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 10 月 29 日疫情

数据来源：WHO

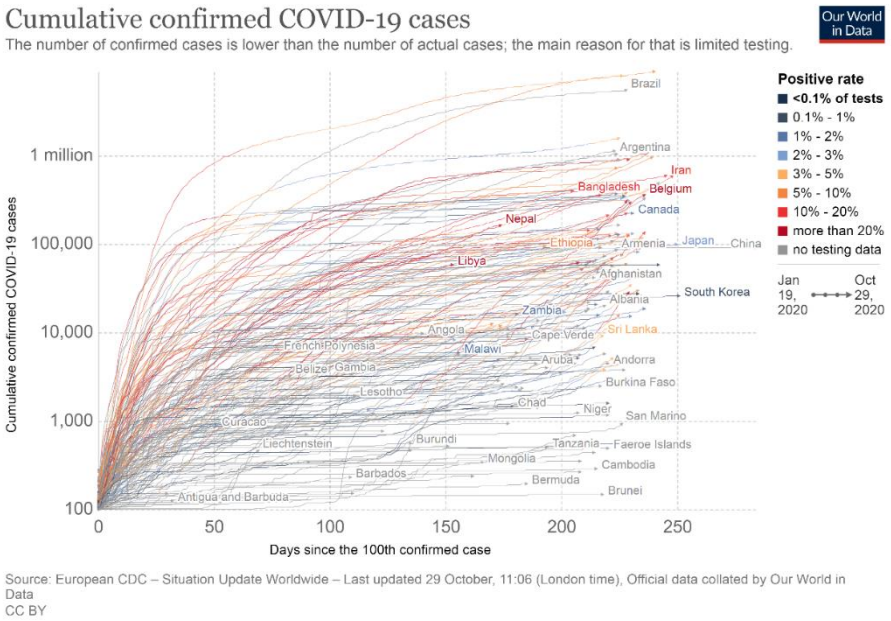
发布时间：2020 年 10 月 29 日北京时间下午 4 点

链接：https://covid19.who.int/

根据 WHO 提供的数据，2020 年 10 月 29 日全球累计确诊新型冠状病毒病人 **44,351,506** 例，当日新增确诊 **479,417** 例，累计死亡 **1,171,255** 例，当日新增死亡 **7,126**。

美国累计确诊**超过 9，000，000** 例，单日新增**超过 90，000** 例。

中国累计确诊 **91,821** 例，累计死亡 **4,746** 例，当日新增确诊 **49** 例，新增死亡 **0** 例。



Source: European CDC – Situation Update Worldwide – Last updated 29 October, 11:06 (London time), Official data collated by Our World in Data
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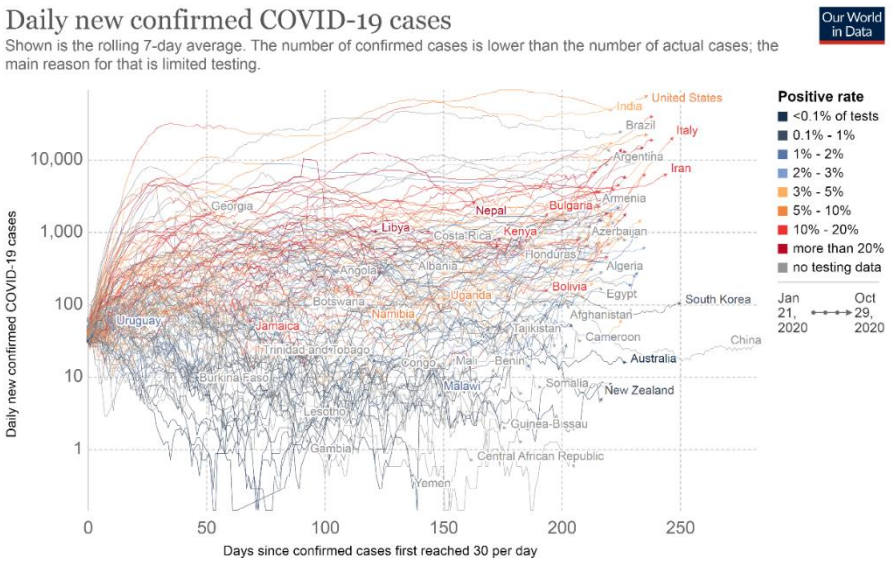
重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



Source: European CDC – Situation Update Worldwide – Last updated 29 October, 11:06 (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 29 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 新疆喀什：目前已可基本排除疏附县疫情蔓延扩散的可能性

转自丁香园公众号：https://mp.weixin.qq.com/s/W9Evv4-hxVwL1M2_4_GNRg

10 月 28 日下午，新疆维吾尔自治区人民政府新闻办公室召开喀什疫情第四场新闻发布会，通报新疆喀什地区疏附县疫情相关情况。

喀什地区疾病预防控制中心副主任王希江介绍：10 月 27 日 0 时至 24 时，喀什地区疏附县新增新冠肺炎确诊病例 22 例，全部为无症状感染者转确诊，截至 10 月 27 日 24 时，喀什市现有确诊病例 22 例，无症状感染者 161 例，均为疏附县报告，24 日报告首例无症状感染者。

当地经过 3 昼夜的连续奋战，到 27 日 17 时完成喀什地区全员核酸检测，除已报告的疏附县 183 人呈阳性外，其余均为阴性，目前已可以基本排除疫情蔓延扩散的可能性。（来源：央视新闻）

3. 北京新发地疫情病毒源头最新结论：可能来自受污染冷链进口食品

转自丁香园公众号：https://mp.weixin.qq.com/s/W9Evv4-hxVwL1M2_4_GNRg

研究文章链接：

https://academic.oup.com/nsr/advance-article/doi/10.1093/nsr/nwaa264/5936602

Cold-chain food contamination as the possible origin of Covid-19 resurgence in Beijing

10 月 23 日，清华大学、北京市疾病预防控制中心、中国医学科学院病原生物学研究所、北京大学、中国科学院北京基因组研究所联合在 *National Science Review* 发文，通过分析相关病例、环境与食品等样品的核酸测序和病毒基因组序列，结合全面的流行病学调查和大数据分析，揭示了北京新发地市场聚集性疫情中的病毒源头极有可能是境外疫情高发区的冷链进口食品。

研究指出，虽然尚不清楚三文鱼身上的病毒载量是否足以造成感染，但食物和环境污染的风险仍然存在。对于那些社区传播得到控制的国家来说，病毒有可能通过冷链运输被污染物导

致再次传播，并可能引发疫情。因此，应将监控冷链进口产品、尤其是来自新冠流行地区的冷链产品，纳入预防、控制新冠的区域指南中。（来源：*National Science Review*）

4. 对冰岛人群 SARS-CoV-2 的体液免疫应答的研究

Humoral Immune Response to SARS-CoV-2 in Iceland

来源：NEJM

发布时间：2020-10-29

链接：https://www.nejm.org/doi/full/10.1056/NEJMoa2026116?query=featured_home

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通讯作者单位：Amgen

DOI 或 PUBMED ID：10.1056/NEJMoa2026116

编译者：张丽双

中文摘要：

对冰岛 30576 人血清样本中的抗体进行了检测，在 1797 名从 SARS-CoV-2 感染中恢复的患者中，1215 名受检者中有 1107 人（91.1%）血清阳性；经 qPCR 确诊后 2 个月内，经两次 pan-Ig 检测的抗病毒抗体滴度升高，并在确诊后 4 个月内，抗 SARS-2 抗体没有下降。在被隔离者中，血清阳性率为 2.3%；在不明接触者中，阳性率为 0.3%。估计有 0.9%的冰岛人感染了 SARS-CoV-2，其中 0.3%的人是致命的。研究人员估计，在冰岛，56%的 SARS-CoV-2 感染被 qPCR 确诊，44%的 SARS-CoV-2 感染者未经 qPCR 确诊。14%发生在未经 qPCR 检测的隔离人群中（或者检测为阴性结果），30%发生在隔离区之外，没有进行 qPCR 检测的人。

Abstract:

BACKGROUND

Little is known about the nature and durability of the humoral immune response to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

METHODS

We measured antibodies in serum samples from 30,576 persons in Iceland, using six assays (including two pan-immunoglobulin [pan-Ig] assays), and we determined that the appropriate measure of seropositivity was a positive result with both pan-Ig assays. We tested 2102 samples collected from 1237 persons up to 4 months after diagnosis by a quantitative polymerase-chain-reaction (qPCR) assay. We measured antibodies in 4222 quarantined persons who had been exposed to SARS-CoV-2 and in 23,452 persons not known to have been exposed.

RESULTS

Of the 1797 persons who had recovered from SARS-CoV-2 infection, 1107 of the 1215 who were tested (91.1%) were seropositive; antiviral antibody titers assayed by two pan-Ig assays increased during 2 months after diagnosis by qPCR and remained on a plateau for the remainder of the study. Of quarantined persons, 2.3% were seropositive; of those with unknown exposure, 0.3% were positive. We estimate that 0.9% of Icelanders were infected with SARS-CoV-2 and that the infection was fatal in 0.3%. We also estimate that 56% of all SARS-CoV-2 infections in Iceland had been diagnosed with qPCR, 14% had occurred in quarantined persons who had not been tested with qPCR (or who had not received a positive result, if tested), and 30% had occurred in persons outside quarantine

and not tested with qPCR.
CONCLUSIONS
Our results indicate that antiviral antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis. We estimate that the risk of death from infection was 0.3% and that 44% of persons infected with SARS-CoV-2 in Iceland were not diagnosed by qPCR.

5. SARS-CoV-2 感染可产生持续数月的稳定中和抗体

Robust neutralizing antibodies to SARS-CoV-2 infection persist for months
简报 7 月 24 日第 3 条报道过该工作的预印本
链接：https://science.sciencemag.org/content/early/2020/10/27/science.abd7728

6. 通过新的 SARS-CoV-2 全基因组测序反向互补 PCR 技术能快速和准确的疫情分析

Novel SARS-CoV-2 Whole-genome sequencing technique using Reverse Complement PCR enables fast and accurate outbreak analysis
来源：bioRxiv
发布时间：2020-10-29
链接：https://www.biorxiv.org/content/10.1101/2020.10.29.360578v1.full.pdf
第一作者：Femke Wolters, Jordy P.M. Coolen
通讯作者：Femke Wolters
通讯作者单位：Radboud university medical center, Geert Grooteplein Zuid 10, 6525 GA, Nijmegen, The Netherlands
DOI 或 PUBMED ID：
编译者：宋张悦
中文摘要：

目前 SARS-CoV-2 的传播率仍在上升，许多国家正面临第二波感染。快速的 SARS-CoV-2 全基因组测序(WGS)通常是不可用的，但可以支持公共卫生组织和医院监测和确定传播链。本文报道了一种新的用于 SARS-CoV-2 WGS 的反向互补聚合酶链式反应(RC-PCR)技术（Figure 1)。这项技术的独特之处在于，它可以在单一 PCR 中制备文库，节省时间和资源，并实现高通量筛选。这项研究包含了在 2020 年 3 月至 9 月期间，检测出 SARS-CoV-2 阳性的共 173 份样本。在包含卫生工作者和患者样本的六个预定义集群上测试了 RC-PCR WGS 在公共卫生服务和医院设置中用于疫情分析的适用性。RC-PCR 得到 146 份样品的 WGS 数据。对 Ct 值最大为 32 的样本，其基因组覆盖率高达 98,2%。6 个疑似群集中的 3 个已得到完全确认，而在其他群集中，4 名医疗工作者没有关联。重要的是，在公共卫生服务样本中确认了以前未知的传播链。这些发现证实了用于 SARS-CoV-2 测序的 RC-PCR 技术在疫情分析和监测中的可靠性和适用性。

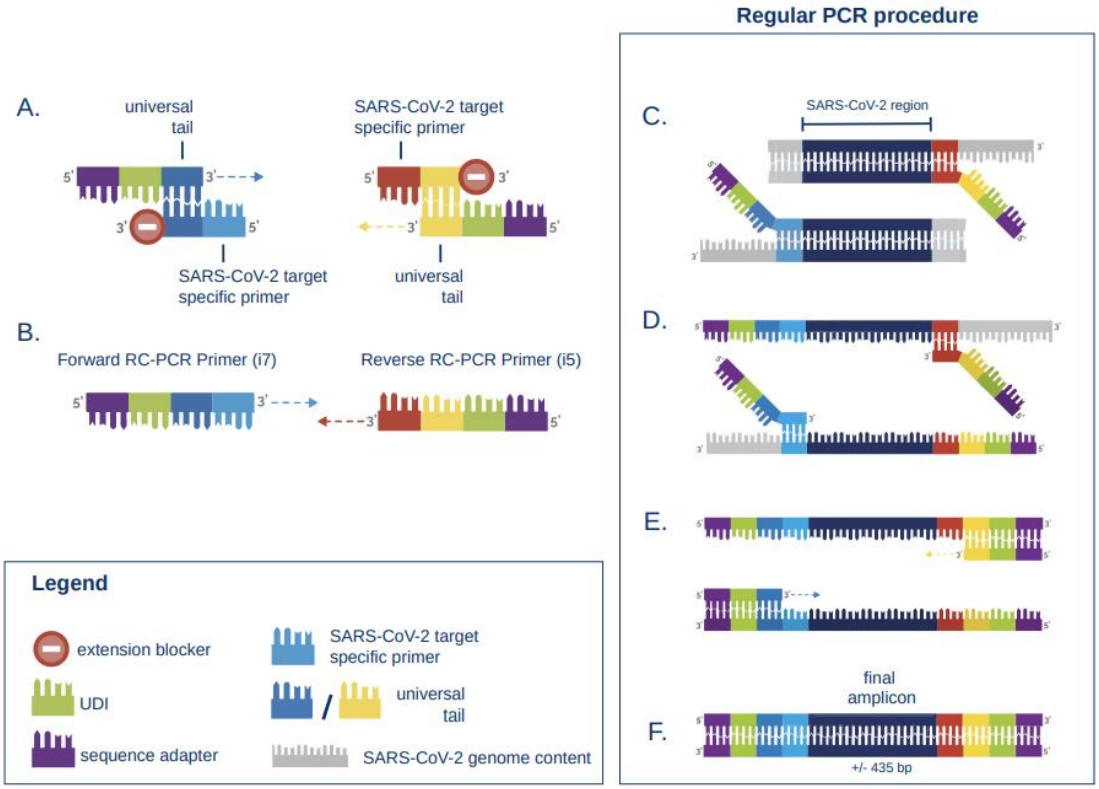


Figure 1. Schematic representation of the RC-PCR technology to WGS SARS-CoV-2. The protocol consists of one single PCR-like reaction consisting of 2 steps. The schematic is adapted from Kieser et al. (Kieser et al., 2020) A. Two types of oligo's are present, 1) the universal barcoding primer which includes a Unique Dual Index (UDI), sequence adapter, and universal tail. 2) the RC probe which contains an extension blocker, universal sequence, and the reverse complement of the SARS-CoV-2 genomic target sequence. B. The universal tail sequences anneal and form a SARS-CoV-2 specific PCR primer. C - E. A regular PCR in which the SARS-CoV-2 specific amplicons are created. F. The final amplicons are ready to sequence on an Illumina sequencer.

Abstract:

Current transmission rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are still increasing and many countries are facing second waves of infections. Rapid SARS-CoV-2 whole genome sequencing (WGS) is often unavailable but could support public health organizations and hospitals in monitoring and determining transmission links. Here we report a novel reverse complement polymerase chain reaction (RC-PCR) technology for WGS of SARS-CoV-2. This technique is unique as it enables library preparation in a single PCR saving time, resources and enables high throughput screening. A total of 173 samples tested positive for SARS-CoV-2 between March and September 2020 were included. RC-PCR WGS applicability for outbreak analysis in public health service and hospital settings was tested on six predefined clusters containing samples of healthcare workers and patients. RC-PCR resulted in WGS data for 146 samples. It showed a genome coverage of up to 98,2% for samples with a maximum Ct value of 32. Three out of six suspected clusters were fully confirmed, while in other

clusters four healthcare workers were not associated. Importantly, a previously unknown chain of transmission was confirmed in the public health service samples. These findings confirm the reliability and applicability of the RC-PCR technology for SARS-CoV-2 sequencing in outbreak analysis and surveillance.

7. 多组学研究揭示了 COVID-19 从轻症急转为中度症状的特征

Multi-omics resolves a sharp disease-state shift between mild and moderate COVID-19

来源：Cell

发布时间：2020-10-26

链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31444-6

第一作者：Yapeng Su

通讯作者：James R Heath

通讯作者单位：ISB, Seattle, USA

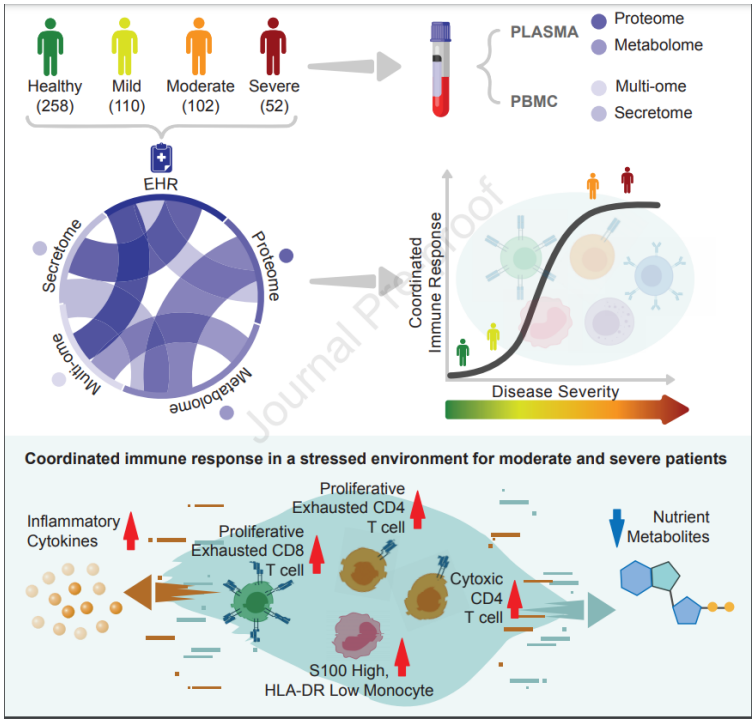
DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2020.10.037

编译者：蒋立春

注：简报 7 月 31 日第 10 条报道过该工作预印本，该文相比预印本增加了分析的病人数目（从 50 人增加到 139 人）

中文摘要：

作者对 139 个代表了疾病的各种不同严重程度 COVID-19 病人的临床检验结果、免疫细胞以及在确诊之后一个星期的一系列血样的血浆多组学分析的结果进行了整合分析。作者们鉴定出一个在轻症和中度症状之间的一个主要的转折，此时炎症信号增加并且伴随特定族的代谢物和代谢过程缺乏。在压力之下的中度症状的血浆环境中，出现了多种不同寻常的免疫细胞表型，这些表型随疾病症状加重而放大。作者们将 120，000 个免疫特征压缩为一个特征值来抓取不同免疫细胞群协同应对 SARS-CoV-2 的特征。这个免疫反应特征值可以独立反映主要血浆成分变化、凝血的临床数据以及从轻微症状到中度症状的突变。这个研究提示中度症状可能可以是治疗干预最有效的场景。



Abstract:
We present an integrated analysis of the clinical measurements, immune cells and plasma multi-omics of 139 COVID-19 patients representing all levels of disease severity, from serial blood draws collected during the first week of infection following diagnosis. We identify a major shift between mild and moderate disease, at which point elevated inflammatory signaling is accompanied by the loss of specific classes of metabolites and metabolic processes. Within this stressed plasma environment at moderate disease, multiple unusual immune cell phenotypes emerge and amplify with increasing disease severity. We condensed over 120,000 immune features into a single axis to capture how different immune cell classes coordinate in response to SARS-CoV-2. This immune-response axis independently aligns with the major plasma composition changes, with clinical metrics of blood clotting, and with the sharp transition between mild and moderate disease. This study suggests that moderate disease may provide the most effective setting for therapeutic intervention.

8. 增强剂量加强 COVID-19 疫苗候选株 chadox1ncov-19 在老年小鼠中的免疫原性

A booster dose enhances immunogenicity of the COVID-19 vaccine candidate ChAdOx1 nCoV-19 in aged mice

来源：bioRxiv

发布时间：2020-10-27

链接：https://www.biorxiv.org/content/10.1101/2020.10.27.357426v1

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DOI 或 PUBMED ID：

编译者：张鹏伟

中文摘要：
SARS-CoV-2 的蔓延引起了全球性大流行，几乎影响了人类生活的各个方面。有效 COVID-19 疫苗的开发可以限制感染引起的发病率和死亡率，并可以放松社会隔离措施。年龄是 SARS-CoV-2 感染后健康状况不佳的最重要危险因素之一，因此，希望任何新的候选疫苗都能引起老年人强烈的免疫反应。在这里，我们测试了腺病毒载体疫苗 ChAdOx1 nCoV-19（AZD-1222）在老年小鼠中的免疫原性。我们发现，单剂量的这种疫苗可在老年小鼠中诱导细胞和体液免疫，但程度要比年轻成年小鼠低。此外，我们报道第二剂可增强老年小鼠对该疫苗的免疫反应，表明初免-加强策略可能是增强老年人免疫原性的合理方法。

Abstract:
The spread of SARS-CoV-2 has caused a global pandemic that has affected almost every aspect of human life. The development of an effective COVID-19 vaccine could limit the morbidity and mortality caused by infection, and may enable the relaxation of social distancing measures. Age is one of the most significant risk factors for poor health outcomes after SARS-CoV-2 infection, therefore it is desirable that any new vaccine candidates should elicit a robust immune response in older adults. Here, we test the immunogenicity of the adenoviral

vectored vaccine ChAdOx1 nCoV-19 (AZD-1222) in aged mice. We find that a single dose of this vaccine induces cellular and humoral immunity in aged mice, but at a reduced magnitude than in younger adult mice. Furthermore, we report that a second dose enhances the immune response to this vaccine in aged mice, indicating that a prime-boost strategy may be a rational approach to enhance immunogenicity in older persons.

9. 阿斯利康的 COVID-19 疫苗能增强老年人和年轻人的免疫反应

AstraZeneca's COVID-19 Vaccine Boosts Immune Response in Older, Younger Adults
来源：BioSpace
发布时间：2020-10-26
链接：https://www.biospace.com/article/astrazeneca-covid-19-vaccine-shows-efficacy-in-older-and-younger-trial-participants/
第一作者：Alex Keown
通讯作者：Alex Keown
通讯作者单位：BioSpace
DOI 或 PUBMED ID：
编译者：张丽双
中文摘要：
阿斯利康腺病毒载体疫苗候选品 AZD1222 第一阶段数据显示，该疫苗可诱导产生针对 SARS-CoV-2 的中和抗体和免疫 T 细胞。基于这项数据，阿斯利康称该疫苗能增强老年人和年轻人对新冠病毒的免疫应答。据阿斯利康开发候选疫苗的合作伙伴牛津大学称，该疫苗在接种后 14 天内引起 T 细胞反应，28 天内引起抗体反应。目前人们相信，这种疫苗可以在一年内对这种新型冠状病毒提供保护。
Abstract:
Days after the U.S. Food and Drug Administration greenlit the restart of AstraZeneca's Phase III COVID-19 vaccine trial, the U.K.-based company said the preventative medication boosts immune responses in older and younger adults against the novel coronavirus.
The announcement this morning builds on previous positive Phase I data for the vaccine candidate that showed the preventative medication generated both neutralizing antibodies and immune T-cells that target the virus that causes COVID-19. The vaccine provoked a T cell response within 14 days of vaccination and an antibody response within 28 days, according to Oxford University, AstraZeneca's partner in developing the vaccine candidate. It's believed at this time that the vaccine could provide protection against the novel coronavirus for about a year. Additional protection will require a booster or additional vaccination.

10. 单次注射和修饰的咪唑喹啉 TLR7/8 激动剂-佐剂重组 S 蛋白疫苗在 SARS-CoV-2 小鼠模型中的免疫抗病毒作用

Sterilizing Immunity against SARS-CoV-2 Infection in Mice by a Single-Shot and Modified Imidazoquinoline TLR7/8 Agonist-Adjuvanted Recombinant Spike Protein Vaccine

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DOI 或 PUBMED ID：preprint
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摘要：
面对严峻的 SARS-CoV-2 疫情，开发出对抗病毒的疫苗变的更加紧迫。目前已经有几种候选疫苗进入临床阶段。灭活病毒和重组蛋白疫苗相对比较安全，但需要佐剂才能产生较强的免疫反应。文中研究者报道了一种新型的两性咪唑喹啉(IMDQ-PEG-CHOL)TLR7/8 佐剂。该佐剂由咪唑喹啉与胆固醇-聚(乙二醇)大分子末端共轭形成两亲物。这种水溶性的两亲物在局部给药时，可能通过与白蛋白结合，表现在淋巴结的大量聚集。使用 IMDQ-PEG-CHOL 作为佐剂，用三聚体重组 SARS-CoV-2 S 蛋白单次接种 BALB/c 中国小鼠模型，体内可产生针对 SARS-CoV-2 的保护性免疫应答。使用 IMDQ-PEG-CHOL 作为佐剂的 SARS-CoV-2 S 蛋白疫苗制剂，可增强淋巴结中免疫细胞的募集和活化。与天然可溶性 IMDQ 相比，IMDQ-聚乙二醇-CHOL 具有更好的安全性，前者在局部注射时诱导更局部的免疫反应，防止全身炎症反应的发生。此外，IMDQ-聚乙二醇-CHOL 佐剂疫苗诱导增强的酶联免疫吸附试验和体外微中和滴度，以及更平衡的 IgG2a/IgG1 反应。接种疫苗的小鼠在通过鼻内腺病毒介导的人血管紧张素转换酶 2 (ACE2)基因的表达致敏后，经 SARS-CoV-2 病毒感染以评估疫苗应答与抑制体内病毒复制的效果。结果显示不含佐剂的三聚体重组 S 蛋白疫苗组的小鼠与对照小鼠肺病毒滴度无显著差异，而 IMDQ-聚乙二醇-CHOL-佐剂疫苗组小鼠体内病毒的复制得到显著的抑制。为了测试 IMDQ-PEG-CHOL 是否也可以用于目前已获准用于人类的佐剂疫苗，结果发现使用相同的 IMDQ-PEG-CHOL 佐剂人四价灭活流感病毒裂解疫苗，可增强血凝抑制效价和更平衡的 IgG2a / IgG1 抗体反应。当小鼠被感染致命的流感病毒时，增强的流感疫苗反应与更强的病毒控制相关。文中研究结果强调了将 IMDQ-PEG-CHOL 用作佐剂的潜在用途，可在重组蛋白和灭活病毒疫苗对呼吸道病毒（如 SARS-CoV-2 和流感病毒）进行单次免疫后获得保护。
Abstract:
The search for vaccines that protect from severe morbidity and mortality as a result of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19) is a race against the clock and the virus. Several vaccine candidates are currently being tested in the clinic. Inactivated virus and recombinant protein vaccines can be safe options but may require adjuvants to induce robust immune responses efficiently. In this work we describe the use of a novel amphiphilic imidazoquinoline(IMDQ-PEG-CHOL)TLR7/8 adjuvant,consisting of an imidazoquinoline conjugated to the chain end of a cholesterol-poly(ethylene glycol) macromolecular amphiphile). This amphiphile is water soluble and exhibits massive translocation to lymph nodes upon local administration, likely through binding to albumin. IMDQ-PEG-CHOL is used to induce a protective immune response against SARS-CoV-2 after single vaccination with trimeric recombinant SARS-CoV-2 spike protein in the BALB/c mouse model. Inclusion of amphiphilic IMDQ-PEG-CHOL in the SARS-CoV-2 spike vaccine formulation resulted in enhanced immune cell recruitment and

activation in the draining lymph node. IMDQ-PEG-CHOL has a better safety profile compared to native soluble IMDQ as the former induces a more localized immune response upon local injection, preventing systemic inflammation. Moreover, IMDQ-PEG-CHOL adjuvanted vaccine induced enhanced ELISA and in vitro microneutralization titers, and a more balanced IgG2a/IgG1 response. To correlate vaccine responses with control of virus replication in vivo, vaccinated mice were challenged with SARS-CoV-2 virus after being sensitized by intranasal adenovirus-mediated expression of the human angiotensin converting enzyme 2 (ACE2) gene. Animals vaccinated with trimeric recombinant spike protein vaccine without adjuvant had lung virus titers comparable to non-vaccinated control mice, whereas animals vaccinated with IMDQ-PEG-CHOL-adjuvanted vaccine controlled viral replication and infectious viruses could not be recovered from their lungs at day 4 post infection. In order to test whether IMDQ-PEG-CHOL could also be used to adjuvant vaccines currently licensed for use in humans, proof of concept was also provided by using the same IMDQ-PEG-CHOL to adjuvant human quadrivalent inactivated influenza virus split vaccine, which resulted in enhanced hemagglutination inhibition titers and a more balanced IgG2a/IgG1 antibody response. Enhanced influenza vaccine responses correlated with better virus control when mice were given a lethal influenza virus challenge. Our results underscore the potential use of IMDQ-PEG-CHOL as an adjuvant to achieve protection after single immunization with recombinant protein and inactivated virus vaccines against respiratory viruses, such as SARS-CoV-2 and influenza viruses.

11. 基于 mRNA 的 SARS-CoV-2 候选疫苗 CVnCoV 诱导高水平的病毒中和抗体并介导对啮齿动物的保护作用

mRNA based SARS-CoV-2 vaccine candidate CVnCoV induces high levels of virus neutralizing antibodies and mediates protection in rodents

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中文摘要：

SARS-CoV-2 疾病需要快速的疫苗开发和大规模生产来满足全球需求。 mRNA 疫苗已成为解决这一空前挑战的最有前途的技术之一。在这里，我们展示了临床候选 CVnCoV 的临床前数据，CVnCoV 是一种脂质纳米颗粒（LNP）封装的非修饰 mRNA 疫苗，编码全长、融合前稳定的 SARS-CoV-2 的 S 蛋白。从 CVnCoV 翻译得到的 S 被切割，翻译后修饰并呈现在细胞表面，突显了 mRNA 疫苗在病毒感染过程中模仿抗原呈递的能力。用 CVnCoV 免疫可在小鼠和仓鼠中产生高滴度的病毒中和抗体，并在小鼠中产生强烈的 CD4+和 CD8+ T 细胞反应，从而引起强烈的体液反应。最重要的是，接种 CVnCoV 疫苗可以完全保护仓鼠肺免受野生型 SARS-CoV-2

的攻击。为了深入了解疫苗增强疾病的风险，对接种了次优剂量的 CVnCoV 导致突破性病毒复制的仓鼠进行了疫苗增强疾病的体征分析。没有发现增加病毒复制或加剧炎症以及病毒靶器官受损的证据，这为 CVnCoV 安全性提供了有力证据。总体而言，这里的数据证明 CVnCoV 是一种有效和安全的 SARS-CoV-2 疫苗候选品。

Abstract:
The devastating SARS-CoV-2 pandemic demands rapid vaccine development and large scale production to meet worldwide needs. mRNA vaccines have emerged as one of the most promising technologies to address this unprecedented challenge. Here, we show preclinical data for our clinical candidate CVnCoV, a lipid nanoparticle (LNP) encapsulated non-modified mRNA vaccine that encodes the full length, pre-fusion stabilised SARS-CoV-2 Spike (S) protein. S translated from CVnCoV is cleaved, post-translationally modified, and presented on the cell surface, highlighting the ability of mRNA vaccines to mimic antigen presentation during viral infection. Immunisation with CVnCoV induced strong humoral responses with high titres of virus neutralizing antibodies in mice and hamsters and robust CD4+ and CD8+ T cell responses in mice. Most importantly, vaccination with CVnCoV fully protected hamster lungs from challenge with wild type SARS-CoV-2. To gain insights in the risk of vaccineenhanced disease, hamsters vaccinated with a suboptimal dose of CVnCoV leading to breakthrough viral replication were analysed for signs of vaccine-enhanced disease. No evidence of increased viral replication or exacerbated inflammation and damage to viral target organs was detectable, giving strong evidence for a favourable safety profile of CVnCoV. Overall, data presented here provide evidence that CVnCoV represents a potent and safe vaccine candidate against SARS-CoV-2.

12. 从早期恢复期的 COVID-19 患者中分离出的一种有效的 SARS-CoV-2 中和抗体 SC31 的 Fc 介导效应功能对于抗体的最佳治疗效果至关重要

The Fc-mediated effector functions of a potent SARS-CoV-2 neutralizing antibody, SC31, isolated from an early convalescent COVID-19 patient, are essential for the optimal therapeutic efficacy of the antibody

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中文摘要：

SARS-CoV-2 中和抗体是有望治疗 COVID-19 的药物。然而，这些抗体的作用机制或其有效给药窗口尚不清楚。文中报道了 SC31 的发现和发展，一种强有力的 SARS-CoV-2 中和 IgG1 抗体，最初从一名康复病人在症状出现后的第 27 天分离。中和作用通过在 SARS-CoV-2 刺突蛋白 ACE2 的结合表位发生，该表位在所有常见的 SARS-CoV-2 突变体中保守。在感染了 SARS-

CoV-2 的 k18 人 ACE2 转基因小鼠中，SC31 通过显著降低病毒载量，同时减轻与严重系统性疾病相关的促炎反应(如 IL-6)，证明了其有效的益处。与 Fc 缺失的 LALA 变体 SC31 的比较表明，SC31 的最佳治疗效果需要完整的 Fc 介导的效应功能，从而进一步诱导 IFNγ 驱动的抗病毒免疫应答。在激活肺部炎症反应前，给药后 SC31 的剂量依赖性疗效下降到 5mg/kg。重要的是，尽管 FcγR 结合，即使是在亚治疗剂量的情况下，也没有证据表明 Fc 的 SC31 具有抗体依赖性增强。治疗效果在感染 SARS-CoV-2 的仓鼠中得到证实，其中 SC31 再次显著降低病毒载量，减少肺部病变，并抑制严重疾病表现的进展。这项研究强调了 SC31 抗体对 COVID-19 患者的潜在益处，这证明了快速的临床进展，同时也强调了在开发过程中适当的机制和功能研究的重要性。

Abstract:
SARS-CoV-2-neutralizing antibodies are promising therapeutics for COVID-19. However, little is known about the mechanisms of action of these antibodies or their effective dosing windows. We report the discovery and development of SC31, a potent SARS-CoV-2 neutralizing IgG1 antibody, originally isolated from a convalescent patient at day 27 after the onset of symptoms. Neutralization occurs via a binding epitope that maps within the ACE2 interface of the SARS-CoV-2 Spike protein, conserved across all common circulating SARS-CoV-2 mutants. In SARS-CoV-2 infected K18-human ACE2 transgenic mice, SC31 demonstrated potent survival benefit by dramatically reducing viral load concomitant with attenuated pro-inflammatory responses linked to severe systemic disease, such as IL-6. Comparison with a Fc-null LALA variant of SC31 demonstrated that optimal therapeutic efficacy of SC31 requires intact Fc-mediated effector functions that can further induce an IFNγ-driven anti-viral immune response. Dose-dependent efficacy for SC31 was observed down to 5mg/kg when dosed before the activation of lung inflammatory responses. Importantly, despite FcγR binding, no evidence of antibody dependent enhancement was observed with the Fc-competent SC31 even at sub-therapeutic doses. Therapeutic efficacy was confirmed in SARS-CoV-2-infected hamsters, where SC31 again significantly reduced viral load, decreased lung lesions and inhibited progression to severe disease manifestations. This study underlines the potential for significant COVID-19 patient benefit for the SC31 antibody that justifies rapid advancement to the clinic, as well as highlighting the importance of appropriate mechanistic and functional studies during development.

13. 通过中和人单克隆抗体，SARS-CoV-2 感染 K18-hACE2 转基因小鼠的暴露后保护

Post-exposure protection of SARS-CoV-2 lethal infected K18-hACE2 transgenic mice by neutralizing human monoclonal antibody

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摘要

中和抗体是治疗和预防 COVID-19 这种新病原体感染的一种极有前途的方法。在本研究中，通过对最近鉴定的人单克隆 MD65 抗体进行了表征，并进一步评价了其对 K18-hACE2 转基因小鼠 SARS-CoV-2 致命感染的保护能力。75%未处理的小鼠在感染后 6-9 天内死亡，而在感染后 3 天内给予 MD65 抗体，拯救了所有感染的动物。这些数据史无前例地证明了人类单克隆抗体对 COVID-19 重症感染的救命治疗价值。

Abstract

Coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), exhibits high levels of mortality and morbidity and has dramatic consequences on human live, sociality and global economy. Neutralizing antibodies constitute a highly promising approach for treating and preventing infection by this novel pathogen. In the present study, we characterized and further evaluated the recently identified human monoclonal MD65 antibody for its ability to provide protection against a lethal SARS-CoV-2 infection of K18-hACE2 transgenic mice. 75% of the untreated mice succumbed 6-9 days post-infection while administration of the MD65 antibody as late as 3 days after exposure, rescued all infected animals. The data unprecedentedly demonstrate, the therapeutic value of human monoclonal antibodies as a life-saving treatment of severe COVID-19 infection.

14. 用肺和结肠类器官鉴定 SARS-CoV-2 抑制剂

Identification of SARS-CoV-2 Inhibitors using Lung and Colonic Organoids

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中文摘要：

迫切需要使用与人类疾病相关的细胞来创建新颖的模型，以研究 SARS-CoV-2 生物学并促进药物筛选。由于 SARS-CoV-2 主要感染呼吸道，因此我们开发了使用人类多能干细胞（hPSC-LOs）的肺类器官模型。 hPSC-LOs，特别是 II 型肺泡细胞，允许 SARS-CoV-2 感染，并在 SARS-CoV-2 感染后表现出强烈的趋化因子诱导作用，类似于在 COVID-19 患者中所见。这些患者中将近 25％的人也有胃肠道表现，这与 COVID-19 结果恶化有关。因此，我们还产生了互补的 hPSC 衍生的结肠类器官（hPSC-COs），以探索结肠细胞对 SARS-CoV-2 感染的反应。我们发现多种结肠细胞类型，尤其是肠上皮细胞，表达 ACE2，并允许 SARS-CoV-2 感染。使用 hPSC-LOs，我们对 FDA 批准的药物进行了高通量筛选，并确定了 SARS-CoV-2 的进入抑制剂，包括伊马替尼、麦考酚酸（MPA）和奎纳克林二盐酸盐（QNHC）。这些药物在生理上相关

的水平上的治疗显着抑制了 hPSC-LOs 和 hPSC-COs 的 SARS-CoV-2 感染。总之，这些数据表明，SARS-CoV-2 感染的 hPSC-LOs 和 hPSC-COs 可以用作研究 SARS-CoV-2 感染的疾病模型，并为筛选药物以鉴定候选 COVID-19 治疗剂提供有价值的资源。

Abstract:

There is an urgent need to create novel models using human disease-relevant cells to study SARS-CoV-2 biology and to facilitate drug screening. As SARS-CoV-2 primarily infects the respiratory tract, we developed a lung organoid model using human pluripotent stem cells (hPSC-LOs). The hPSC-LOs, particularly alveolar type II-like cells, are permissive to SARS-CoV-2 infection, and showed robust induction of chemokines upon SARS-CoV-2 infection, similar to what is seen in COVID-19 patients. Nearly 25% of these patients also have gastrointestinal manifestations, which are associated with worse COVID-19 outcomes1. We therefore also generated complementary hPSC-derived colonic organoids (hPSC-COs) to explore the response of colonic cells to SARS-CoV-2 infection. We found that multiple colonic cell types, especially enterocytes, express ACE2 and are permissive to SARS-CoV-2 infection. Using hPSC-LOs, we performed a high throughput screen of FDA-approved drugs and identified entry inhibitors of SARS-CoV-2, including imatinib, mycophenolic acid (MPA), and quinacrine dihydrochloride (QNHC). Treatment at physiologically relevant levels of these drugs significantly inhibited SARS-CoV-2 infection of both hPSC-LOs and hPSC-COs. Together, these data demonstrate that hPSC-LOs and hPSC-COs infected by SARS-CoV-2 can serve as disease models to study SARS-CoV-2 infection and provide a valuable resource for drug screening to identify candidate COVID-19 therapeutics.

15. SARS-CoV-2 中和性抗体 LY-CoV555 对新冠病毒感染门诊病人的保护性评估

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

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DOI 或 PUBMED ID：10.1056/NEJMoa2029849

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中文摘要：

背景：急性呼吸综合征冠状 2 型病毒(SARS-CoV-2)导致 2019 年新冠肺炎流行，最常见为轻度感染，但严重时会威胁生命。而病毒中和性单抗可降低体内病毒载量，改善临床症状以缓和住院压力

方法:目前进行的单抗 LY-CoV5552Ⅱ期临床试验中，我们将 452 名最近诊断为轻度或中度新冠肺炎的门诊患者随机分配成三组，接受不同剂量的中和抗体 LY-CoV555(700 mg、2800mg 或 7000mg)的单次静脉输注，并与安慰剂使用患者对比评估病毒清除效果及临床表现。主要数据显示患者体内病毒载量在第 11 天时基线发生变化。该数据为 2020 年 9 月 5 日的中期时的分析结果。

结果：中期实验数据显示，可观察到的整体人群对数病毒载量的基线对数值平均下降为 3.81，

99.97%以上患者体内检测不到病毒 RNA 基因。接受 2800 mg 中和抗体 LY-CoV555 治疗的患者，与安慰剂组相比，其基线下降差异为 0.53 (95% CI, -0.98 至-0.08；P=0.02)，病毒载量降低了 3.4 倍。700mg 抗体治疗患者组或 7000mg 治疗剂量组与对照组的差异不显著，基线分别下降为 0.20（95% CI，0.66 至 0.25；P=0.38)和 0.09 (95%，0.37 至 0.55；P=0.70)。在抗体治疗的第 2 至 6 天，抗体治疗的患者的症状略好于安慰剂使用患者。同时 LY-CoV555 抗体治疗组患者因新冠肺炎住院或急诊的比例为 1.6%，而安慰剂组为 6.3%。

结论：在 LY-CoV555 抗体Ⅱ期临床试验的中期分析结果，2800 mgL 抗体治疗组有助于加速患者体内病毒载量的自然下降，而 700mg 或 7000mg 抗体治疗患者组无类似效果。(由礼来资助；临床试验号码，NCT04427501)。

Abstract:

BACKGROUND

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (Covid-19), which is most frequently mild yet can be severe and life-threatening. Virus-neutralizing monoclonal antibodies are predicted to reduce viral load, ameliorate symptoms, and prevent hospitalization.

METHODS

In this ongoing phase 2 trial involving outpatients with recently diagnosed mild or moderate Covid-19, we randomly assigned 452 patients to receive a single intravenous infusion of neutralizing antibody LY-CoV555 in one of three doses (700 mg, 2800 mg, or 7000 mg) or placebo and evaluated the quantitative virologic end points and clinical outcomes. The primary outcome was the change from baseline in the viral load at day 11. The results of a preplanned interim analysis as of September 5, 2020, are reported here.

RESULTS

At the time of the interim analysis, the observed mean decrease from baseline in the log viral load for the entire population was -3.81, for an elimination of more than 99.97% of viral RNA. For patients who received the 2800-mg dose of LY-CoV555, the difference from placebo in the decrease from baseline was -0.53 (95% confidence interval [CI], -0.98 to -0.08; P=0.02), for a viral load that was lower by a factor of 3.4. Smaller differences from placebo in the change from baseline were observed among the patients who received the 700-mg dose (-0.20; 95% CI, -0.66 to 0.25; P=0.38) or the 7000-mg dose (0.09; 95% CI, -0.37 to 0.55; P=0.70). On days 2 to 6, the patients who received LY-CoV555 had a slightly lower severity of symptoms than those who received placebo. The percentage of patients who had a Covid-19–related hospitalization or visit to an emergency department was 1.6% in the LY-CoV555 group and 6.3% in the placebo group.

CONCLUSIONS

In this interim analysis of a phase 2 trial, one of three doses of neutralizing antibody LY-CoV555 appeared to accelerate the natural decline in viral load over time, whereas the other doses had not by day 11. (Funded by Eli Lilly; BLAZE-1 ClinicalTrials.gov number, NCT04427501. opens in new tab)

16. 大规模单细胞分析揭示 COVID-19 患者的关键免疫特性

Large-scale single-cell analysis reveals critical immune characteristics of

COVID-19 patients
来源：bioRxiv
发布时间：2020-10-29
链接：https://www.biorxiv.org/content/10.1101/2020.10.29.360479v1
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通讯作者：Penghui Zhou, Qinghua Jiang, Zhiwei Huang, Jin-Xin Bei, Lai Wei1, Xindong Liu, Tao Cheng, Xiangpan Li, Pingsen Zhao, Fu-Sheng Wang, Hongyang Wang, Bing Su, Zheng Zhang, Kun Qu, Xiaoqun Wang, Jiekai Chen, Ronghua Jin, Zemin Zhang[1]
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DOI 或 PUBMED ID：
编译者：王玮
中文摘要：

COVID-19 患者的免疫功能失调是影响症状和死亡率的一个反复出现的主题，但是我们对相关免疫细胞的了解还不完整。该研究对 205 例 COVID-19 患者的 284 个样品进行了全面的 RNA 测序。淋巴细胞减少和 T 细胞及 B 细胞反应活跃是共存的，并与年龄、性别及其与 COVID-19 的相互作用有关。不同类型的上皮细胞和免疫细胞病毒呈阳性，并且显示出显著的转录组变化。病毒阳性鳞状上皮细胞中 ANXA1 和 S100A9 的升高可能通过 ANXA1-FPR1 和 S100A8/9-TLR4 轴启动中性粒细胞和巨噬细胞反应。S100A8/A9 的系统性上调，主要源于外周血中的巨核细胞和单核细胞上调，可能是重症患者常见的细胞因子风暴的原因之一。该数据为了解 COVID-19 的发病机制和设计有效的治疗策略提供了丰富的资源。
Abstract:
Dysfunctional immune response in the COVID-19 patients is a recurrent theme impacting symptoms and mortality, yet the detailed understanding of pertinent immune cells is not complete. We applied single-cell RNA sequencing to 284 samples from 205 COVID-19 patients and controls to create a comprehensive immune landscape. Lymphopenia and active T and B cell responses were found to coexist and associated with age, sex and their interactions with COVID-19. Diverse epithelial and immune cell types were observed to be virus-positive and showed dramatic transcriptomic changes. Elevation of ANXA1 and S100A9 in virus-positive squamous epithelial cells may enable the initiation of neutrophil and macrophage responses via the ANXA1-FPR1 and S100A8/9-TLR4 axes. Systemic up-regulation of S100A8/A9, mainly by megakaryocytes and monocytes in the peripheral blood, may contribute to the cytokine storms frequently observed in severe patients. Our data provide a rich resource for understanding the pathogenesis and designing effective therapeutic strategies for COVID-19.

17. 基于转录组学的药物重新定位的管道，用以识别 COVID-19 的候选治疗方案

Transcriptomics-based drug repositioning pipeline identifies therapeutic

candidates for COVID-19
来源：bioRxiv
发布时间：2020-10-23
链接：https://www.biorxiv.org/content/10.1101/2020.10.23.352666v1
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DOI 或 PUBMED ID：
编译者：王玮
中文摘要：

新型 SARS-CoV-2 病毒于 2019 年 12 月出现，目前几乎没有有效的治疗方法。该研究将一个计算药物重新定位的管道（pipeline）应用于从公开数据中获得的 SARS-CoV-2 差异基因表达特征。从三个独立发表的研究中获得并生成对照组和 SARS-CoV-2 感染样本之间差异表达基因的列表。利用基于 Kolmogorov-Smirnov 统计量并基于秩的模式匹配策略，从 Connectivity Map（CMap）中查询药物特征码。在 Calu-3 或 293T-ACE2 细胞中验证了 16 个种预测化合物的抗 SARS-CoV-2 病毒的活性。在人类细胞系中的验证实验表明，测试的 16 种化合物中有 11 种（包括氯法齐明、氟哌啶醇等）对 SARS-CoV-2 具有可测量的抗病毒活性。该研究团队将继续致力于进一步分析这些预测化合物可否作为治疗 COVID-19 的潜在疗法。

Abstract:

The novel SARS-CoV-2 virus emerged in December 2019 and has few effective treatments. We applied a computational drug repositioning pipeline to SARS-CoV-2 differential gene expression signatures derived from publicly available data. We utilized three independent published studies to acquire or generate lists of differentially expressed genes between control and SARS-CoV-2-infected samples. Using a rank-based pattern matching strategy based on the Kolmogorov-Smirnov Statistic, the signatures were queried against drug profiles from Connectivity Map (CMap). We validated sixteen of our top predicted hits in live SARS-CoV-2 antiviral assays in either Calu-3 or 293T-ACE2 cells. Validation experiments in human cell lines showed that 11 of the 16 compounds tested to date (including clofazimine, haloperidol and others) had measurable antiviral activity against SARS-CoV-2. These initial results are encouraging as we continue to work towards a further analysis of these predicted drugs as potential therapeutics for the treatment of COVID-19.

18. SARS-CoV-2 病毒 RNA 基因组翻译过程中核糖体移码的结构基础

Structural basis of ribosomal frameshifting during translation of the SARS-CoV-2 RNA genome
来源：bioRxiv
发布时间：2020-10-26
链接：https://www.biorxiv.org/content/10.1101/2020.10.26.355099v1
第一作者：Pramod R. Bhatt, Alain Scaiola
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DOI 或 PUBMED ID：
编译者：宋珂
中文摘要：

程序性核糖体移码是 SARS-CoV-2 病毒 RNA 基因组翻译过程中的关键步骤，用于合成病毒 RNA 依赖的 RNA 聚合酶以及下游的病毒蛋白。本文中，作者解析了哺乳动物核糖体处于病毒 RNA 翻译过程中的 cryo-EM 结构，而且此时的病毒 RNA 暂停在预备移码的构象。作者观察到病毒 RNA 形成一种伪结的结构，结合在核糖体的 mRNA 进入通道位置，并产生了对 mRNA 的拉力，从而导致移码过程。在核糖体中新合成的初始病毒多聚蛋白停留在移码位置，与核糖体多肽出口通道间形成了独特的相互作用。作者利用生化实验方法验证了结构生物学的观察结果，并揭示了影响移码效率的机理和调控因素。最后，作者发现之前证明可以降低移码过程的化合物也能够抑制 SARS-CoV-2 病毒在感染细胞中的复制，从而建立了以冠状病毒的移码过程为抗病毒干预的靶标。
注：作者未提供结构文件 ID。

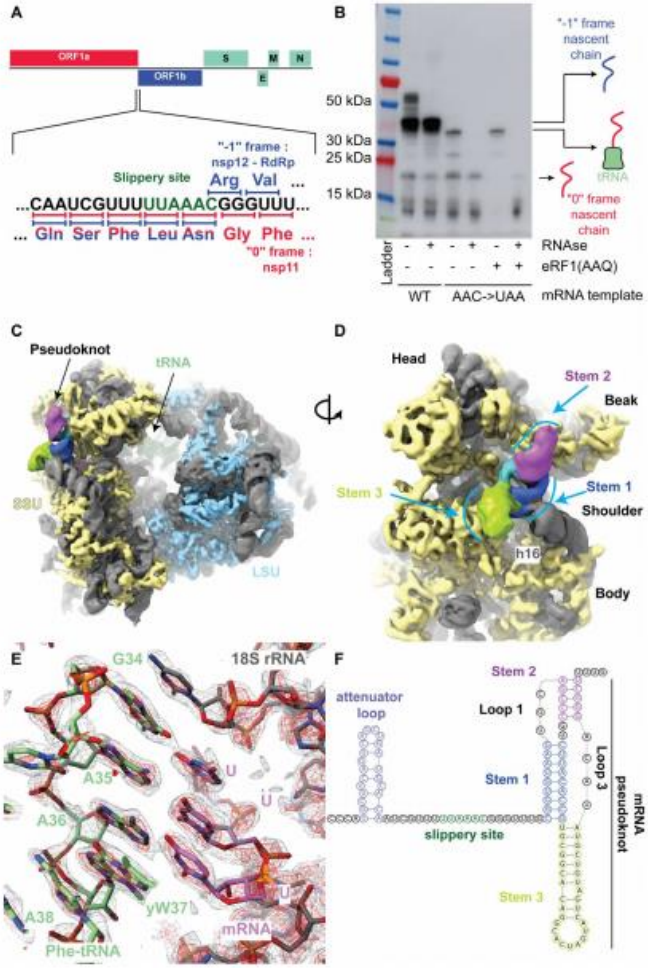

Fig. 1 The SARS-Cov-2 pseudoknot interacts with the ribosome and pauses translation upstream of the slippery site.

(A) Schematic of the SARS-CoV-2 main ORF. In the close up view of the frameshift event, codons and corresponding amino acids are shown. During -1 frameshifting, the 'slippery site' codons UUA (Leu) and AAC (Asn) are the last codons decoded in the 0 frame. Upon -1 frameshifting of the AAC codon to AAA, translation resumes at the CGG (Arg) triplet, where elongation proceeds uninterrupted to produce full-length Nsp12. **(B)** In vitro translation reaction depicting pausing at the frameshift site. Efficient frameshifting is observed for the WT template. Samples for cryo-EM originally intended to be trapped by dominant negative eRF1 (AAQ) show a tRNA-bound pause in proximity of the frameshift site. The tRNA-associated band is lost upon RNAse treatment. Reactions without added eRF1 (AAQ) produce a similarly paused product. **(C)** Overview of the density low pass filtered to 6Å with the pseudoknot found close to the entry of the mRNA channel on the small subunit (SSU). The SSU proteins are colored in yellow, the large subunit (LSU) proteins in blue and the rRNA in grey. The pseudoknot is colored according to its secondary structure as in panel (F), and the P-site tRNA is colored in dark green. **(D)** Close-up view of the pseudoknot from the solvent-exposed side of the SSU. Helix h16 of the 18S rRNA interacts with the base of Stem 1. Unpaired loop-forming nucleotides are colored in cyan. **(E)** P-site codon-anticodon interactions reveal a Phe (UUU) codon interacting with Phe-tRNA. **(F)** Schematic of the revised secondary structure elements in the pseudoknot necessary for -1 PRF with different functional regions labeled and colored accordingly.

Abstract:
Programmed ribosomal frameshifting is the key event during translation of the SARS-CoV-2 RNA genome allowing synthesis of the viral RNA-dependent RNA polymerase and downstream viral proteins. Here we present the cryo-EM structure of the mammalian ribosome in the process of translating viral RNA paused in a conformation primed for frameshifting. We observe that the viral RNA adopts a pseudoknot structure lodged at the mRNA entry channel of the ribosome to generate tension in the mRNA that leads to frameshifting. The nascent viral polyprotein that is being synthesized by the ribosome paused at the frameshifting site forms distinct interactions with the ribosomal polypeptide exit tunnel. We use biochemical experiments to validate our structural observations and to reveal mechanistic and regulatory features that influence the frameshifting efficiency. Finally, a compound previously shown to reduce frameshifting is able to inhibit SARS-CoV-2 replication in infected cells, establishing coronavirus frameshifting as target for antiviral intervention.

19. 人类细胞中 SARS-CoV-2 感染所需宿主因子的鉴定

Identification of required host factors for SARS-CoV-2 infection in human cells

来源：Cell
发布时间：2020-10-24
链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31394-5

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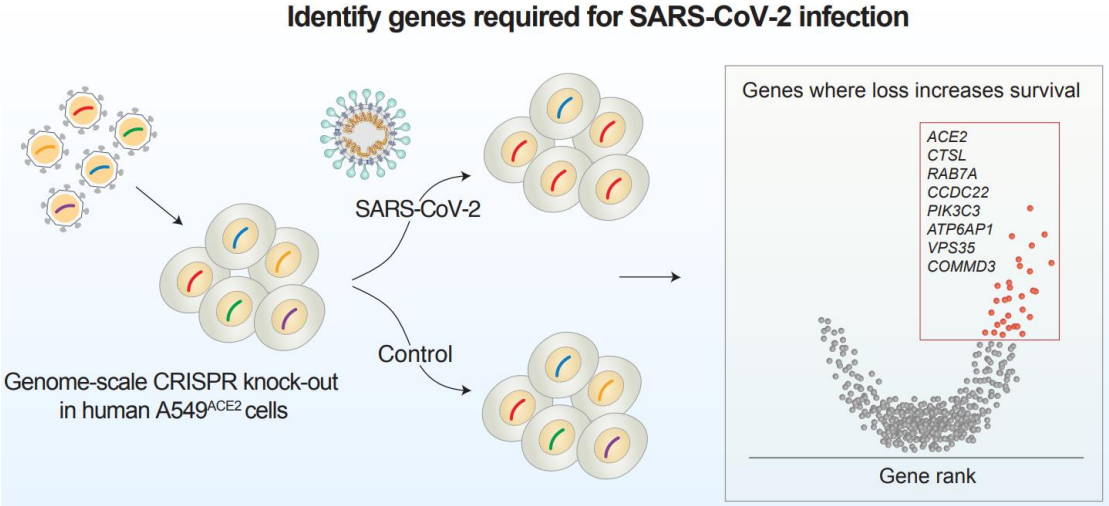
DOI 或 PUBMED ID：10.1016/j.cell.2020.10.030
编译者：宋张悦
中文摘要：

- 全基因组 CRISPR 敲除筛选确定了 SARS-CoV-2 感染的宿主因子。
- 排名靠前的基因包括 vacuolar ATPases, Retromer, Commander 和 Arp2/3 复合物。
- 使用 CRISPR 敲除，RNA 干扰和小分子抑制剂进行验证。
- 通过增加胆固醇生物合成和隔离 ACE2 减少感染。

为了更好地了解宿主-病毒的遗传依赖关系，并找到 COVID-19 的潜在治疗靶点，我们进行了一项全基因组规模的 CRISPR 功能缺失筛查，以确定人类肺泡上皮细胞感染 SARS-CoV-2 病毒所需的宿主因子。排名靠前的基因聚集成不同的通路，包括 vacuolar ATPase 质子泵、Retromer 和 Commander 复合物。我们使用几种正交的方法验证这些基因目标，如 CRISPR 敲除、RNA 干扰敲除和小分子抑制剂。通过使用单细胞 RNA 测序，我们发现了排名靠前的基因缺失时胆固醇生物合成的共同转录变化。此外，鉴于 ACE2 受体在病毒进入的早期阶段的关键作用，我们发现 RAB7A 的缺失通过将 ACE2 受体隔离在细胞内降低了病毒的进入。总的来说，这项工作为每个宿主基因的缺失对病毒感染适应度/反应的影响提供了一个基因组尺度的定量资源。



Abstract:

Highlights

- Genome-wide CRISPR knockout screen identifies host factors for SARS-CoV-2 infection
- Top-ranked genes include vacuolar ATPases, Retromer, Commander and Arp2/3 complex
- Validation using CRISPR knockout, RNA interference and small molecule inhibitors
- Reduced infection via increased cholesterol biosynthesis and sequestration of ACE2

Summary

To better understand host-virus genetic dependencies and find potential therapeutic targets for COVID-19, we performed a genome-scale CRISPR loss-of-

function screen to identify host factors required for SARS-CoV-2 viral infection of human alveolar epithelial cells. Top-ranked genes cluster into distinct pathways, including the vacuolar ATPase proton pump, Retromer, and Commander complexes. We validate these gene targets using several orthogonal methods such as CRISPR knock-out, RNA interference knock-down, and small-molecule inhibitors. Using single-cell RNA-sequencing, we identify shared transcriptional changes in cholesterol biosynthesis upon loss of top-ranked genes. In addition, given the key role of the ACE2 receptor in the early stages of viral entry, we show that loss of *RAB7A* reduces viral entry by sequestering the ACE2 receptor inside cells. Overall, this work provides a genome-scale, quantitative resource of the impact of the loss of each host gene on fitness/response to viral infection.

20. β-冠状病毒利用溶酶体而不是生物合成中的分泌通路进行病毒粒子释放

β-Coronaviruses use lysosomes for egress instead of the biosynthetic secretory pathway

简报 7 月 31 日第 27 条报道过该工作的预印本

链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31446-X

21. SARS-CoV-2 病毒的非结构蛋白 1 是重要的致病因子，能够重定向宿主的蛋白合成机制转而合成病毒 RNA

Nonstructural protein 1 of SARS-CoV-2 is a potent pathogenicity factor redirecting host protein synthesis machinery toward viral RNA.

简报 8 月 14 日第 24 条报道过

链接：https://www.cell.com/molecular-cell/fulltext/S1097-2765(20)30741-3

22. 刺突蛋白 D614G 突变改变了 SARS-CoV-2 的适应力

Spike mutation D614G alters SARS-CoV-2 fitness

来源：Nature 加速发表

发布时间：2020-10-26

链接：https://www.nature.com/articles/s41586-020-2895-3

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编译者：蒋立春

中文摘要：

随着疫情流行，刺突蛋白突变株 D614G 成为 SARS-CoV-2 的主要毒株（编译者注，D614 是我国疫情期间最为流行的病毒株，疫情在欧美国家流行之后 D614G 才成为主要病毒株）。该突变对病毒的传播和疫苗响应的影响还不清楚。作者们将 USA-WA1/2020 人工改造为 D614G 来研究该突变的影响。D614G 加强了病毒粒子的感染性，使得病毒在人肺部上皮细胞以及人气道原代组织中的复制能力增强。感染 G614 病毒株的仓鼠的鼻洗液和气管中病毒感染滴度更高，肺部的病毒感染滴度不变，这验证了临床上感染 D614G 的病人上呼吸道中病毒载量增加的现象，意味着突变导致了更强的传染力。感染 D614 病毒株的仓鼠的血清对 G614 病毒的中和滴度稍微高于对 D614 病毒的中和滴度，这提示（i）突变不降低临床实验中的

疫苗对 COVID-19 的防护作用 （ii）应该测试治疗性抗体对循环系统中的 G614 病毒的中和能力。和临床发现一起，该工作强调了 D614G 突变对病毒传播的重要性，以及对疫苗和抗体治疗有效性的影响。

Abstract

A spike protein mutation D614G became dominant in SARS-CoV-2 during the COVID-19 pandemic1,2. However, the impact on viral spread and vaccine efficacy remains to be defined.

Here, we engineer the D614G mutation in the USA-WA1/2020 strain and characterize its effect. D614G enhances replication on human lung epithelial cells and primary human airway tissues through an improved infectivity of virions. Hamsters infected with the G614 variant produced higher infectious titers in the nasal washes and trachea, but not lungs, confirming clinical evidence that the D614G mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increases transmission. Sera from D614-infected hamsters exhibit modestly higher neutralization titers against G614 virus than against D614 virus, indicating that (i) the mutation may not reduce the ability of vaccines in clinical trials to protect against COVID-19 and (ii) therapeutic antibodies should be tested against the circulating G614 virus. Together with clinical findings, our work underscores the importance of this mutation in viral spread, vaccine efficacy, and antibody therapy.

23. SARS-CoV-2 核衣壳蛋白阻断了应急颗粒的形成，通过直接和宿主的 mRNA 相互作用而改变宿主基因表达

SARS-CoV-2 Nucleocapsid protein attenuates stress granule formation and alters gene expression via direct interaction with host mRNAs

来源：Cell

发布时间：2020-10-23

链接：https://www.biorxiv.org/content/10.1101/2020.10.23.342113v1

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通讯作者：Jack F. Greenblatt

通讯作者单位：University of Toronto，Canada

编译者：蒋立春

中文摘要：

SARS-CoV-2 核衣壳蛋白（N 蛋白）在感染时大量表达，使得该蛋白成为抗病毒和 发展疫苗的潜在靶标。从一个功能蛋白组的工作流程，作者们在 HEK293 细胞中鉴定了 21 个 SARS-CoV-2 蛋白的蛋白-蛋白结合图谱。作者们发现应急颗粒中的蛋白 G3BP1 和 G3BP2 和 SARS-CoV-2 的 N 蛋白发生了非常特异的共纯化。作者们揭示在人细胞中 N 蛋白表达通过和 G3BP1 和 G3BP2 的物理结合而阻断这些蛋白，阻碍应急颗粒的形成。在表达 N 蛋白的细胞系中过表达 G3BP1 可以反转这个表型。N 蛋白是一个 RNA 结合蛋白，作者们在存在氧自由基压力和不存在氧自由基压力的情况下通过细胞中 iCLIP 测序实验鉴定了被 N 蛋白结合的宿主 RNAs. 这些结果显示在两种情况下，SARS-CoV-2 的 N 蛋白直接和上千个宿主 mRNA 结合。和应急颗粒中的 G3BP 蛋白一样，N 蛋白主要结合在靶 mRNAs 的 3UTRs. RNA 测序揭示表达 N 蛋白在非应急情况以及存在氧应急情况下都导致了细胞中发生广泛的基因表达变化。

Abstract:

The COVID-19 pandemic has caused over one million deaths thus far. There is an urgent need for the development of specific viral therapeutics and a vaccine. SARS-CoV-2 nucleocapsid (N) protein is highly expressed upon infection and is essential for viral replication, making it a promising target for both antiviral drug and vaccine development. Here, starting from a functional proteomics workflow, we initially catalogued the protein-protein interactions of 21 SARS-CoV-2 proteins in HEK293 cells, finding that the stress granule resident proteins G3BP1 and G3BP2 co-purify with N with high specificity. We demonstrate that N protein expression of in human cells sequesters G3BP1 and G3BP2 through its physical interaction with these proteins, attenuating stress granule (SG) formation. The ectopic expression of G3BP1 in N-expressing cells was sufficient to reverse this phenotype. Since N is an RNA-binding protein, we performed iCLIP- sequencing experiments in cells, with or without exposure to oxidative stress, to identify the host RNAs targeted by N. Our results indicate that SARS-CoV-2 N protein binds directly to thousands of host mRNAs under both conditions. Like the G3BPs stress granule proteins, N was found to predominantly bind its target mRNAs in their 3UTRs. RNA sequencing experiments indicated that expression of N results in wide-spread gene expression changes in both unstressed and oxidatively stressed cells. We suggest that N regulates host gene expression by both attenuating stress granules and binding directly to target mRNAs.

24. 整合单细胞分析揭示了口腔感染 SARS-CoV-2 以及传染轴

Integrated Single-Cell Atlases Reveal an Oral SARS-CoV-2 Infection and Transmission Axis

来源：medxriv

发布时间：2020-10-27

链接：https://www.medrxiv.org/content/10.1101/2020.10.26.20219089v1

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通讯作者：Kevin M. Byrd

通讯作者单位：ADA Science & Research Institute, Gaithersburg, MD, USA

编译者：蒋立春

中文摘要：

即便有感染的迹象，口腔怎么参与到 COVID-19 的感染还所知甚少。

作者整合了人得小唾液腺和 牙龈单细胞测序数据，鉴定出 11 个上皮细胞、7 个间叶细胞以及 15 个免疫细胞群。对 SARS-CoV-2 病毒进入因子的表达显示它们富集在唾液腺的导管和腺泡上皮细胞以及粘膜的上基部细胞中。对 COVID-19 病人的尸检组织中也验证了唾液腺和粘膜中的体内感染。感染 SARS-CoV-2 的个体的唾液中存在表达 ACE2 和 SARS-CoV-2 RNA 的上皮细胞。配对的鼻咽拭子和唾液样品中的病毒脱落动力学差异很大，唾液中的病毒载量和包括失去味觉等 COVID-19 症状相关。随着病人的康复，这些病人唾液中开始出现针对 SARS-CoV-2 的抗体。这些研究表明口腔是 COVID-19 感染的一个稳定场所，唾液可以传播病毒。

Abstract:

Despite signs of infection, the involvement of the oral cavity in COVID-19 is

poorly understood. To address this, single-cell RNA sequencing datasets were integrated from human minor salivary glands and gingiva to identify 11 epithelial, 7 mesenchymal, and 15 immune cell clusters.Analysis of SARS-CoV-2 viral entry factor expression showed enrichment in epithelia including the ducts and acini of the salivary glands and the suprabasal cells of the mucosae. COVID-19 autopsy tissues confirmed in vivo SARS-CoV-2 infection in the salivary glands and mucosa. Saliva from SARS-CoV-2-infected individuals harbored epithelial cells exhibiting ACE2 expression and SARS-CoV-2 RNA. Matched nasopharyngeal and saliva samples found distinct viral shedding dynamics and viral burden in saliva correlated with COVID-19 symptoms including taste loss. Upon recovery, this cohort exhibited salivary antibodies against SARS-CoV-2 proteins. Collectively, the oral cavity represents a robust site for COVID-19 infection and implicates saliva in viral transmission.

25. 全基因组的 CRISPR/Cas9 基因敲除实验筛选出 DEAD box RNA 解螺旋酶 DDX42 是一个广谱的病毒抑制因子

A genome-wide CRISPR/Cas9 knock-out screen identifies the DEAD box RNA helicase DDX42 as a broad antiviral inhibitor

链接：https://www.biorxiv.org/content/10.1101/2020.10.28.359356v1

26. SARS-CoV-2 通过抑制 JAK-STAT 信号通路使得它对于宿主的干扰素不敏感

SARS-CoV-2 desensitizes host cells to interferon through inhibition of the JAK-STAT pathway

https://www.biorxiv.org/content/10.1101/2020.10.27.358259v1

27. COVID-19 疾病图谱，一个可执行计算的 SARS-CoV-2 病毒-宿主间相互作用机制的知识库

COVID-19 Disease Map, a computational knowledge repository of SARS-CoV-2 virus-host interaction mechanisms

来源：bioRxiv

发布时间：2020-10-28

链接：https://www.biorxiv.org/content/10.1101/2020.10.26.356014v1

第一作者：Marek Ostaszewski

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通讯作者单位：COVID-19 Disease Map Community

DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

通过大规模的团体协作，合作者们搭建了一个允许公开访问，能够交互操作，而且可执行计算的 COVID-19 分子机制知识库 - “COVID-19 疾病图谱”。由来自生物数据管理，各领域专家，以及生物信息学家和计算生物学家等多方参与者组成的团体对“COVID-19 疾病图谱”的内容进行分布式开发所使用的工具，平台和指南进行了讨论。作者强调了相关数据库和文本挖掘方法对丰富和验证展示出的机制的重要性。作者还介绍了图谱的内容，及其与 COVID-19 分子病理生理学的相关性。同时还可以对“COVID-19 疾病图谱”的内容进行分析

和计算建模，用于对机制研究数据的解释和预测。最后，作者通过几个使用实例演示其工作的具体应用。

相关链接：https://fairdomhub.org/projects/190 , https://covid.pages.uni.lu/

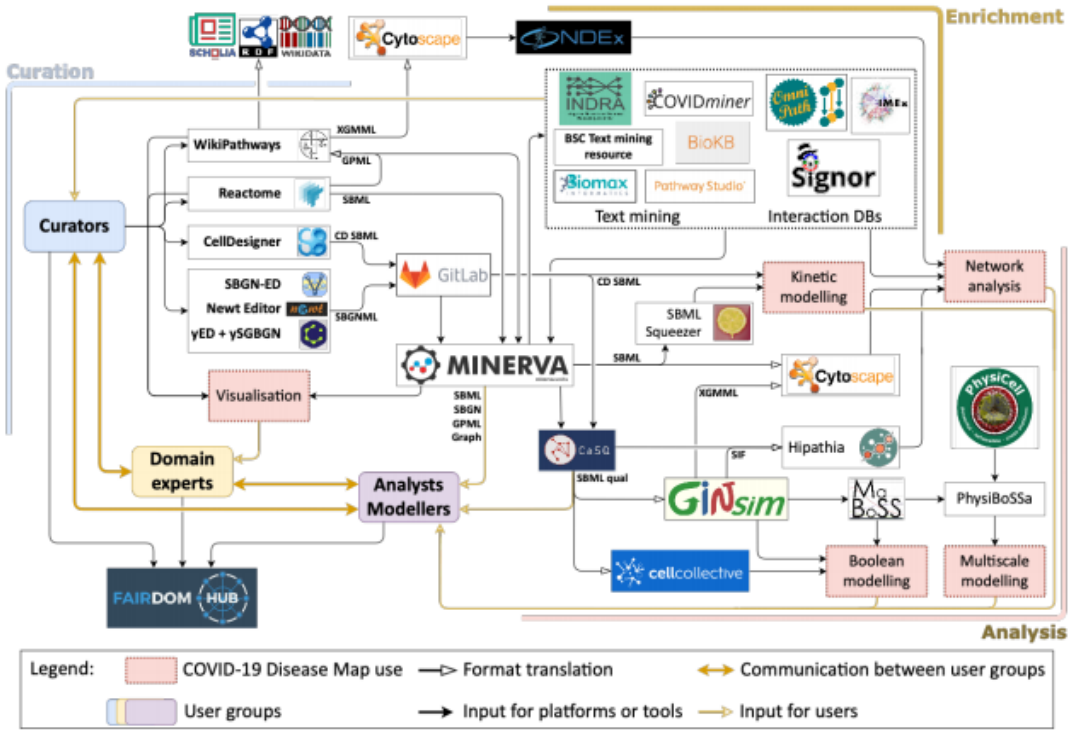

Figure 1: The ecosystem of the COVID-19 Disease Map Community. The main groups of COVID19 Disease Map Community are biocurators, domain experts, analysts, and modellers; communicating to refine, interpret and apply COVID-19 Disease Map diagrams. These diagrams are created and maintained by biocurators, following pathway database workflows or standalone diagram editors, and reviewed by domain experts. The content is shared via pathway databases or a GitLab repository; all can be enriched by integrated resources of text mining and interaction databases. The COVID-19 Disease Map diagrams, available in layout-aware systems biology formats and integrated with external repositories, are available in several formats allowing a range of computational analyses, including network analysis and Boolean, kinetic or multiscale simulations.

Abstract:

We hereby describe a large-scale community effort to build an open-access, interoperable, and computable repository of COVID-19 molecular mechanisms - the COVID-19 Disease Map. We discuss the tools, platforms, and guidelines necessary for the distributed development of its contents by a multi-faceted community of biocurators, domain experts, bioinformaticians, and computational biologists. We highlight the role of relevant databases and text mining approaches in enrichment and validation of the curated mechanisms. We describe the contents of the map and their relevance to the molecular pathophysiology of COVID-19 and the analytical and computational modelling approaches that can be applied to the contents of the COVID-19 Disease Map for mechanistic data interpretation and predictions. We conclude by demonstrating concrete applications of our work through several use cases.

28. 资源：COVID-19 单细胞图谱

由 Sanger 中心，人类细胞图谱项目以及扎克伯格基金会共同发起的对健康人以及 COVID-19 病人的单细胞测序数据的展示系统。里面提供了这些机构对病人进行的单细胞测序数据的图形化展示，包括未发表数据。

链接:https://www.covid19cellatlas.org/

29. 疫苗伤害的无过错赔偿——公平获得新冠肺炎疫苗的另一面

No-Fault Compensation for Vaccine Injury — The Other Side of Equitable Access to Covid-19 Vaccines

来源： NEJM

发布时间：2020-10-28

链接：https://www.nejm.org/doi/full/10.1056/NEJMp2030600?query=featured_home

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DOI 或 PUBMED ID： 10.1056/NEJMp2030600

编译者：孔娟

摘要：

新冠疫苗全球获取机制（COVAX）是为了应对当前流行的所谓“疫苗民族主义”的威胁而成立的，这一政策旨在为主要疫苗候选人提供财政支持，并确保低收入国家获得疫苗。同样重要的是，如果新冠肺炎疫苗对接种者造成真实的伤害，制造商应获得针对因使用其疫苗产品而产生的法律索赔的保护。对大多数国家（尤其是低收入和中等收入国家）来说，向制药公司提供赔偿或完全免于诉讼在宪法上或财政上是不可能的。研究者提出解决这一问题的办法包括利用现有的两种无过失疫苗伤害补偿系统，并在 COVAX 的授权下建立第三种制度。首先，目前已经有 24 个国家和加拿大魁北克省为常规免疫接种建立了无过失疫苗伤害补偿系统。其次，世卫组织对紧急使用授权下部署的疫苗制定一种保险机制。这一机制要求受援国同意赔偿世卫组织、捐助者、制造商和为人们接种疫苗的卫生保健工作者。为了满足这一需求，研究者认为 COVAX 基金应建立一个程序，对免疫接种后出现严重不良事件的人进行补偿。因为 COVAX 将要求国家疫苗部署计划，它可以使国家包括上市后安全监督计划。补偿基金服务于大量人群，包括中低收入国家。此外受害者信托基金是另一个适用的模式。这些赔偿制度表明，有可能为与新冠肺炎疫苗有关的伤害建立一个全球性的中央赔偿委员会。此外 COVAX 的补偿体系可以通过指定高收入国家的承诺资源或向制造商征收每剂税来支持其目的。设在 COVAX 基金的全球赔偿委员会是一个现实、可实现的解决方案，它将促进新冠肺炎疫苗的采购，同时确保弱势人群能够寻求伤害赔偿，并可能为未来的疫苗接种开创先例。

Abstract：

The Covid-19 pandemic has triggered a global vaccine race. The response to vaccine nationalism has been the creation of the COVAX Facility, an international partnership that aims to financially support leading vaccine candidates and ensure access to vaccines for lower-income countries. But large, up-front financial commitments to manufacturers are only half the solution when it comes to ensuring that companies will be willing to participate in the COVAX mechanism for vaccine distribution. Equally important is offering companies protection against potentially substantial liability should Covid-19 vaccines cause real or

perceived injuries to recipients. For most countries, offering pharmaceutical companies indemnity or complete immunity from lawsuits is constitutionally or financially impossible. The dilemma for low- and middle-income countries, therefore, involves whether to refuse to offer manufacturers protection against liability and go without Covid-19 vaccines or to extend liability protections (if doing so is constitutionally possible) and risk having a large number of people injured to whom the government is unable to offer compensation. First, 24 countries and the Canadian province of Quebec have no-fault vaccine-injury compensation systems for routine immunizations. Countries with existing no-fault vaccine-injury compensation systems could incorporate Covid-19 vaccines into these programs. For most countries, offering pharmaceutical companies indemnity or complete immunity from lawsuits is constitutionally or financially impossible. We believe that the solution to this problem involves leveraging two existing no-fault vaccine-injury regimens and constructing a third regimen under COVAX's authority. Second, the World Health Organization (WHO) has an insurance mechanism for vaccines deployed under emergency use authorizations. This mechanism requires that the recipient country agree to indemnify the WHO, donors, manufacturers, and health care workers who vaccinate people; the WHO then provides compensation to people who have a serious adverse event. To meet this need, we believe that the COVAX Facility should establish a procedure for compensating people who have a severe adverse event after immunization. Compensation funds have served large groups of people, including in low- and middle-income countries. Compensation funds have served large groups of people, including in low- and middle-income countries. The Trust Fund for Victims is another applicable model. These compensation systems demonstrate that it would be possible to create a global, centralized compensation commission for injuries related to Covid-19 vaccines. A COVAX compensation system could be funded by earmarking committed resources from higher-income countries or by charging manufacturers a per-dose tax to support its purpose. A global commission for compensation based at the COVAX Facility is a realistic, achievable solution that would facilitate the procurement of Covid-19 vaccines while ensuring that vulnerable people are able to seek compensation for injuries, and it could set a precedent for future vaccination campaigns.