV infection of CC mice results in a variety of viral load trajectories and disease outcomes. Further, early control of virus in the lung correlates with an increased abundance of activated CD4 and CD8 T cells and regulatory T cells prior to infections across strains. A basal propensity of T cells to express IFNg and IL17 over TNFa also correlated with early viral control. Overall, a dysregulated, pro-inflammatory signature of circulating T cells at baseline was associated with severe disease upon infection. While future studies of human samples prior to infection with SARS-CoV-2 are required, our studies in mice with SARS-CoV serve as proof of concept that circulating T cell signatures at baseline can predict clinical and virologic outcomes upon SARS-CoV infection. Identification of basal immune predictors in humans could allow for identification of individuals at highest risk of severe clinical and virologic

outcomes upon infection, who may thus most benefit from available clinical interventions to restrict infection and disease.

Summary We used a screen of genetically diverse mice from the Collaborative Cross infected with mouse-adapted SARS-CoV in combination with comprehensive pre-infection immunophenotyping to identify baseline circulating immune correlates of severe virologic and clinical outcomes upon SARS-CoV infection.

20. 恒河猴和食蟹猴作为 COVID-19 模型的比较

Comparison of Rhesus and Cynomolgus macaques as an authentic model for COVID-19

来源：biorxiv

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中文摘要：

新型冠状病毒 SARS-CoV-2 已被确认为是当前 COVID-19 大流行的致病因子。动物模型，尤其是非人灵长类动物，对于了解新出现疾病的发病机制，新型疫苗和疗法的安全性和有效性至关重要。该研究发现 SARS-CoV-2 在上呼吸道和下呼吸道复制，并导致恒河猴和食蟹猴的肺部病变，类似于人类 COVID-19 的轻度临床病例。两个物种对 SARS-CoV-2 的免疫反应也相似，与轻度感染和恢复期人类患者的免疫反应相同。重要的是，该研究设计了一种新的肺部组织病理学评分方法，它将提供一个指标，使关键终点的决策更加明确。之前的研究说明，恒河猴被认为是最佳的研究物种，该研究又提供了令人信服的证据，这两种猕猴代表了在大多数人类群体中观察到的 COVID-19 的轻度到中度症状，这两种物种都应该被用来评估新型和重新利用的 SARS-CoV-2 干预措施的安全性和有效性。食蟹猴的模型使用将大大减轻目前恒河猴库存的压力。

Abstract:

A novel coronavirus, SARS-CoV-2, has been identified as the causative agent of the current COVID-19 pandemic. Animal models, and in particular non-human primates, are essential to understand the pathogenesis of emerging diseases and to the safety and efficacy of novel vaccines and therapeutics. Here, we show that SARS-CoV-2 replicates in the upper and lower respiratory tract and causes pulmonary lesions in both rhesus and cynomolgus macaques, resembling the mild clinical cases of COVID-19 in humans. Immune responses against SARS-CoV-2 were also similar in both species and equivalent to those reported in milder infections and convalescent human patients. Importantly, we have devised a new method for lung histopathology scoring that will provide a metric to enable clearer decision making for this key endpoint. In contrast to prior publications, in which rhesus are accepted to be the optimal study species, we provide convincing evidence that both macaque species authentically represent mild to moderate forms of

COVID-19 observed in the majority of the human population and both species should be used to evaluate the safety and efficacy of novel and repurposed interventions against SARS-CoV-2. Accessing cynomolgus macaques will greatly alleviate the pressures on current rhesus stocks.

21. Coronascape ：COVID-19 相关 OMICS 数据

由诺华、UCSD 和加州 SBP 研究所联合构建的 Coronascape 系统，收录了 21 个研究里在 28 个组织和细胞系的采集的 7 种组学技术的数据，包括了 362 个和 Covid-19 相关的宿主基因列表。

链接:https://metascape.org/COVID

About：

Cronoascape is a free COVID-related reference host gene lists collected from published and unpublished studies, processed and curated by the Metascape team. Users can compare their own gene list with a selected panel of COVID lists using the powerful Metascape Express Analysis tool. There are three basic steps, provide your gene list, use purple tabs to select reference lists, then run Metascape Analysis. To learn more regarding the underlying bioinformatics analysis, please visit Metascape web site.

This system includes 362 COVID gene lists generated with 7 technologies from 28 tissues and cell lines and 21 studies.