新型冠状病毒信息简报

第 66 期（2020 年 8 月 1-7 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 8 月 6 日疫情

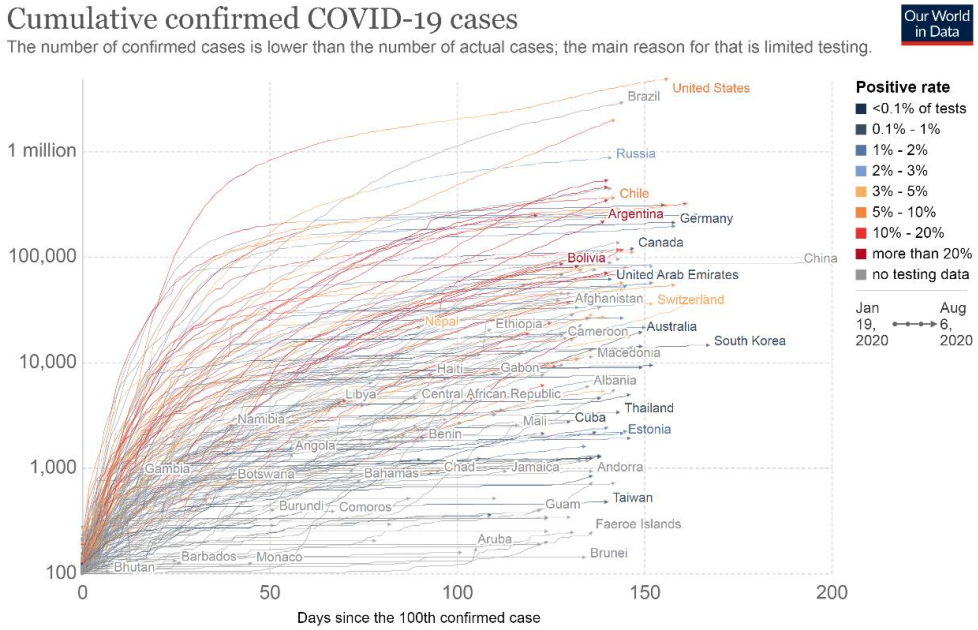
数据来源：WHO

发布时间：2020 年 8 月 6 日北京时间下午 4 点

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

根据 WHO 提供的数据，2020 年 8 月 6 日全球累计确诊新型冠状病毒病人 **18614177** 例，当日新增确诊 **259344** 例，累计死亡 **702642** 例，当日新增死亡 **6488**。

中国累计确诊 88804 例，累计死亡 4684 例，当日新增确诊 122 例，新增死亡 1 例。



Source: European CDC – Situation Update Worldwide – Last updated 6 August, 10:04 (London time), Official data collated by Our World in Data
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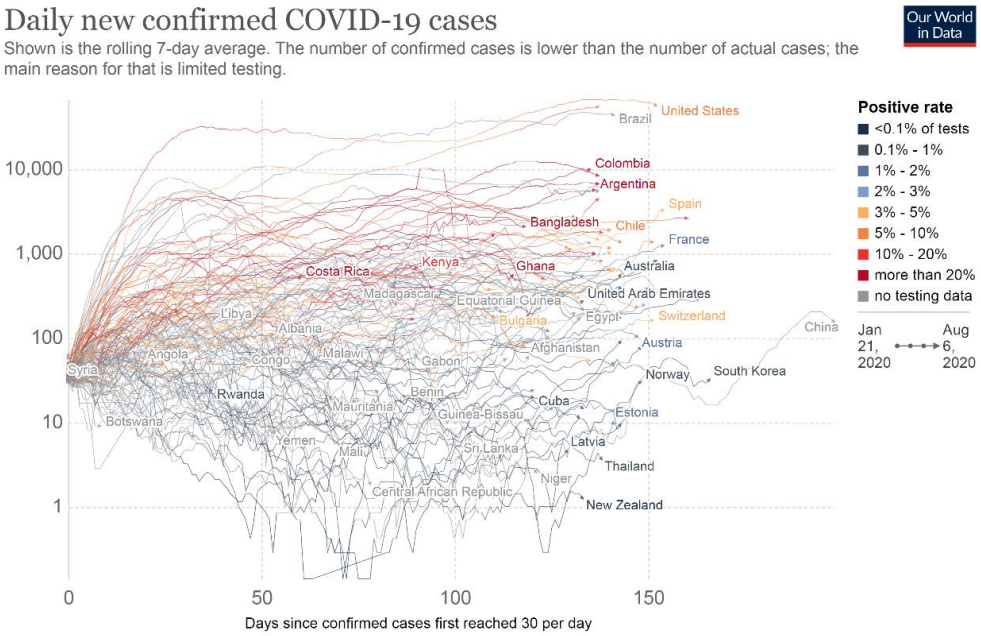
重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



Source: European CDC – Situation Update Worldwide – Last updated 6 August, 10:04 (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（8 月 6 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. Sound Pharmaceuticals 申请 IND 进行 SPI-1005 治疗 COVID-19 的临床二期试验

Sound Pharmaceuticals files IND to test SPI-1005 in Phase 2 COVID-19 trials

来源：prnewswire

发布时间：2020-07-30

链 接 ： https://www.prnewswire.com/news-releases/sound-pharmaceuticals-files-ind-to-test-spi-1005-in-phase-2-covid-19-trials-301103291.html

编译者：雷颖

中文摘要：

Sound Pharmaceuticals（SPI）欣然宣布向 FDA 提交了新药研究性测试申请，以开始进行预防和治疗 COVID-19 的临床二期研究。成年中度疾病患者将在一项双盲试验中随机分组，并接受 7 天的治疗，而病情较严重的患者将接受 14 天的治疗。在这些最初的安全性和探索性功效研究中，将对两种不同的 SPI-1005 口服剂量（400 和 800mg，每天两次）进行测试，并在 30 天的随访期内与安慰剂进行比较。Sound Pharmaceuticals 的创始人兼首席执行官，医学博士 Jonathan Kil 说：“除了 ebselen 具有潜在的抗病毒活性外，我们还将测试 SPI-1005 是否可以减少对 COVID-19 患者的肺和肾脏造成破坏性的炎症反应和细胞损伤。” 主持该临床二期研究的两位研究者之一是耶鲁大学医学院细胞生物学系教授、遗传系教授、妇产科系教授、干细胞中心创始主任林海帆，林教授也是上海科技大学免疫化学研究所特聘教授和生命科学与技术学院创始院长。

今年 4 月上海科技大学饶子和/杨海涛团队及其合作者发表在科学期刊《自然》上的一项最新研究中，成功解析了新型冠状病毒关键药物靶点——主蛋白酶（Mpro）的高分辨率三维空间结构，并综合利用三种不同的药物发现策略，找到针对新冠病毒的若干潜在药物，其中就包括 ebselen。SPI-1005 是一种正在研究中的新型抗炎药，主要成分为 ebselen。ebselen

是一种新型小分子，其模仿并诱导内耳，视网膜，脑，肺和肾中的谷胱甘肽过氧化物酶（GPx）的活性。有关这个临床二期试验的更多信息，请访问 Clinicaltrials.gov 和 NCT04484025。

Abstract

Sound Pharmaceuticals (SPI) is pleased to announce the filing of an Investigational New Drug Application with the FDA to begin Phase 2 studies to prevent and treat COVID-19. Adult patients with moderate disease will be randomized in a double-blind trial and treated for 7 days, while patients with more severe disease will be treated for 14 days. In these initial safety and exploratory efficacy studies, two different oral doses of SPI-1005 (400 and 800 mg, twice daily) will be tested and compared to placebo over a 30-day period of follow-up.

"In addition to ebselen's potential anti-viral activity, we will test if SPI-1005 can reduce the inflammatory response and cellular injury that is devastating to the lungs and kidneys of COVID-19 patients," said Dr. Jonathan Kil, MD, Co-Founder and CEO of Sound Pharmaceuticals.

SPI-1005 is an investigational new drug that contains ebselen, a novel small molecule that mimics and induces the activity of Glutathione Peroxidase (GPx) in the inner ear, retina, brain, lung, and kidney. SPI-1005 represents a novel class of anti-inflammatory and is under clinical investigation in several neurotologic diseases where GPx activity is reduced including sensorineural hearing loss, tinnitus, ototoxicity, Meniere's disease, and neuropsychiatric illness including bipolar mania. SPI-1005 is currently being tested in a Phase 2b study where Cystic Fibrosis patients with acute pulmonary exacerbations are receiving IV antibiotics to treat their respiratory infection. In this study, three different oral doses of SPI-1005 are being compared to placebo following 21 days of treatment.

For more information regarding these Phase 2 trials please see clinicaltrials.gov and NCT04484025.

3. SalivaDirect：用唾液对 SARS-CoV-2 监测的简单而敏感的分子诊断测试

SalivaDirect: Simple and sensitive molecular diagnostic test for SARS-CoV-2 surveillance

来源：medRxiv

发布时间：2020-08-04

链接：https://www.medrxiv.org/content/10.1101/2020.08.03.20167791v1

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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.08.03.20167791

编译者：张鹏伟

中文摘要：

目前提高 SARS-CoV-2 检测可访问性和可扩展性的瓶颈包括诊断分析成本、复杂性和供应链短缺。为了解决这些问题，我们开发了 SalivaDirect。我们的方法的关键部分是使用唾液

而不是呼吸拭子，这使得无创的频繁采样成为可能，并减少了在采集过程中对训练有素的医疗专业人员的需求。此外，我们简化了我们的诊断测试，在样本收集时不需要核酸防腐剂，用简单的蛋白酶 K 和热处理步骤代替核酸提取，并用双重定量逆转录聚合酶链反应（RT-qPCR）检测标本。我们使用来自多个供应商的试剂和仪器对唾液直接进行验证，以将供应链问题的风险降至最低。不管我们测试的试剂和仪器组合来自不同的供应商，我们发现唾液直接检测是高度敏感的，检测限为 6-12 个 SARS-CoV-2 copies / μL。当使用经授权的 ThermoFisher Scientific TaqPath COVID-19 组合试剂盒和我们的唾液直接方案比较配对的鼻咽拭子和唾液标本时，我们发现检测结果的一致性很高（>94%）。由于其灵活和廉价（1.29-4.37 美元/样本），SalivaDirect 是一个可行且容易获得的选择，有助于缓解 SARS-CoV-2 检测需求。我们于 2020 年 7 月 14 日向美国食品和药物管理局提交了一份实验室开发的测试报告，以获得紧急使用授权，目前的详细信息可以在我们的网站上找到(covidtrackerct.com/about-salivadirect/)。

Abstract

Current bottlenecks for improving accessibility and scalability of SARS-CoV-2 testing include diagnostic assay costs, complexity, and supply chain shortages. To resolve these issues, we developed SalivaDirect. The critical component of our approach is to use saliva instead of respiratory swabs, which enables non-invasive frequent sampling and reduces the need for trained healthcare professionals during collection. Furthermore, we simplified our diagnostic test by not requiring nucleic acid preservatives at sample collection, replacing nucleic acid extraction with a simple proteinase K and heat treatment step, and testing specimens with a dualplex quantitative reverse transcription PCR (RT-qPCR) assay. We validated SalivaDirect with reagents and instruments from multiple vendors to minimize the risk for supply chain issues. Regardless of our tested combination of reagents and instruments from different vendors, we found that SalivaDirect is highly sensitive with a limit of detection of 6-12 SARS-CoV-2 copies/μL. When comparing paired nasopharyngeal swabs and saliva specimens using the authorized ThermoFisher Scientific TaqPath COVID-19 combo kit and our SalivaDirect protocol, we found high agreement in testing outcomes (>94%). Being flexible and inexpensive ($1.29-$4.37/sample), SalivaDirect is a viable and accessible option to help alleviate SARS-CoV-2 testing demands. We submitted SalivaDirect as a laboratory developed test to the US Food and Drug Administration for Emergency Use Authorization on July 14th, 2020, and current details can be found on our website (covidtrackerct.com/about-salivadirect/).

4. 与 SARS-CoV-2 生存率密切相关的早期血清学特征

Distinct early serological signatures track with SARS-CoV-2 survival

来源：Immunity

发布时间：2020-07-30

链接：https://www.cell.com/immunity/fulltext/S1074-7613(20)30327-7

第一作者：Caroline Atyeo, Stephanie Fischinger, Tomer Zohar

通讯作者：Helen Chu5, and Galit Alter1

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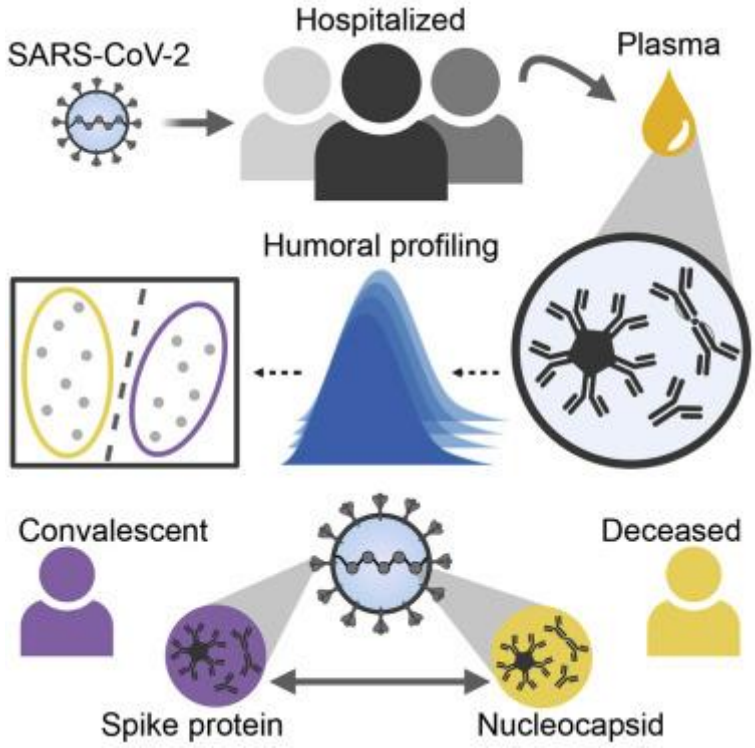
DOI 或 PUBMED ID：https://doi.org/10.1016/j.immuni.2020.07.020
编译者：宋张悦
中文摘要：
随着 SARS-CoV-2 感染和死亡人数继续上升，仍不清楚为什么一些人从感染中康复，而另一些人迅速发展并死亡。本文分析了 22 名住院患者的 SARS-CoV-2 特异性体液反应。尽管个体间存在异质性，但不同的抗体标记使个体具有不同的结局。虽然在 SARS-CoV-2 特异性 IgG 水平没有观察到差异，**spike-特异性体液反应在恢复期个体中有富集，而功能性抗体对核衣壳的反应在死亡个体中升高**。此外，这一丰富的免疫优势 S-特异性抗体谱在恢复期更大的验证队列中得到证实。这些结果表明，SARS-CoV-2 特异性抗体的早期抗原特异性和定性特征表明了疾病轨迹的差异，强调功能性抗原特异性体液免疫对指导患者护理和疫苗开发的潜在重要性。
Graphical Abstract



Highlights
• Limited early differences across groups were observed in titers and neutralization
• Five antibody features collectively could differentiate convalescents and deceased
• A shift in the balance of spike versus nucleocapsid immunity separated the groups
• Spike-specific phagocytic and complement fixing activity was enriched in convalescents

5. SARS-CoV-2 感染恢复期患者的持续细胞免疫失调

Sustained Cellular Immune Dysregulation in Individuals Recovering from SARS-CoV-2 Infection

来源：medrxiv
发布时间：2020-08-01
链接：https://www.medrxiv.org/content/10.1101/2020.07.30.20165175v1
第一作者：Jacob K. Files
通讯作者：Paul A. Goepfert, Nathan Erdmann
通讯作者单位：Division of Infectious Diseases, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL 35294, USA
DOI 或 PUBMED ID：
编译者：王玮
中文摘要：
SARS-CoV-2 感染会引起很多的临床表现和显著的死亡率。研究潜在的免疫特性是了解疾病发病机制和疫苗设计所必需的。该研究检测了住院和非住院患者的免疫细胞亚群。住院患者的许多适应性和先天性免疫细胞较健康人和恢复期患者减少，但是 B 淋巴细胞增加。该研究结果显示，与健康人和非住院患者相比，住院患者的 T 细胞活化标记物阳性（CD69、Ox40、HLA-DR 和 CD154）的细胞增加，以及其他 T 细胞活化/耗竭标记物（CD25、PD-L1 和 TIGIT）升高。B 细胞的激活/衰竭模式相似，住院患者的 CD69 和 CD95 的阳性细胞增加，非住院患者的 PD1 阳性细胞增加。有趣的是，在非住院患者的纵向样本中，这些变化中有许多随着时间的推移而增加，这表明 SARS-CoV-2 感染后的免疫失调期延长。非住院患者 T 细胞活化/衰竭的变化与年龄呈正相关。重症患者的活化和衰竭标志物表达增加。这些数据表明，SARS-CoV-2 感染后免疫失调的持续时间延长，这表明需要进一步研究恢复期患者的免疫失调。

Abstract
SARS-CoV-2 causes a wide spectrum of clinical manifestations and significant mortality. Studies investigating underlying immune characteristics are needed to understand disease pathogenesis and inform vaccine design. In this study, we examined immune cell subsets in hospitalized and non-hospitalized individuals. In hospitalized patients, many adaptive and innate immune cells were decreased in frequency compared to healthy and convalescent individuals, with the exception of B lymphocytes which increased. Our findings show increased frequencies of T-cell activation markers (CD69, Ox40, HLA-DR and CD154) in hospitalized patients, with other T-cell activation/exhaustion markers (CD25, PD-L1 and TIGIT) remaining elevated in hospitalized and non-hospitalized individuals. B cells had a similar pattern of activation/exhaustion, with increased frequency of CD69 and CD95 during hospitalization, followed by an increase in PD1 frequencies in non-hospitalized individuals. Interestingly, many of these changes were found to increase over time in non-hospitalized longitudinal samples, suggesting a prolonged period of immune dysregulation following SARS-CoV-2 infection. Changes in T-cell activation/exhaustion in non-hospitalized patients were found to positively correlate with age. Severely infected individuals had increased expression of activation and exhaustion markers. These data suggest a prolonged period of immune dysregulation following SARS-CoV-2 infection highlighting the need for additional studies investigating immune dysregulation in convalescent individuals.

6. 被 SARS-CoV-2 病毒感染的肺泡巨噬细胞和 T 细胞之间的自持性循环导致了重症 SARS-

CoV-2 肺炎患者的肺泡炎

Alveolitis in severe SARS-CoV-2 pneumonia is driven by self-sustaining circuits between infected alveolar macrophages and T cells

来源：bioRxiv
发布时间：2020-08-05
链接：https://www.biorxiv.org/content/10.1101/2020.08.05.238188v1

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DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

部分被 SARS-CoV-2 病毒感染的患者会发展为严重的肺炎和急性呼吸窘迫综合症（ARDS）。根据这些患者明显的临床特征，人们推测被 SARS-CoV-2 感染的肺泡对病毒的免疫反应与其他类型的肺炎不同。本文中，作者收集了 86 例因感染 SARS-CoV-2 而引起呼吸衰竭的患者的支气管肺泡灌洗液样本，以及 252 例因感染其他病原体而导致的已知或疑似肺炎患者的支气管肺泡灌洗液样本，随后对其进行了流式细胞术和混池转录组分析。作者从重症 COVID-19 患者在插管后 48 小时内获取的支气管肺泡灌洗液样本中抽取了 5 例，进行了单细胞 RNA-Seq 检测。发现在机械通气的初始阶段，大多数感染 SARS-CoV-2 的患者中，其肺泡腔内持续地富集肺泡巨噬细胞和 T 细胞，而没有中性白细胞。混池和单细胞转录组分析的结果表明，SARS-CoV-2 病毒感染了肺泡巨噬细胞，并导致了不断招募 T 细胞。这些 T 细胞释放干扰素，从而诱导肺泡巨噬细胞释放炎性细胞因子，同时进一步促进 T 细胞的招募。作者的研究结果表明，SARS-CoV-2 病毒引起了发展缓慢，且空间分布有限的肺泡炎。携带 SARS-CoV-2 病毒转录物质的肺泡巨噬细胞和 T 细胞能够在其中形成正反馈回路，从而引发进行性肺泡炎。

Abstract

Some patients infected with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) develop severe pneumonia and the acute respiratory distress syndrome (ARDS). Distinct clinical features in these patients have led to speculation that the immune response to virus in the SARS-CoV-2-infected alveolus differs from other types of pneumonia. We collected bronchoalveolar lavage fluid samples from 86 patients with SARS-CoV-2-induced respiratory failure and 252 patients with known or suspected pneumonia from other pathogens and subjected them to flow cytometry and bulk transcriptomic profiling. We performed single cell RNA-Seq in 5 bronchoalveolar lavage fluid samples collected from patients with severe COVID-19 within 48 hours of intubation. In the majority of patients with SARS-CoV-2 infection at the onset of mechanical ventilation, the alveolar space is persistently enriched in alveolar macrophages and T cells without neutrophilia. Bulk and single cell transcriptomic profiling suggest SARS-CoV-2 infects alveolar macrophages that respond by recruiting T cells. These T cells release interferon-gamma to induce inflammatory cytokine release from alveolar macrophages and further promote T cell recruitment. Our results suggest SARS-CoV-2 causes a

slowly unfolding, spatially-limited alveolitis in which alveolar macrophages harboring SARS-CoV-2 transcripts and T cells form a positive feedback loop that drives progressive alveolar inflammation.

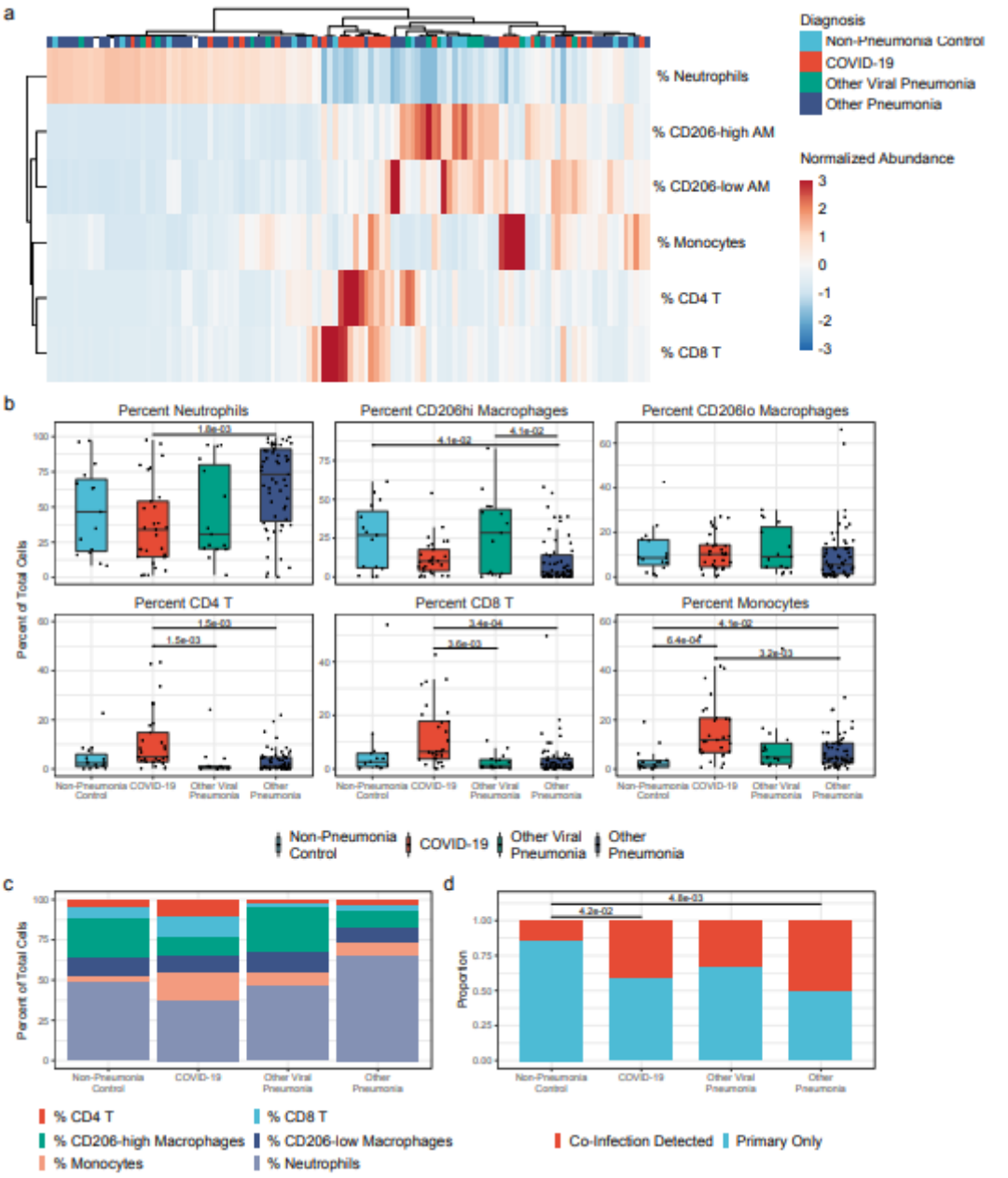


Figure 2. The alveolar space in patients with severe SARS-CoV-2 pneumonia is enriched for T cells and monocytes and lacks neutrophils at the onset of mechanical ventilation. a. Hierarchical clustering of BAL samples collected within 48 hours of intubation based on their composition. Samples from patients with non-COVID19 pneumonia are characterized by neutrophilia while BAL fluid from most patients with SARS-CoV-2 pneumonia is enriched for CD4+ and CD8+ T cells and monocytes. Samples were clustered by Euclidean distance using Ward's method. **b.** Proportions of cells detected within 48 hours of intubation. Proportion of CD4+ and CD8+ T cells is increased in the COVID-19 cohort ($q < 0.05$, pairwise Wilcoxon rank-sum tests with FDR correction) and proportion of neutrophils is reduced in these patients, relative to non-viral pneumonia controls ($q < 0.05$, pairwise Wilcoxon ranksum tests with FDR correction). Comparisons are not significant unless otherwise noted. **c.** Averaged

cell-type compositions in the first 48 hours of intubation, binned by diagnosis. **d.** Comparison of rates of co-infection. Coinfection was defined by detection in a single sample of any bacterial or fungal pathogen listed in Table 2 by culture or multiplex PCR analysis. No significant differences were observed between the COVID-19 cohort and pneumonia controls ($q \geq 0.05$, pairwise Chi-Square tests of proportions with continuity and FDR correction).

7. 针对 SARS-CoV-2 肺部感染的宿主反应具有时空异质性

Temporal and Spatial Heterogeneity of Host Response to SARS-CoV-2 Pulmonary Infection

来源：medrxiv

发布时间：2020-08-02

链接：https://www.medrxiv.org/content/10.1101/2020.07.30.20165241v1

第一作者：Niyati Desai

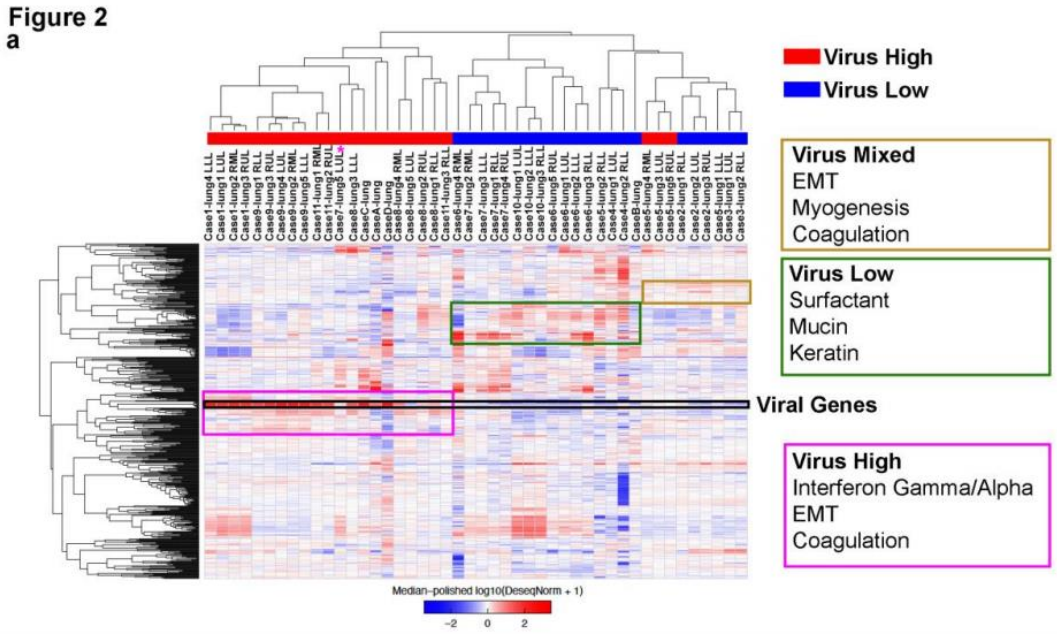
通讯作者：Vikram Deshpande

通讯作者单位： Massachusetts General Hospital

编译者：蒋立春

中文摘要：

我们还没有完全了解 SARS-CoV-2 肺部感染和症状的严重程度的关系。作者们用各种 RNA 和蛋白分析平台分析了 24 个 COVID-19 病人的尸检解剖样品，以了解病人体内以及不同病人之间肺部病毒感染的异质性。在病毒含量高和病毒含量低的病人中，可以看到病程的长度差异以及干扰素通路基因的激活的差异。用数字空间表达谱平台的分析可以看到病毒和干扰素反应基因以及免疫检查点基因的表达相一致，揭示 SARS-CoV-2 感染存在肺内部的异质性。



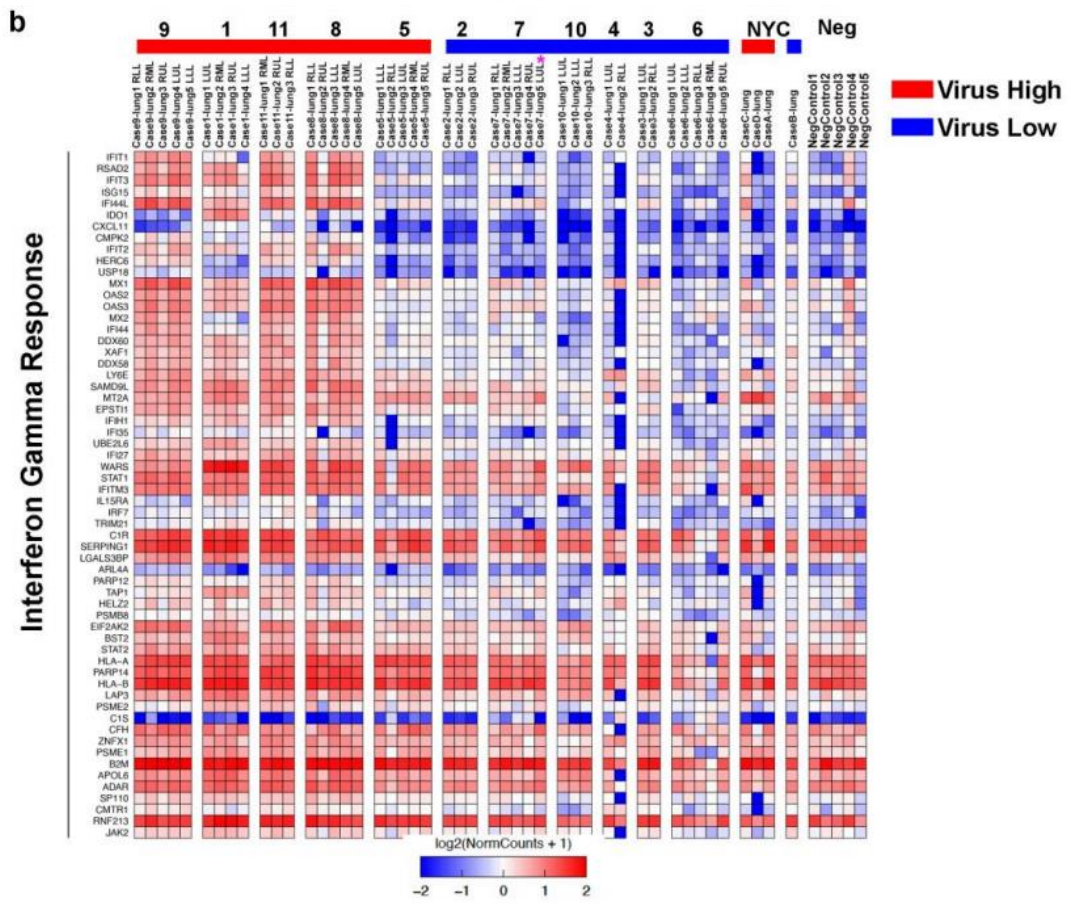


Figure 2: Interferon gamma response genes define high SARS-CoV-2 cases a, Unsupervised hierarchical clustering of 500 most variant genes across lung specimens from SARS-CoV-2 infected patients separating into high, mixed, and low viral RNA cases. b, Gene expression heatmap of interferon gamma response genes differentially expressed between high and low viral RNA cases. The high viral cases were enriched with higher interferon response genes.

Abstract

The relationship of SARS-CoV-2 lung infection and severity of pulmonary disease is not fully understood. We analyzed autopsy specimens from 24 patients who succumbed to SARS-CoV-2 infection using a combination of different RNA and protein analytical platforms to characterize inter- and intra- patient heterogeneity of pulmonary virus infection. There was a spectrum of high and low virus cases that was associated with duration of disease and activation of interferon pathway genes. Using a digital spatial profiling platform, the virus corresponded to distinct spatial expression of interferon response genes and immune checkpoint genes demonstrating the intra-pulmonary heterogeneity of SARS-CoV-2 infection.

8. 抗 MDA5 抗体的增强意味着 COVID-19 患者患有严重疾病

Augmentation of anti-MDA5 antibody implies severe disease in COVID-19 patients

来源：medRxiv

发布时间：2020-08-01

链接：https://www.medrxiv.org/content/10.1101/2020.07.29.20164780v1
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DOI 或 PUBMED ID：
编译者：张鹏伟
中文摘要：
最近的研究为严重急性呼吸综合征冠状病毒 2 型（SARS-CoV2）感染引发的自身炎症提供了见解，这与 2019 年冠状病毒病（COVID-19）的高死亡率有关。COVID-19 与抗黑色素瘤分化相关基因 5（MDA5）抗体（Ab）相关皮肌炎（DM）之间存在显著的相似性，这意味着共同的自身炎症异常。然而，目前尚不清楚 COVID-19 中是否存在抗 MDA5 抗体，并与 COVID-19 患者的严重程度和不良结局相关。在这里，我们发现 COVID-19 患者中抗 MDA5-Ab 的阳性率为 48.2%，并且抗 MDA5-Ab 阳性的患者有发展为严重疾病的趋势（88.6%比 66.9%，P<0.0001）。特别是，抗 MDA5 抗体滴度在非存活组升高（5.95±5.16 vs 8.22±6.64，P=0.030），阳性率也高于存活组（23.5%vs12.0%，P=0.012）。对于严重的 COVID-19 患者，我们发现抗 MDA5 抗体的高滴度（≥10.0 U/mL）在非存活患者中更为普遍（31.2%比 14.0%，P=0.006）。此外，早期检测抗 MDA5 抗体可以区分重症患者和非重症患者。总的来说，我们的数据显示抗 MDA5 抗体在 COVID-19 患者中普遍存在，这种抗体的高滴度与严重疾病和不良结局相关。
Abstract
Recent studies have provided insights into the autoinflammation triggered by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection, which is associated with high mortality of coronavirus disease 2019 (COVID-19). Striking similarities has been noted between COVID-19 and anti-melanoma differentiation-associated gene 5 (MDA5) antibody (Ab)-related dermatomyositis (DM), implying a shared autoinflammatory aberrance. However, it is unclear whether anti-MDA5 Ab is present in COVID-19 and correlates with the severity and adverse outcome of COVID-19 patients. Here, we found that the positive rate of anti-MDA5 Ab in patients with COVID-19 was 48.2% and the anti-MDA5 Ab positive patients tended to develop severe disease (88.6% vs 66.9%, P<0.0001). In particular, the titer of anti-MDA5 Ab was increased in the non-survivals (5.95±5.16 vs 8.22±6.64, P=0.030) and the positive rate was also higher than that in the survivals (23.5% vs 12.0%, P=0.012). Regarding to severe COVID-19 patients, we found that high titer of anti-MDA5 Ab (≥10.0 U/mL) was more prevalent in the non-survivals (31.2% vs 14.0%, P=0.006). Moreover, early profiling of anti-MDA5 Ab could distinguish severe patients from those with non-severe ones. Overall, our data reveal that anti-MDA5 Ab is prevalent in the COVID-19 patients and high titer of this antibody is correlated with severe disease and unfavorable outcomes.

9. Warp Speed 承诺对赛诺菲和葛兰素史克 COVID-19 计划投资 21 亿美元，美国对七种疫苗的总投资达到 83 亿美元

Warp Speed’s $2.1B commitment to Sanofi-GSK COVID-19 program brings total to $8.3B across seven vaccines
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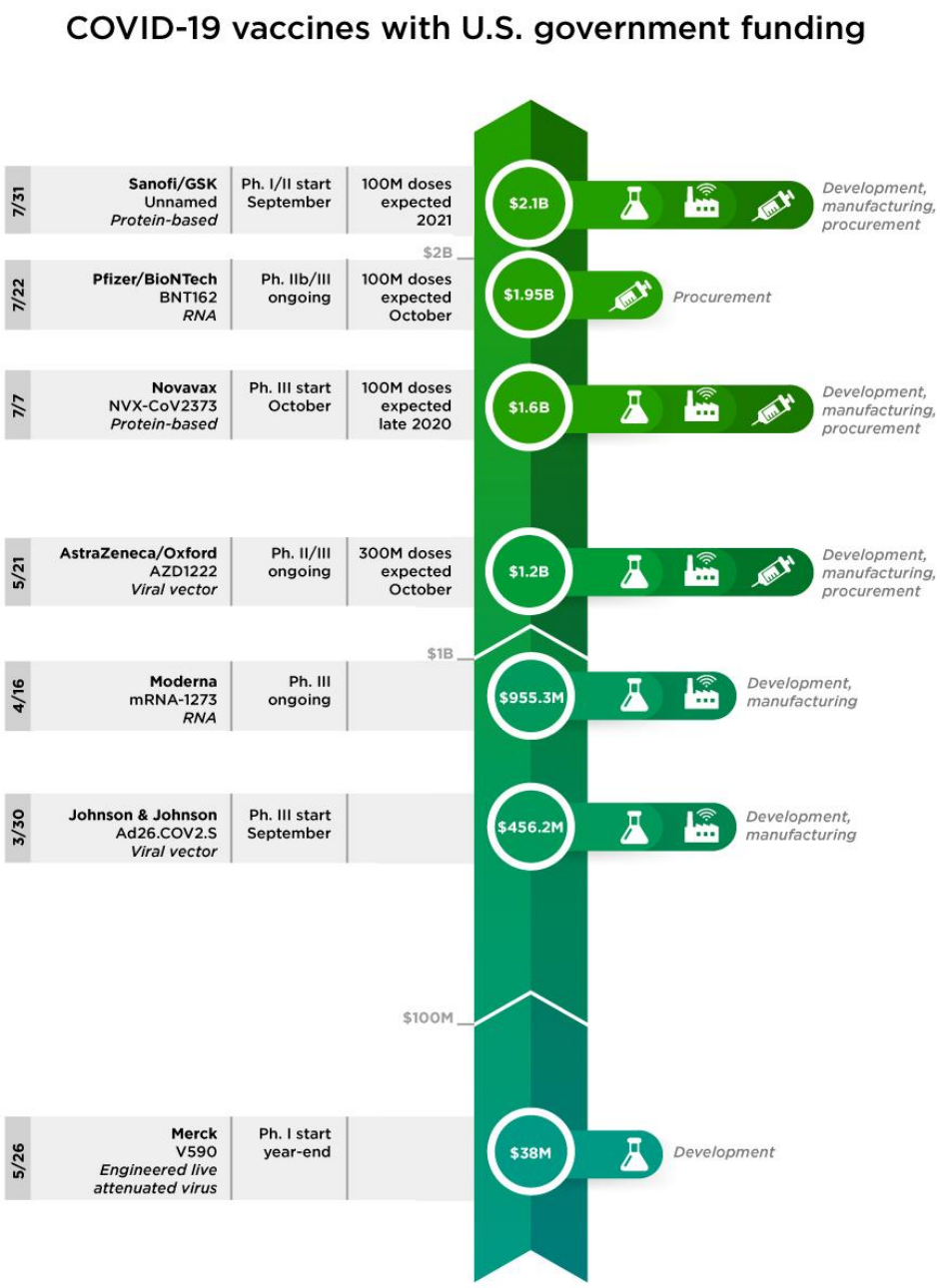
链接：
https://www.biocentury.com/article/305831?editionId=ckdb1c8pk1vz3017487f90pkj&editionType=daily
第一作者：PAUL BONANOS
通讯作者：
通讯作者单位：
DOI 或 PUBMED ID：
编译者：王玮
中文摘要：
赛诺菲和葛兰素史克的一种临床前疫苗可能比其他研制中的 COVID-19 疫苗晚几个月，但美国政府已经为其研发和制造做出了迄今最大的财政承诺，承诺在“Warp Speed”中投入 21 亿美元。
这使得美国政府在使用四种不同模式的 7 个疫苗项目中总共承诺约 83 亿美元，其中大部分已在临床上使用。
大部分新资金将流向赛诺菲，超过一半的资金被指定用于疫苗的研发，包括 9 月份开始的临床试验。余款将用于第一批 1 亿剂的疫苗生产和交付；美国还有另外 5 亿剂供应的选择。
这两家公司在疫苗领域历来是竞争对手，但目前正在合作研制 COVID-19 产品。该疫苗使用了赛诺菲公司的一种抗原，基于该公司流感疫苗中使用的重组蛋白技术，以及葛兰素史克公司的佐剂。将于 9 月进入临床 I 期/II 期，并在年底前进行 III 期。
“Warp Speed”的目标是获得数百万剂量的安全有效的 COVID-19 疫苗。第一份紧急使用授权书可能在年底前到达，其他授权书也将在 2021 年出台。另外五种获得了“Warp Speed”资助的疫苗已经投入临床，其中三种正在进行后期测试。
葛兰素史克的一位发言人告诉 BioCentury，现在报告疫苗的任何临床前数据还为时过早。这两家公司预计采用两次给药方案，但也在测试单剂量给药。
赛诺菲计划将一部分剂量用于 Access to COVID-19 Tools (ACT) Accelerator，并已开始与 COVID-19 Vaccine Global Access Facility (COVAX)进行对话，以确保全球获得疫苗。今年由全球公共卫生和私营部门组织发起，ACT 加速器创建了 COVAX 作为全球采购池，为世界各地的优先人群提供疫苗。
英国政府与赛诺菲和葛兰素史克达成了 6000 万剂疫苗的协议。
Abstract
A preclinical vaccine from Sanofi and GSK may be months behind other COVID-19 vaccines in development, but the U.S. government has made its largest financial commitment yet to its development and manufacturing, pledging up to $2.1 billion as part of Operation Warp Speed.
That brings the U.S. government’s total commitment to about $8.3 billion across seven vaccine programs that use four different modalities, most of which are already in the clinic (see “COVID-19 Vaccines with U.S. Government Funding”).
The majority of the new cash will go to Sanofi (Euronext:SAN; NASDAQ:SNY). More than half is earmarked for the vaccine’s development, including clinical testing that is due to start in September. The balance will go toward manufacturing and delivery of the first 100 million doses; the U.S. has an option for the supply of an additional 500 million.
The two companies have historically been competitors in the vaccine sector, but are collaborating on the COVID-19 product. The vaccine uses an antigen from

Sanofi, based on the recombinant protein technology used in the company's flu vaccine, along with an adjuvant from GlaxoSmithKline plc (LSE:GSK; NYSE:GSK).
It is due to enter a Phase I/II trial in September, with a Phase III trial to follow by year-end.
Operation Warp Speed is aiming to secure many millions of doses of a safe and effective COVID-19 vaccine. The first Emergency Use Authorization could arrive by year-end, with others to follow in 2021. Five other vaccines that have received Operation Warp Speed funding are already in the clinic, with three in late-stage testing…



10. 核苷修饰的 mRNA 疫苗的单次免疫在小鼠中引起针对 SARS-CoV-2 的强烈细胞和体液免疫反应

A single immunization with nucleoside-modified mRNA vaccines elicits strong cellular and humoral immune responses against SARS-CoV-2 in mice

来源：Immunity

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DOI 或 PUBMED ID：https://doi.org/10.1016/j.immuni.2020.07.019

编译者：张丽双

中文摘要：

研究人员提供了对脂质纳米颗粒包裹的，核苷修饰的 mRNA（mRNA-LNP）疫苗（编码全长 SARS-CoV-2 刺突蛋白或刺突蛋白受体结合域）在小鼠中的免疫原性的详细评估。我们证明这些疫苗单剂量可诱导强烈的 1 型 CD4+和 CD8+ T 细胞反应，以及长时间的血浆和记忆 B 细胞反应。此外，我们检测到强大且持续的中和抗体反应，而核苷修饰的 mRNA 疫苗引发的抗体在体外并未表现出抗体依赖性的感染增强作用。疫苗诱导的 T 细胞很容易离开脉管系统并进入肺实质。这些发现表明，核苷修饰的 mRNA-LNP 疫苗平台可以诱导强大的免疫反应，并且是对抗 COVID-19 的有希望的候选者。

Abstract

SARS-CoV-2 infection has emerged as a serious global pandemic. Because of the high transmissibility of the virus and the high rate of morbidity and mortality associated with COVID-19, developing effective and safe vaccines is a top research priority. Here, we provide a detailed evaluation of the immunogenicity of lipid nanoparticle-encapsulated, nucleoside-modified mRNA (mRNA-LNP) vaccines encoding the full length SARS-CoV-2 spike protein or the spike receptor binding domain in mice. We demonstrate that a single dose of these vaccines induces strong type 1 CD4+ and CD8+ T cell responses, as well as long-lived plasma and memory B cell responses. Additionally, we detect robust and sustained neutralizing antibody responses and the antibodies elicited by nucleoside-modified mRNA vaccines do not show antibody-dependent enhancement of infection in vitro. Our findings suggest that the nucleoside-modified mRNA-LNP vaccine platform can induce robust immune responses and is a promising candidate to combat COVID-19.

11. 中国的冠状病毒疫苗正在大步前进，但面临着病毒消退的挑战

China’s coronavirus vaccines are leaping ahead – but face challenges as virus wanes

来源：nature

发布时间：2020.07.31

文章链接：https://www.nature.com/articles/d41586-020-02244-1

作者：David Cyranoski

作者信息：David Cyranoski reports for Nature from Shanghai, China.

doi: 10.1038/d41586-020-02244-1
编译者：张怡
中文摘要：
中国企业在研制冠状病毒疫苗的全球努力中走在前列，有超过六家候选公司正在临床研发中。上周，位于天津的 CanSino Biologics 公布了一项早期临床试验的结果，表明其疫苗是安全的，可以引发免疫反应。
然而，这些公司在努力推动疫苗通过第三阶段试验时可能面临困难，这是一个关键的测试阶段，需要证明其有效性并获得监管机构的批准。这些试验通常需要数以万计的参与者，而随着中国疫情在很大程度上得到控制，企业不得不在其他地方测试疫苗。但研究人员表示，他们可能仍然难以招收这么多的参与者，并聘请足够的医疗保健专业人员来收集数据。
中国疫苗制造商也将面临其他挑战。科学家们说，鉴于中国严格的监管体系和此前的长春疫苗问题，疫苗可能会面临额外的审查。
作为冠状病毒爆发的国家，中国在开发疫苗方面迅速走出大门。CanSino 的产品是由一种普通感冒病毒制成的，经过调整以模仿冠状病毒。北京的一家国有制药公司国药集团（Sinopharm）正在开发两种疫苗，这种疫苗使用的是已经灭活的冠状病毒颗粒，这样它们就不会再致病了。该公司在 6 月份的新闻发布会上说，这两种疫苗在第一阶段和第二阶段试验的所有参与者中都产生了抗体。北京的科兴公司也宣布了同样有希望的灭活病毒疫苗的结果。
本月，科兴在巴西启动了疫苗的第三阶段试验。国药集团将在阿联酋测试其灭活疫苗。只有另外三种冠状病毒疫苗进入第三阶段试验：一种由马萨诸塞州剑桥市的生物技术公司 Moderna 生产；一种由位于英国剑桥的牛津大学和制药商阿斯利康公司生产；另一种由德国美因茨的生物技术公司 BioNTech 与总部设在纽约的制药公司辉瑞（Pfizer）合作生产。
CanSino 还准备启动第三阶段的试验。但中国政府已经表示，其疫苗可供军方使用，这使得中能科技成为第一家获准在人群中限量使用的 COVID-19 疫苗的公司。法国里昂大学疫苗研究人员 Stéphane Paul 说，中国在这一过程中努力“尽快生产出一种有效的疫苗，并且做到透明”。
但一些研究人员质疑，在阿联酋和巴西进行的试验能否收集到足够的数据，使监管机构相信疫苗有效。在阿联酋，国药集团计划招收 15000 名参与者来研究这两种疫苗，感染 COVID-19 的人相对较少。
尽管巴西爆发了大规模的冠状病毒疫情，但丁坦研究所计划在卫生保健专业人员中测试科诺伐的疫苗，因为据推测，他们将面临比非卫生保健专业人员更多的病毒暴露。领导这项试验的该研究所临床研究员里卡多·帕拉西奥斯说，正因为如此，这项试验将只招收 9000 人来测试它是否有效。帕拉西奥斯说：“我们设计了一个试验，以更有效的方式获得答案。”。
Abstract
Chinese companies are at the forefront of global efforts to create a vaccine for the coronavirus, with more than half a dozen candidates in clinical development. Last week, Tianjin-based CanSino Biologics published results1 from an early-stage clinical trial showing that its vaccine is safe and can trigger an immune response.
Yet the companies could face difficulty as they try to push vaccines through phase III trials, a crucial stage of testing that is needed to prove efficacy and secure approval from regulators. These trials usually require tens of thousands of participants, and with the outbreak in China largely under control, companies are having to test their vaccines elsewhere. But researchers say they

might still struggle to enrol so many participants and employ enough health-care professionals to collect data.

Chinese vaccine-makers will face other challenges, too. Vaccines will probably face extra scrutiny, given the country's opaque regulatory system and previous vaccine scandals, say scientists.

As the country where the coronavirus outbreak began, China was fast out of the gate in developing vaccines. CanSino's offering is made from a common-cold virus, tweaked to mimic the coronavirus. Sinopharm, is developing two vaccines made using particles of the coronavirus that have been inactivated so that they can no longer cause disease. The company said in press releases in June that both vaccines had produced antibodies in all participants in preliminary phase I and II trials. And Sinovac has announced similarly promising results for its own inactivated-virus vaccine.

This month, Sinovac launched a phase III trial of its vaccine in Brazil. Sinopharm will be testing its inactivated vaccines in the United Arab Emirates (UAE). Only three other coronavirus vaccines have entered phase III trials: one produced by biotech company Moderna in Cambridge, Massachusetts; one by the University of Oxford and drug maker AstraZeneca, based in Cambridge, UK; and one by biotech company BioNTech of Mainz, Germany, in collaboration with New York City-based drug firm Pfizer.

CanSino is also poised to launch a phase III trial. But the Chinese government has already said that its vaccine can be used by the military — making CanSino the first company to have a vaccine for COVID-19 approved for limited use in people. China has worked hard "to generate an efficient vaccine as soon as possible and to be transparent" when doing so, says Stéphane Paul, a vaccine researcher at the University of Lyon in France.

But some researchers question whether the trials in the UAE and Brazil will gather enough data to convince regulatory agencies that the vaccines work. In the UAE, where Sinopharm plans to enrol 15,000 participants to study its two vaccines, relatively few people are infected with COVID-19.

And although Brazil has a large coronavirus outbreak, the Butantan Institute plans to test Sinovac's vaccine among health-care professionals because it is assumed they will face greater exposure to the virus than will non-health-care professional. Because of this, the trial will enrol only 9,000 people to test whether it works, says Ricardo Palacios, a clinical researcher at the institute who is leading the trial. "We designed a trial in order to obtain answers in a more efficient way," says Palacios.

12. 工程化的 ACE2 受体陷阱能有效中和 SARS-CoV-2

Engineered ACE2 receptor traps potently neutralize SARS-CoV-2

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第一作者：Anum Glasgow

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DOI 或 PUBMED ID：preprint
编译者：孔娟
中文摘要：
SARS-CoV-1 和 SARS-CoV-2 感染的基本机制始于病毒 S 蛋白与 ACE2 的结合。文中研究者通过一种逐步工程化的方法产生一组亲和力优化的、酶灭活的 ACE2 突变体，这些突变体能够有效地阻断 SARS-CoV-2 对细胞的感染。这些优化的受体陷阱与病毒 S 蛋白的受体结合域(RBD)紧密结合，抑制其进入宿主细胞。我们首先通过计算设计了 ACE2-RBD 界面，使用两阶段灵活的蛋白质主链设计过程将其对 RBD 的亲和力提高了 12 倍。随后通过随机诱变和酵母表面展示筛选，这些设计的受体突变体亲和力进一步提高 14 倍。亲和力最高的突变体包含 7 个氨基酸的变化，其与 RBD 蛋白的结合强度是野生型 ACE2 的 170 倍。通过天然 ACE2 集合结构域及人 Fc 结构域的融合，提高了突变体的稳定性和亲和力，最优的 ACE2 受体陷阱能够中和 SARS-CoV-2 假型慢病毒及真 SARS-CoV-2 病毒，其半最大抑制浓度(IC50)在几十纳克/毫升范围内。工程化的 ACE2 受体陷阱可能成为抗 SARS-CoV 和其他 ACE2 利用冠状病毒感染的有效途径，其主要优点是病毒耐药性也可能会抑制病毒的进入。此外，可以为具有已知进入受体的病毒预先设计这种陷阱，以获得更快的治疗反应，而不需要从恢复期患者中分离或产生中和抗体。

Abstract
An essential mechanism for SARS-CoV-1 and -2 infection begins with the viral spike protein binding to the human receptor protein angiotensin-converting enzyme II (ACE2). Here we describe a stepwise engineering approach to generate a set of affinity optimized, enzymatically inactivated ACE2 variants that potently block SARS-CoV-2 infection of cells. These optimized receptor traps tightly bind the receptor binding domain (RBD) of the viral spike protein and prevent entry into host cells. We first computationally designed the ACE2-RBD interface using a two-stage flexible protein backbone design process that improved affinity for the RBD by up to 12-fold. These designed receptor variants were affinity matured an additional 14-fold by random mutagenesis and selection using yeast surface display. The highest affinity variant contained seven amino acid changes and bound to the RBD 170-fold more tightly than wild-type ACE2. With the addition of the natural ACE2 collectrin domain and fusion to a human Fc domain for increased stabilization and avidity, the most optimal ACE2 receptor traps neutralized SARS-CoV-2 pseudotyped lentivirus and authentic SARS-CoV-2 virus with half-maximal inhibitory concentrations (IC50) in the tens of ng/ml range. Engineered ACE2 receptor traps offer a promising route to fighting infections by SARS-CoV-2 and other ACE2-utilizing coronaviruses, with the key advantage that viral resistance would also likely impair viral entry. Moreover, such traps can be pre- designed for viruses with known entry receptors for faster therapeutic response without the need for neutralizing antibodies isolated or generated from convalescent patients.

13. 礼来和 AbCellera 的抗病毒治疗 COVID-19 的单克隆抗体开始了移动式的三期预防性临床试验

Lilly, AbCellera antiviral COVID-19 mAb begins mobile Phase III prevention study
来源：biocentury
发布时间：2020-08-04
链 接 ： https://www.biocentury.com/article/305860/lilly-abcellera-antiviral-covid-19-mab-begins-mobile-phase-iii-prevention-study?return_feed=%2Fcoronavirus
编译：蒋立春
中文摘要：
礼来制药和 Abcellera 生物公司本周一宣布开始 Ly-CoV555 的三期临床试验，以预防 COVID-19。当日再生元公司披露其抗病毒治疗 COVID-19 的单克隆抗体在猕猴和仓鼠中的实验数据。礼来-Abcellera 临床试验在再生元开始测试 REGN-COV-2 的预防作用三期临床试验之后一个月开始。再生元公司将招募 2000 位在家庭内接触 SARS-CoV-2 感染者的健康家庭成员。
礼来制药和 Abcellera 生物公司将招募约 2400 位最近感染 COVID-19 的在长期护理机构（比如养老院）工作以及居住的人员。
目前至少有三个抗病毒治疗 COVID-19 的单克隆抗体。除了礼来制药和 Abcellera 生物公司的 Ly-CoV555,再生元的 REGN-COV2,还有上海君实和礼来合作的 JS016。今年 5 月，中科院团队的研究表明该抗体在非人灵长类中可以降低喉咙部位病毒 RNA 并且减少肺部损失。

14. 随机对照临床试验的初步结果：联合使用干扰素 α-2b 和干扰素-γ 或单独使用干扰素 α-2b 对消除 SARS-CoV-2 病毒 RNA 的效果

Effect of combination of interferon alpha-2b and interferon-gamma or interferon alpha-2b alone for elimination of SARS-CoV-2 viral RNA. Preliminary results of a randomized controlled clinical trial
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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.07.29.20164251
编译者：刘焕珍
中文摘要：
目的：IFN-α 2b 和 IFN-γ 联合应用对 SARS-CoV-2 感染宿主防御的抗病毒活性基因具有良好的药效学作用。考虑到这种协同作用，我们进行了一项随机对照临床试验，以评估 SARS-CoV-2 阳性患者皮下注射 IFN-α 2b 和 IFN-γ 的有效性和安全性。
方法：在古巴哈瓦那的军事中心医院招募了 19-82 岁的住院患者，患者以 1：1 的比例随机分配成两组，HeberFERON 组接受 3.0 MIU IFN-α 2b 和 0.5 MIU IFN-γ 的联合皮下治疗，每周两次，持续两周；Heberon Alpha R 组每周三次肌肉注射 3.0 MIU IFN-α 2b。此外，所有患者均接受 lopinavir/ritonavir（每 12 小时 200/50 mg）和氯喹（每 12 h 250 mg）。此次试验的主要终点是,从治疗开始到病毒 RNA 消除的时间或发展成严重 COVID-19 的时间。
结果：对符合纳入标准的 79 例患者进行了随机分组，HeberFERON 组和 Heberon Alpha R 组

分别有 33 名受试者。治疗 4 天后，HeberFERON 组中 78.6％的受试者消除了病毒，而 Heberon Alpha R 组中的比例为 40.6％。对于 HeberFERON 组和 Heberon Alpha R 组，通过 RT-PCR 测定达到 SARS-CoV-2 消除的时间分别为 3.0 天和 5.0 天，与 Heberon Alpha R 治疗组相比，HeberFERON 显着改善了消除病毒的时间。HeberFERON 组和 Heberon Alpha R 组分别有 2 名（6.6％）和 1 名（3.3％）患者出现呼吸道症状恶化。但是，在研究期间或在随后的临床评估中，没有受试者转变为严重的 COVID-19。在开始治疗后第 14 天，这两个组的所有患者均康复，并且其实验室参数恢复到正常值。

结论：在 63 名（19 至 82 岁）SARS-CoV-2 阳性住院患者中，与单独使用 IFN-α2b 相比，HeberFERON 在治疗的第 4 天显著清除了该病毒。然而，单独使用 Heberon Alpha R 也显示出治疗病毒感染的疗效。两种治疗都是安全的，对症状的缓解有积极的影响。没有患者出现严重的 COVID-19。

Abstract

Objectives: An IFN-α2b and IFN-γ combination has demonstrated favorable pharmacodynamics for genes underlying antiviral activity which might be involved in the defense of a host from a SARS-CoV-2 infection. Considering this synergy, we conducted a randomized controlled clinical trial for efficacy and safety evaluation of subcutaneous IFN-α2b and IFN-γ administration in patients positive for SARS-CoV-2.

Methods: We enrolled 19-82 years-old inpatients at the Military Central Hospital Luis Diaz Soto, Havana, Cuba. They were hospitalized after confirmed diagnosis for SARS-CoV-2 RNA by real-time reverse transcription polymerase chain reaction. Patients were randomly assigned in a 1:1 ratio to receive either, subcutaneous treatment with a co-lyophilized combination of 3.0 MIU IFN-α2b and 0.5 MIU IFN-γ (HeberFERON, CIGB, Havana, Cuba), twice a week for two weeks, or thrice a week intramuscular injection of 3.0 MIU IFN-α2b (Heberon® Alpha R, CIGB, Havana, Cuba). Additionally, all patients received lopinavir/ritonavir (200/50 mg every 12 h) and chloroquine (250 mg every 12 h, i.e.standard of care). The primary endpoints were, from the start of treatment, the time to elimination of viral RNA and the time to progression to severe COVID-19. The protocol was approved by the Ethics Committee on Clinical Investigation from the Hospital and the Center for the State Control of Medicines, Equipment and Medical Devices in Cuba. Informed consent was obtained from each participant (INSTITUTION PROTOCOL IG/IAG/CV/2001).

Results: A total of 79 patients with laboratory-confirmed SARS-CoV-2 infection, including symptomatic or asymptomatic conditions, fulfilled the inclusion criteria and underwent randomization. Thirty-three subjects were assigned to the HeberFERON group, and 33 to the Heberon Alpha R group. Sixty-three patients were analyzed for viral elimination, of these 78.6% in the HeberFERON group eliminated the virus after 4 days of treatment versus 40.6% of patients in the Heberon Alpha R groups (p=0.004). Time to reach the elimination of SARS-CoV-2, as measured by RT-PCR was 3.0 and 5.0 days for the HeberFERON and Heberon Alpha R groups, respectively. A significant improvement in the reduction of time for virus elimination was attributable to HeberFERON (p=0.0027, Log-rank test) with a Hazard Ratio of 3.2 and 95% CI of 1.529 to 6.948, as compared to the Heberon

Alpha R treated group. Worsening of respiratory symptoms was detected in two (6.6%) and one (3.3%) patients in HeberFERON and IFN-2b groups, respectively. However, none of the subjects transited to severe COVID-19 during the study or during the following clinical evaluation (21 more days). RT-PCR on day 14 after the start of the treatment was negative to SARS-CoV-2 in 100% and 91% of patients of the combination of IFNs and IFN-α2b, respectively. Elimination in HeberFERON treated patients was related to a significant increase in lymphocytes counts and also a significant reduction in CRP as early as 7 days after commencing the therapeutic schedule. All the patients in both cohorts recovered and had their laboratory parameters return to normal values by day 14 after treatment initiation. Adverse events were identified in 31.5% of patients, 28.5% in the control group, and 34.4% in the HeberFERON group, with the most frequent adverse event being headaches (17.4%).

Conclusions: In a cohort of 63 hospitalized patients between 19 to 82 years-old with positive SARS-CoV-2, HeberFERON significantly eliminated the virus on day 4 of treatment when compared to treatment with IFN-α2b alone. However, Heberon Alpha R alone also showed efficacy for the treatment of the viral infection. Both treatments were safe and positively impacted on the resolution of the symptoms. None of the patients developed severe COVID-19.

15. 风疹病毒高突变基因组与 COVID-19 大流行期间积累的 SARS-CoV-2 基因组突变谱的相似性

Similarity between mutation spectra in hypermutated genomes of rubella virus and in SARS-CoV-2 genomes accumulated during the COVID-19 pandemic

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中文摘要：

全世界数以万计的 SARS-CoV2 分离株的基因组已被测序，这些分离株的变化总数（主要是单碱基替换）超过了 1 万。研究人员将新的 SARS-CoV-2 突变数据集中的突变谱与先前发表的风疹(另一种阳性单链 RNA 病毒)高突变基因组中的突变谱进行了比较。每一株风疹分离株都是在单个主体的传播过程中由于数百个突变的积累而产生的，而 SARS-CoV-2 突变谱代表了来自世界各地多个个体的病毒分离株的一组收集事件。研究人员发现风疹和 SARS-CoV-2 的单碱基取代谱之间有明显的相似性，在每种病毒的正链基因组 RNA 中，C 到 U、A 到 G 和 U 到 C 是最显著的。其中，在预测的 RNA 二级结构中，U 到 C 的变化普遍显示出对环状 RNA 的偏好而不是茎。与风疹相似，C to U 变化在 uCn 基序中富集，提示 APOBEC 胞苷脱氨酶的一个亚类是这些取代的来源。还发现仅在 SARS-CoV-2 中富集了其他几个三核苷酸中心突变基序，这可能表明了该病毒特有的突变过程。总之，该分析的结果表明，**导致风疹疫苗病毒**

在罕见的病理状态下发生超突变的突变机制，也可能在目前在人群中传播的 SARS-CoV-2 病毒的背景下起作用。

Abstract

Genomes of tens of thousands of SARS-CoV2 isolates have been sequenced across the world and the total number of changes (predominantly single base substitutions) in these isolates exceeds ten thousand. We compared the mutational spectrum in the new SARS-CoV-2 mutation dataset with the previously published mutation spectrum in hypermutated genomes of rubella - another positive single stranded (ss) RNA virus. Each of the rubella isolates arose by accumulation of hundreds of mutations during propagation in a single subject, while SARS-CoV-2 mutation spectrum represents a collection events in multiple virus isolates from individuals across the world. We found a clear similarity between the spectra of single base substitutions in rubella and in SARS-CoV-2, with C to U as well as A to G and U to C being the most prominent in plus strand genomic RNA of each virus. Of those, U to C changes universally showed preference for loops versus stems in predicted RNA secondary structure. Similarly, to what was previously reported for rubella, C to U changes showed enrichment in the uCn motif, which suggested a subclass of APOBEC cytidine deaminase being a source of these substitutions. We also found enrichment of several other trinucleotide-centered mutation motifs only in SARS-CoV-2 - likely indicative of a mutation process characteristic to this virus. Altogether, the results of this analysis suggest that the mutation mechanisms that lead to hypermutation of the rubella vaccine virus in a rare pathological condition may also operate in the background of the SARS-CoV-2 viruses currently propagating in the human population.

16. 一种在人的鼻腔和呼吸道支气管上皮细胞中表达的 ACE2 蛋白新亚型，并其能够响应呼吸道 RNA 病毒的感染而被上调

A novel isoform of ACE2 is expressed in human nasal and bronchial respiratory epithelia and is upregulated in response to RNA respiratory virus infection

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中文摘要：

血管紧张素转换酶 2（ACE2）是 SARS-CoV-2 病毒在呼吸道的主要受体。ACE2 与 SARS-CoV-2 病毒的 Spike 蛋白结合，触发病毒与细胞膜融合，从而使病毒 RNA 基因注入宿主中。尽管 ACE2 蛋白在 SARS-CoV-2 的感染过程中起到了关键作用，但人们对 ACE2 的表达（包括

其对病毒感染的响应）仍没有清晰的理解。目前，普遍认为 ACE2 蛋白由 805 个氨基酸组成，拥有 5 个转录本。在本文中，作者发现了 ACE2 的一种新的短亚型。ACE2 短亚型在呼吸道的上皮细胞中表达，这也是 SARS-CoV-2 病毒感染的主要部位。干扰素的刺激和 RV 感染能够明显上调其表达，但对 SARS-CoV-2 感染却无响应，并且在哮喘患者中也表现出不同的调节作用。这种 ACE2 短亚型缺乏与 SARS-CoV-2 Spike 糖蛋白的高亲和力结合位点，作者的数据与 ACE2 短亚型可能会影响宿主对 SARS-CoV-2 感染的敏感性的模型相一致。

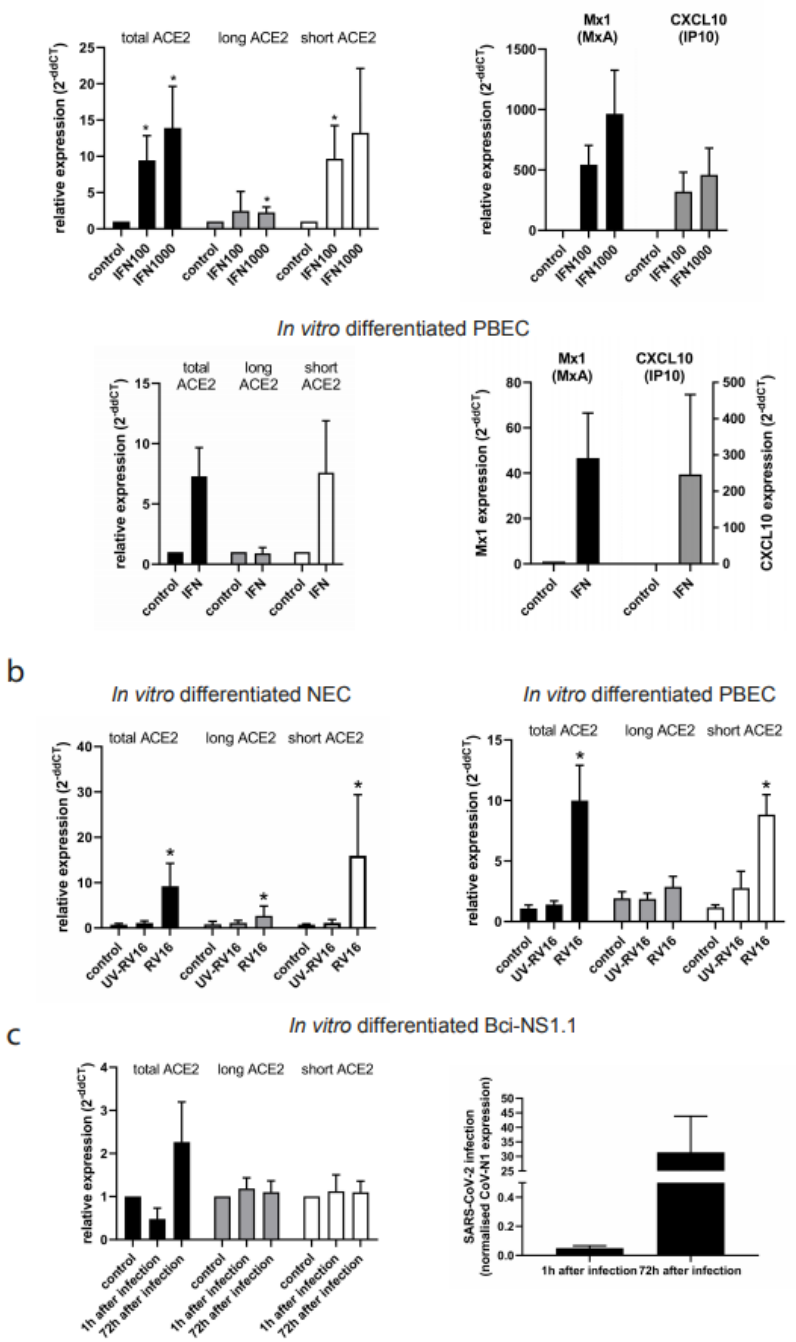

Figure 6. Short ACE2 is upregulated in response to IFN-beta and rhinovirus (RV16) infection but not SARS-CoV-2 infection

6a. Undifferentiated primary bronchial epithelial cell (PBEC) monolayer cultures (N=3) (top) or in vitro differentiated (ALI) PBEC cultures (N=3) (bottom) were treated with IFN-beta (100 or 1000 IU/ml) for 24h and ACE2 transcripts (left panel) and induction of IFN-response genes (MX1 and CXCL10) (right

panel) were measured by RT-qPCR. Data were analysed using Students t-test. **6b.** in vitro differentiated (ALI) nasal epithelia cells (NEC) (n=11) (left panel) or in vitro differentiated (ALI) bronchial epithelia cells (BEC) (n=11) (right panel) were infected with rhinovirus (RV16) (MOI of 1) or mock-infected using a UV-irradiated control (UV-RV16). Nasal cells were collected from 3 female, 8 male patients with a mean age of 45.31+/-3.23 (SEM). After 24h, induction of ACE2 isoform expression was assessed by RT-qPCR with transcript-specific primers. Data were analysed using non-parametric Wilcoxon test. **6c.** BCi-NS1.1 cells were grown at ALI and then infected on the apical side for 1 hour with 100,000 pfu of SARS-Cov-2 strain nCoV/Victoria/1/2020 obtained from Public Health England (PHE), UK. Cells were harvested in QIAzol at 1h post infection and at 72h, RNA extracted and quantitative RT-qPCR performed to detect SARS-CoV-2 using 2019-nCoV_N1 primers and the housekeeping genes HPRT, 18S and RNAse P using the dCt method. 1 hour and 72 hours after infection induction of ACE2 transcript expression was assessed by RT-qPCR with transcript-specific primers (left). SARS-CoV-1 infection was confirmed by CoV-N1 RT-qPCR 1 and 72 hours after infection (right). Data were analysed using non-parametric Wilcoxon test. N=4.

Abstract

Angiotensin-converting enzyme 2 (ACE2) is the main entry point in the airways for SARS-CoV-2. ACE2 binding to SARS-CoV-2 protein Spike triggers viral fusion with the cell membrane, resulting in viral RNA genome delivery into the host. Despite ACE2's critical role in SARS-CoV-2 infection, an understanding of ACE2 expression, including in response to viral infection, remains unclear. Until now ACE2 was thought to encode five transcripts and one 805 amino acid protein. Here we identify a novel short isoform of ACE2. Short ACE2 is expressed in the airway epithelium, the main site of SARS-CoV-2 infection; it is substantially upregulated in response to interferon stimulation and RV infection, but not in response to SARS-CoV-2 infection, and it shows differential regulation in asthma patients. This short isoform lacks SARS-CoV-2 spike glycoprotein high-affinity binding sites and altogether our data are consistent with a model where short ACE2 may influence host susceptibility to SARS-CoV-2 infection.

17. 在个人和群体中对 SARS-CoV-2 型感染的 T 细胞反应的强度和动态水平的评价

Magnitude and Dynamics of the T-Cell Response to SARS-CoV-2 Infection at Both Individual and Population Levels

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中文摘要：

T 细胞参与病毒感染的早期识别和清除，B 细胞产生抗体。T 细胞的这一中心作用使其成为评估对 SARS-CoV-2 型感染的免疫反应的理想目标。文中研究者结合两种高通量的免疫分析方法，建立了一个抗 SARS-CoV-2 的 T 细胞反应的定量图像。首先，在个体水平上，研究者

对 3 名急性感染和 58 名恢复的 COVID-19 受试者进行了深入的特征描述，通过抗原刺激对展示病毒肽段的 545 个人类白细胞抗原(HLA)I 类(即将进行的研究中的 II 类数据)，CD8 T 细胞反应进行了追踪。随后在群体水平上，研究者对 1,015 个样本(来自 827 名 COVID-19 受试者)和 3,500 个对照进行了 T 细胞序列测定，以从 CD8 和 CD4 T 细胞中鉴定与 SARS-CoV-2 感染相关的 “公共”T 细胞受体。总的来说，数据显示 CD8 T 细胞反应通常是由一些免疫显性的、人类白细胞抗原限制的表位驱动。事实表明 T 细胞对 SARS-CoV-2 型的反应在感染后约 1 至 2 周达到峰值，并在康复后的几个月内可检测到。作为这些数据的一个应用，我们测试了一个分类器，仅根据血样中的 TCR 测序来诊断 SARS-CoV-2 型感染，并观察到，在 99.8%的特异性下，在诊断后不久即具有高早期敏感性(第 3-7 天= 83.8% [95%置信区间= 77.6-89.4]；第 8-14 天= 92.4% [87.6-96.6])以及恢复后的持久敏感性(第 29 天+/恢复期 = 96.7% [93.0-99.2])。这些结果证明了一种可靠地评估适应性免疫反应的方法，既可以在病毒抗原暴露后不久(抗体通常可检测到之前)，也可以在以后的时间点进行。这种基于血液的分子方法用于表征细胞免疫反应，可应用于疫苗开发以及临床诊断和监测。

Abstract

T cells are involved in the early identification and clearance of viral infections and also support the development of antibodies by B cells. This central role for T cells makes them a desirable target for assessing the immune response to SARS-CoV-2 infection. Here, we combined two high-throughput immune profiling methods to create a quantitative picture of the T-cell response to SARS-CoV-2. First, at the individual level, we deeply characterized 3 acutely infected and 58 recovered COVID-19 subjects by experimentally mapping their CD8 T-cell response through antigen stimulation to 545 Human Leukocyte Antigen (HLA) class I presented viral peptides (class II data in a forthcoming study). Then, at the population level, we performed T-cell repertoire sequencing on 1,015 samples (from 827 COVID-19 subjects) as well as 3,500 controls to identify shared "public" T-cell receptors (TCRs) associated with SARS-CoV-2 infection from both CD8 and CD4 T cells. Collectively, our data reveal that CD8 T-cell responses are often driven by a few immunodominant, HLA-restricted epitopes. As expected, the T-cell response to SARS-CoV-2 peaks about one to two weeks after infection and is detectable for several months after recovery. As an application of these data, we trained a classifier to diagnose SARS-CoV-2 infection based solely on TCR sequencing from blood samples, and observed, at 99.8% specificity, high early sensitivity soon after diagnosis (Day 3-7 = 83.8% [95% CI = 77.6-89.4]; Day 8-14 = 92.4% [87.6-96.6]) as well as lasting sensitivity after recovery (Day 29+/convalescent = 96.7% [93.0-99.2]). These results demonstrate an approach to reliably assess the adaptive immune response both soon after viral antigenic exposure (before antibodies are typically detectable) as well as at later time points. This blood-based molecular approach to characterizing the cellular immune response has applications in vaccine development as well as clinical diagnostics and monitoring.

18. 消除 COVID-19：它会是什么样的？有可能吗？

Elimination of COVID-19: what would it look like and is it possible?

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DOI 或 PUBMED ID：https://doi.org/10.1016/S1473-3099(20)30633-2
编译者：刘焕珍
中文摘要：
随着全球 SARS-CoV-2 的持续传播，只有在严格限制旅行的情况下，才能在特定的区域内将病例减少到零。尽管可以通过持续的控制努力实现对病原体的区域性消除，但只有当人类是唯一的宿主时，才能在人类中根除一种疾病。只有疫苗接种才能有目的地实现持续且足够高的人群免疫力，以消除诸如 COVID-19 之类的流行性呼吸道感染。如果没有在全国范围内消除 COVID-19，在获得疫苗之前，可能需要在间歇性限制时间内对 COVID-19 进行持续的管理和控制。
Abstract
With ongoing global SARS-CoV-2 transmission, reduction to zero cases in a defined region is only possible with stringent travel restrictions. Although the regional elimination of a pathogen can be achieved through continued control efforts, eradication of a disease in humans might only be feasible if humans are the only host. Only vaccination can purposefully achieve a sustained and sufficiently high population immunity to eliminate epidemic respiratory infections such as COVID-19. Without country-wide elimination, it is likely that continued management and control of COVID-19 with intermittent periods of restrictions is required until a vaccine is available.