新型冠状病毒信息简报

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上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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1. 2020年4月20日疫情

数据来源：WHO

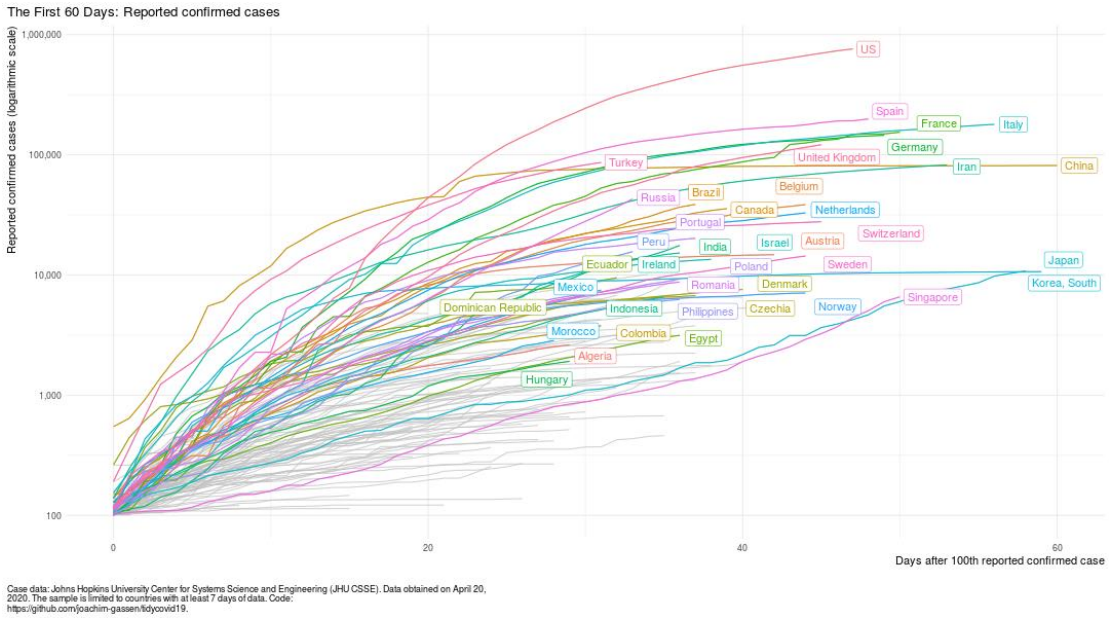
发布时间：2020年4月20日北京时间下午4点

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

根据WHO提供的数据，2020年4月20日全球累计确诊新型冠状病毒病人2314621例，当日新增确诊72846例，累计死亡157847例，当日新增死亡5296。

中国累计确诊84237例，累计死亡4642例，当日新增确诊36例，新增死亡0例。

新：关注美国详细疫情相关统计数据可浏览网站：https://coronavirus.jhu.edu/us-map



重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止4月20日北京时间下午4点）

全国新型冠状病毒肺炎新增确诊病例分布图（4月20日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 适用于 SARS-CoV-2 无症状感染者的一种高通量检测方法

Efficient high throughput SARS-CoV-2 testing to detect asymptomatic carriers

来源：medRxiv

发布时间：2020.04.14

链接：https://www.medrxiv.org/content/10.1101/2020.04.14.20064618v1

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DOI 或 PUBMED ID：Preprint

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中文摘要：

COVID-19 大流行正在全世界迅速蔓延，最近的报告显示 10~30%为无症状感染者。识别此类个体对于有效控制 SARS-CoV-2 的大流行至关重要。迫切需要提高诊断检测能力，以便能够大规模筛查无症状人群。

文中研究者开发了一种基于 PCR 的 SARS-CoV-2 非适应性群体检测方法——P-BEST(Pooling-Based Efficient SARS-CoV-2 Testing)。使用 P-BEST 检测方法，显著减少了在大量样本中识别所有阳性受试者所需的检测次数。研究者基于梯度投影稀疏重建 GPSR(Gradient Projection for Sparse Reconstruction)的方法对组合池策略进行了设计。将 384 个患者样本汇集成 48 个样本池，每个池包含一组 48 个独特的样品，测试效率提高了 8 倍。研究者对 4 组 384 个样品进行了测试，每组中包含了 2~5 个的阳性样本，结果显示每组中的所有阳性样本均被检测到。该方法能够正确识别多达 5/384(1.3%)的携带者，平均假阳性数小于 2.75，平均假阴性数小于 0.33。

该研究中 P-BEST 针对低风险(本例中为 1.3%)的人群进行了高效测试。如果测试样本组中携带者的百分比足够低（~1%），与单独测试每个样本相比，该方法可以使用更少数量的诊断测试来正确识别所有阳性个体。

Abstract

The COVID-19 pandemic is rapidly spreading throughout the world. Recent reports suggest that 10-30% of SARS-CoV-2 infected patients are asymptomatic. Other studies report that some subjects have significant viral shedding prior to symptom onset. Since both asymptomatic and pre-symptomatic subjects can spread the disease, identifying such individuals is critical for effective control of the SARS-CoV-2 pandemic. Therefore, there is an urgent need to increase diagnostic testing capabilities in order to also screen asymptomatic carriers. In fact, such tests will be routinely required until a vaccine is developed. Yet, a major bottleneck of managing the COVID-19 pandemic in many countries is diagnostic testing, due to limited laboratory capabilities as well as limited access to genome-extraction and Polymerase Chain Reaction (PCR) reagents. We developed P-BEST - a method for Pooling-Based Efficient SARS-CoV-2 Testing, using a non-adaptive group testing approach, which significantly reduces the number of tests required to identify all positive subjects within a large set of samples. Instead of testing each sample separately, samples are pooled into groups and each pool is tested for SARS-CoV-2 using the standard clinically approved PCR based diagnostic assay. Each sample is part of multiple pools, using

a combinatorial pooling strategy based on compressed sensing designed for maximizing the ability to identify all positive individuals. We evaluated P-BEST using leftover samples that were previously clinically tested for COVID-19. In our current proof-of-concept study we pooled 384 patient samples into 48 pools providing an 8-fold increase in testing efficiency. Five sets of 384 samples, containing 1-5 positive carriers were screened and all positive carriers in each set were correctly identified. P-BEST provides an efficient and easy-to-implement solution for increasing testing capacity that will work with any clinically approved genome-extraction and PCR-based diagnostic methodologies.

3. 应用 ELISA 和侧流免疫检测对 SARS-COV-2 抗体检测的评价

Evaluation of antibody testing for SARS-Cov-2 using ELISA and lateral flow immunoassays

来源：medRxiv

发布时间：2020-04-20

链接：https://www.medrxiv.org/content/10.1101/2020.04.15.20066407v1

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DOI 或 PUBMED ID：Preprint

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摘要

背景：SARS-CoV-2 大流行在 2020 年 1 月至 3 月期间造成 100 万人感染。迫切需要强有力的抗体检测方法，以支持诊断、疫苗开发、安全解除个人隔离和人口解封的策略。侧流免疫分析（LFIA）装置的早期前景受到了质疑，因为人们担心其敏感性和特异性。

方法：作者使用了一组血浆样本，命名为 SARS-CoV-2 阳性（来自 SARS-CoV-2RT-PCR 阳性个体；n=40）和阴性（2019 年 12 月之前在英国存放的样本（n=142））。作者用 ELISA 和 9 种不同的商业上可用的 LFIA 装置测试了血浆中的 SARS-Cov-2 IgM 和 IgG 抗体。

结果：ELISA 在 RT-PCR 确诊为 SARS-CoV-2 感染组中检测出 34/40 例 SARS-CoV-2 IgM 或 IgG（敏感性为 85%，95%CI 为 70-94%），而流行前对照组中 0/50（特异性为 100%[95% CI 为 93-100%]）。在症状发作后 10 天检测的 31/31 例 RT-PCR 阳性个体中检测到 IgG 水平(灵敏度为 100%，95% CI 为 89-100%)。在症状发作后 3 周内 IgG 滴度上升，8 周后开始下降，但仍高于检测阈值。LFIA 仪器敏感范围估计为 55-70%（与 RT-PCR 相比），和 65-85%（与 ELISA 相比），特异性分别为 95-100%和 93-100%。在研究规模的范围内，大多数 LFIA 仪器的性能相似。

结论：目前 LFIA 设备的性能不足以满足大多数患者的需要。ELISA 可被校准为特异性检测和量化 SARS-CoV-2 IgM 和 IgG，并从症状出现后 10 天起对 IgG 高度敏感。

注: 侧流免疫检测（lateral flow immunoassay），编者的理解是试纸条类型的免疫检测方法。

Abstract

Background: The SARS-CoV-2 pandemic caused >1 million infections during January-March 2020. There is an urgent need for robust antibody detection approaches to support diagnostics, vaccine development, safe individual release from quarantine and population lock-down exit strategies. The early promise of lateral flow immunoassay (LFIA) devices has been questioned following concerns

about sensitivity and specificity.
Methods: We used a panel of plasma samples designated SARS-CoV-2 positive (from SARS-CoV-2 RT-PCR-positive individuals; n=40) and negative (samples banked in the UK prior to December-2019 (n=142)). We tested plasma for SARS-Cov-2 IgM and IgG antibodies by ELISA and using nine different commercially available LFIA devices.
Results: ELISA detected SARS-CoV-2 IgM or IgG in 34/40 individuals with an RT-PCR-confirmed diagnosis of SARS-CoV-2 infection (sensitivity 85%, 95%CI 70-94%), vs 0/50 pre-pandemic controls (specificity 100% [95%CI 93-100%]). IgG levels were detected in 31/31 RT-PCR-positive individuals tested ≥10 days after symptom onset (sensitivity 100%, 95%CI 89-100%). IgG titres rose during the 3 weeks post symptom onset and began to fall by 8 weeks, but remained above the detection threshold. Point estimates for the sensitivity of LFIA devices ranged from 55-70% versus RT-PCR and 65-85% versus ELISA, with specificity 95-100% and 93-100% respectively. Within the limits of the study size, the performance of most LFIA devices was similar.
Conclusions: The performance of current LFIA devices is inadequate for most individual patient applications. ELISA can be calibrated to be specific for detecting and quantifying SARS-CoV-2 IgM and IgG and is highly sensitive for IgG from 10 days following symptoms onset.

4. SARS-CoV-2 抗体在早期 COVID-19 感染中差异表达的全蛋白质组分析

Proteome-wide analysis of differentially-expressed SARS-CoV-2 antibodies in early COVID-19 infection

来源：medRxiv

发布时间：2020-04-14
链接：https://www.medrxiv.org/content/10.1101/2020.04.14.20064535v1
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DOI 或 PUBMED ID：Preprint
编译者：张鹏伟
中文摘要：
快速而准确的检测 SARS-CoV-2 蛋白 IgM 和 IgG 抗体的检测对于通过识别感染 COVID-19 的患者来减缓 COVID-19 的传播至关重要。利用本实验室研制的 SARS-CoV-2 蛋白组芯片，对 40 例早期 COVID-19、流感或有类似症状的非流感患者的 IgM 和 IgG 抗体进行了综合分析。结果表明，SARS-CoV-2 N 蛋白免疫原性低，不适合作为诊断 COVID-19 的生物标志物，因此单纯依靠该标志物的检测假阴性率较高。作者的数据进一步表明，S 蛋白亚单位 1 受体结合区（S1-RBD）可能是 IgM 抗体检测的最佳抗原，而 S 蛋白胞外区（S1+S2 ECD）可能是 IgM 和 IgG 抗体检测的最佳抗原。值得注意的是，结合所有的 IgM 和 IgG 生物标记物，可分别识别 87%和 73.3%的 COVID-19 患者。最后，COVID-19 特异性抗体与病毒感染和急性心肌损伤的临床指标显著相关($\rho \leq 0.05$)。这些数据可能有助于了解抗 SARS-CoV-2 抗体的功能，改进快速筛查 COVID-19 的血清学试验。

Abstract:
Rapid and accurate tests that detect IgM and IgG antibodies to SARS-CoV-2 proteins are essential in slowing the spread of COVID-19 by identifying patients who are infected with COVID-19. Using a SARS-CoV-2 proteome microarray developed in our lab, we comprehensively profiled both IgM and IgG antibodies in forty patients with early-stage COVID-19, influenza, or non-influenza who had similar symptoms. The results revealed that the SARS-CoV-2 N protein is not an ideal biomarker for COVID-19 diagnosis because of its low immunogenicity, thus tests that rely on this marker alone will have a high false negative rate. Our data further suggest that the S protein subunit 1 receptor binding domain (S1-RBD) might be the optimal antigen for IgM antibody detection, while the S protein extracellular domain (S1+S2ECD) would be the optimal antigen for both IgM and IgG antibody detection. Notably, the combination of all IgM and IgG biomarkers can identify 87% and 73.3% COVID-19 patients, respectively. Finally, the COVID-19-specific antibodies are significantly correlated with the clinical indices of viral infection and acute myocardial injury ($p \leqslant 0.05$). Our data may help understand the function of anti-SARS-CoV-2 antibodies and improve serology tests for rapid COVID-19 screening.

5. 比较 SARS-CoV-2 和 SARS-CoV 在人肺部的复制以及免疫激活图谱：离体研究提示 COVID-19 的致病机理

Comparative replication and immune activation profiles of SARS-CoV-2 and SARS-CoV in human lungs: an ex vivo study with implications for the pathogenesis of COVID-19

来源：Clinical Infectious Diseases
发布时间：2020-04-09
链接：
https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa410/5818134?searchresult=1#
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DOI：https://doi.org/10.1093/cid/ciaa410
编译者：蒋立春
中文简介
香港大学袁国勇团队采用离体的肺组织全面的分析比较了 SARS-CoV-2 和 SARS-CoV 的复制、细胞偏好性以及免疫激活谱。
该研究使用了 6 个非感染者肺癌病人（3 男，3 女）手术切割下来的肺部组织进行离体培养，以及感染 SARS-CoV-2 和 SARS-CoV 的实验。在 48 小时内，SARS-CoV-2 产生的有感染性的病毒比 SARS-CoV 多 3.2 倍。两种病毒对细胞的偏好性相似，都侵染 I 和 II 型肺细胞，以及肺泡巨噬细胞。尽管病毒复制更有效，SARS-CoV-2 没有在被感染的肺组织中显著的诱导 I，II，或者 III 干扰素的表达。相比 SARS-CoV 的感染使得 13 个代表性的促炎细胞因子、趋化因子中的 11 个表达上调，SARS-CoV-2 只上调了其中的 5 个。

该研究首次定量比较了 SARS-CoV-2 和 SARS-CoV 感染肺细胞时病毒复制能力。该研究对研究 SARS-CoV-2 的致病机理、高传染性以及无症状感染提供了重要的线索。

备注：
这篇文章在 2020-04-17 的同期刊中被 NCI 的 Thomas R. O’Brien 评论，该研究支持干扰素用于治疗 COVID-19
（https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa453/5821272）
这篇文章的结论和我们 4 月 20 日简报第 10 条结果一致，指出 SARS-CoV-2 没有像流感那样在宿主中诱导出干扰素的高表达。

Abstract
Background
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an emerging coronavirus that has resulted in nearly 1,000,000 laboratory-confirmed cases including over 50,000 deaths. Although SARS-CoV-2 and SARS-CoV share a number of common clinical manifestations, SARS-CoV-2 appears to be highly efficient in person-to-person transmission and frequently cause asymptomatic infections. However, the underlying mechanism that confers these viral characteristics on high transmissibility and asymptomatic infection remain incompletely understood.
Methods
We comprehensively investigated the replication, cell tropism, and immune activation profile of SARS-CoV-2 infection in human lung tissues with SARS-CoV included as a comparison.
Results
SARS-CoV-2 infected and replicated in human lung tissues more efficiently than that of SARS-CoV. Within the 48-hour interval, SARS-CoV-2 generated 3.20 folds more infectious virus particles than that of SARS-CoV from the infected lung tissues (P<0.024). SARS-CoV-2 and SARS-CoV were similar in cell tropism, with both targeting types I and II pneumocytes, and alveolar macrophages. Importantly, despite the more efficient virus replication, SARS-CoV-2 did not significantly induce types I, II, or III interferons in the infected human lung tissues. In addition, while SARS-CoV infection upregulated the expression of 11 out of 13 (84.62%) representative pro-inflammatory cytokines/chemokines, SARS-CoV-2 infection only upregulated 5 of these 13 (38.46%) key inflammatory mediators despite replicating more efficiently.
Conclusions
Our study provided the first quantitative data on the comparative replication capacity and immune activation profile of SARS-CoV-2 and SARS-CoV infection in human lung tissues. Our results provided important insights on the pathogenesis, high transmissibility, and asymptomatic infection of SARS-CoV-2.

6. COVID-19 病人在疾病发展过程中的基因表达下调以及免疫反应变化

Down-regulated gene expression spectrum and immune responses changed during the

disease progression in COVID-19 patients
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DOI：https://doi.org/10.1093/cid/ciaa462
编译者：蒋立春
中文简介
该研究总共招募了 11 个初诊方案相似的 COVID-19 的确诊病人。对这些病人的样品进行了血浆细胞因子、质谱流式以及微流控 qPCR 检测基因表达研究。
5 例轻症，6 例重症病人以及 7 个正常人样品被纳入研究。在重症病人中，年龄更大的病人，中性粒细胞数目更多，C 反应蛋白水平也更高。IL-10 的水平随疾病的进展以及治疗的开展而发生显著变化。
在 COVID-19 病人尤其是重症病人中 T 细胞比例有所下降，轻症病人的 T 细胞比例在治疗后就回到正常水平。重症病人经过治疗后只有 CD4+的 T 细胞数目回到正常水平。差异表达基因的数目随着疾病进展增加，初始治疗后差异表达基因数目有所下降（注:作者采用了微流控 qPCR 对 108 个基因进行了检测，基因列表见 Supplementary Table S1）。所有在重症病人中下调的基因和 Th17 细胞的分化、细胞因子介导的信号通路以及 T 细胞的激活有关系。重症病人经过治疗后，MAP2K7 和 SOS1 基因的表达比入院时有提高。
作者总结说该研究表明在 COVID-19 重症中 T 细胞比例下降，伴随和 T 细胞活化和分化相关基因的表达下调。这些可能对探寻 COVID-19 的有效治疗方案有帮助。
Abstract
Background
WHO characterizes novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a pandemic. Here, we investigated the clinical, cytokine levels, T cell proportion and related gene expression occurring in COVID-19 patients on admission and after intial treatment.
Methods
11 patients diagnosed as COVID-19 with similar initial treatment regimen were enrolled in the hospital. Plasma cytokines, CyTOF and microfluidic qPCR for gene expression were conducted.
Results
5 mild and 6 severe patients were included. Cough and fever were the top symptoms in the 11 COVID-2019 cases. The elder age, more neutrophils numbers and higher C-reactive protein level were found in severe cases. IL-10 level was significantly varied with disease progression and treatment. The decreased T cell proportions were observed in COVID-19 patients especially in severe cases, and all elevated to normal in mild patients after initial treatment but only CD4+T cells return to normal in severe cases. The number of DEGs increased with the disease progress, and decreased after initial treatment. All down-regulated DEGs in severe cases mainly involved in Th17 cell differentiation, cytokine-

mediated signaling pathway and T cell activation. After initial treatment in severe cases, MAP2K7 and SOS1 were upregulated relative to that on admission.
Conclusions
Our findings show a decreased T cell proportion with down-regulated gene expression related to T cell activation and differentiation were occurred in COVID-19 severe patients, which may help to provide effective treatment strategies for COVID-19 .

Supplementary Table S1 108 specific target genes for Microfluidic qPCR

ABCC4	FOS	MAP2K7	PARP2	PYCARD	TGM2
AHR	FOXP3	MAPK14	PIAS1	RANBP10	TMEM57
AKR1C4	GRB2	MAPK8	PIAS2	RIPK2	TNF
ATG13	HSPA8	MCL1	PIAS4	RPS21	TNFRSF10A
B3GAT1	HSPBAP1	MRPL13	PIK3R3	RPS6	TNFRSF10B
CALM3	IL17F	MYT1	PPIA	RXRB	TNFRSF1A
CARM1	IL2RA	NAIP	PPP3CA	S100A7A	TNFRSF1B
CBL	IL2RB	NBAS	PPP3CB	SCP2	TNFRSF25
CD86	IL6ST	NDUFA2	PRKAA1	SELL	TNFRSF8
CEBPB	IRGM	NDUFS1	PRKAB1	SNX5	TNFRSF9
CFLAR	JAK1	NFATC1	PRKCH	SOAT1	TNFSF10
COMMD4	JUNB	NFATC2	PRKCQ	SOCS3	TRADD
DENND4A	JUND	NFATC3	PTEN	SOS1	TRAF2
E2F2	LCK	NFATC4	PTPN11	SRC	TRAF3
E2F7	LCP2	NMI	PTPN6	STAT3	TRAP1
E2F8	LTA	NOD1	PTPRC	STAT5A	TYK2
EGF	LTBR	NPC1	PTPRF	SYK	UBXN1
FKBP1A	M6PR	PARP1	PUS1	TGFB1	VDR

7. COVID-19 大流行的多学科研究重点：心理健康科学的行动呼吁

Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science
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链接：
https://www.sciencedirect.com/science/article/pii/S2215036620301681?via%3Dihub
第一作者：Emily A Holmes, Rory C O’Connor
通讯作者：Claire Cope
通讯作者单位：英国医学科学院
DOI：https://doi.org/10.1016/S2215-0366(20)30168-1
编译者：宋张悦
中文摘要：
2019 年冠状病毒病(COVID-19)大流行正在对社会的各个方面产生深远影响，包括心理健康和生理健康。研究人员探讨了 COVID-19 在心理、社会和神经科学方面的影响，并为心理健康科学研究制定了当前的研究重点和长期战略。本文使用的术语 “心理健康科学”(mental

health science）反映了许多不同的学科，包括但不限于心理学、精神病学、临床医学、行为与社会科学、神经科学。在 2020 年 3 月英国大流行的最初几周，通过公众以及英国医学科学院和心理健康研究慈善机构召集的专家小组（MQ: transformation mental health）的调查，为这些心理健康科学研究重点提供了信息。作者敦促英国研究资助机构与研究人员、有精神疾病生活经历的人以及其他人士合作，建立一个高水平协调小组，以确保这些研究重点得到处理，并允许随着时间的推移确定新的研究重点。保持高质量的研究标准是当务之急。国际合作和全球视野将是有益的。首要的研究重点是收集关于 COVID-19 大流行对整个人口和弱势群体的心理健康影响以及对 COVID-19 患者的大脑功能、认知和心理健康影响的高质量数据。迫切需要研究在大流行情况下，以及在围绕 COVID-19 的反复媒体报道和传播卫生信息的影响下，如何才能减轻易受影响群体的心理健康痛苦。需要发现、评估和改进机械驱动的干预措施，以解决大流行的心理、社会和神经科学方面的问题。应对这一挑战将需要跨学科和部门的整合，并且应该与有精神疾病生活经历的人一起完成。还需要新的资金来满足这些研究重点，英国世界领先的基础设施可以有效地利用这些资金。本意见书提供了一种战略，既可适用于其他国家的研究工作，也可与其他国家的研究工作相结合。

Abstract:

The coronavirus disease 2019 (COVID-19) pandemic is having a profound effect on all aspects of society, including mental health and physical health. We explore the psychological, social, and neuroscientific effects of COVID-19 and set out the immediate priorities and longer-term strategies for mental health science research. These priorities were informed by surveys of the public and an expert panel convened by the UK Academy of Medical Sciences and the mental health research charity, MQ: Transforming Mental Health, in the first weeks of the pandemic in the UK in March, 2020. We urge UK research funding agencies to work with researchers, people with lived experience, and others to establish a high level coordination group to ensure that these research priorities are addressed, and to allow new ones to be identified over time. The need to maintain high-quality research standards is imperative. International collaboration and a global perspective will be beneficial. An immediate priority is collecting high-quality data on the mental health effects of the COVID-19 pandemic across the whole population and vulnerable groups, and on brain function, cognition, and mental health of patients with COVID-19. There is an urgent need for research to address how mental health consequences for vulnerable groups can be mitigated under pandemic conditions, and on the impact of repeated media consumption and health messaging around COVID-19. Discovery, evaluation, and refinement of mechanistically driven interventions to address the psychological, social, and neuroscientific aspects of the pandemic are required. Rising to this challenge will require integration across disciplines and sectors, and should be done together with people with lived experience. New funding will be required to meet these priorities, and it can be efficiently leveraged by the UK’s world-leading infrastructure. This Position Paper provides a strategy that may be both adapted for, and integrated with, research efforts in other countries.

8. 一种 SARS-CoV-2 灭活疫苗的快速开发

Rapid development of an inactivated vaccine for SARS-CoV-2

来源：bioRxiv
发布时间：2020-04-19
链接：https://www.biorxiv.org/content/10.1101/2020.04.17.046375v1
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通讯作者：卢金星、李长贵、王祥喜、尹卫东、张严峻、秦川
通讯作者单位：中国医学科学院等
DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：
这个团队开发了一种纯化的 SARS-CoV-2 病毒灭活候选疫苗（PiCoVacc），该疫苗能诱导小鼠、大鼠和非人类灵长类动物产生 SARS-CoV-2 特异性中和抗体。这些抗体能有效中和 10 株具有代表性的 SARS-CoV-2 病毒株，表明对全球流行的 SARS-CoV-2 病毒株可能具有更广泛的中和能力。两种不同剂量（每剂量 3μg 或 6μg）的免疫均能部分或完全保护猕猴免受 SARS-CoV-2 的攻击，且无抗体依赖性的感染增强（ADE）现象。通过对猕猴临床症状、血液生化指标的监测和组织病理学分析，系统评价 PiCoVacc 是安全的。这些数据支持了 SARS-CoV-2 人用疫苗的快速临床开发。
Abstract:
The COVID-19 caused by SARS-CoV-2 has brought about an unprecedented crisis, taking a heavy toll on human health, lives as well as the global economy. There are no SARS-CoV-2-specific treatments or vaccines available due to the novelty of this virus. Hence, rapid development of effective vaccines against SARS-CoV-2 is urgently needed. Here we developed a pilot-scale production of a purified inactivated SARS-CoV-2 virus vaccine candidate (PiCoVacc), which induced SARS-CoV-2-specific neutralizing antibodies in mice, rats and non-human primates. These antibodies potently neutralized 10 representative SARS-CoV-2 strains, indicative of a possible broader neutralizing ability against SARS-CoV-2 strains circulating worldwide. Immunization with two different doses (3 μg or 6 μg per dose) provided partial or complete protection in macaques against SARS-CoV-2 challenge, respectively, without any antibody-dependent enhancement of infection. Systematic evaluation of PiCoVacc via monitoring clinical signs, hematological and biochemical index, and histophathological analysis in macaques suggests that it is safe. These data support the rapid clinical development of SARS-CoV-2 vaccines for humans.
编者注：
该疫苗在 4 月 13 日已经进入临床一期试验

9. SARS-CoV-2 病毒 nsp10-nsp16 蛋白异二聚体与 S-adenosylmethionine 复合物的晶体结构

The crystal structure of nsp10-nsp16 heterodimer from SARS-CoV-2 in complex with S-adenosylmethionine
来源：bioRxiv
发布时间：2020-04-20
链接：https://www.biorxiv.org/content/10.1101/2020.04.17.047498v1
第一作者：Monica Rosas-Lemus

通讯作者：Karla J.F. Satchell
通讯作者单位：Northwestern University，Chicago，IL，USA
编译者：宋珂

中文摘要：导致 COVID-19 疫情的 SARS-CoV-2 属于冠状病毒科。截至 2020 年 4 月 17 日，病毒在世界范围内迅速传播，已导致超过 200 万人感染，近 15 万人死亡。目前，尚无针对 SARS-CoV-2 的疫苗和用于治疗 COVID-19 的特效药物。由感染引起的呼吸道并发症让世界各国的医疗系统不堪重负。这种病毒与 2002-2004 年间导致 SARS 的 SARS-CoV-1 病毒有一定的亲缘关系。2020 年 1 月，Center for Structural Genomics of Infectious Diseases 建立起一套结构基因组学工作流程，用来解析在冠状病毒复制和转录过程中所必需的蛋白质结构。本文中，作者首次展示了 SARS-CoV-2 病毒 nsp10-nsp16 2'-O-methyltransferase 与 S-adenosylmethionine 复合物的结构，分辨率为 1.8 Å。该异二聚体复合物结构是病毒 mRNA 戴帽所需的，病毒 Mrna 戴帽后才能有效地翻译和逃避免疫监督具。

Abstract: SARS-CoV-2 is a member of the coronaviridae family and is the etiological agent of the respiratory Coronavirus Disease 2019. The virus has spread rapidly around the world resulting in over two million cases and nearly 150,000 deaths as of April 17, 2020. Since no treatments or vaccines are available to treat COVID-19 and SARS-CoV-2, respiratory complications derived from the infections have overwhelmed healthcare systems around the world. This virus is related to SARS-CoV-1, the virus that caused the 2002-2004 outbreak of Severe Acute Respiratory Syndrome. In January 2020, the Center for Structural Genomics of Infectious Diseases implemented a structural genomics pipeline to solve the structures of proteins essential for coronavirus replication-transcription. Here we show the first structure of the SARS-CoV-2 nsp10-nsp16 2'-O-methyltransferase complex with S-adenosylmethionine at a resolution of 1.8 Å. This heterodimer complex is essential for capping viral mRNA transcripts for efficient translation and to evade immune surveillance.

PDB Accession Code	6w4h	6w61
Crystallization Conditions		
Screen conditions	0.2M Calcium acetate, 0.1M HEPES pH 7.5, 18% (w/v) PEG8000	0.1 M sodium citrate, pH 5.6, 10% (w/v) PEG4000, 10%(w/v) isopropanol
Protein concentration (mg/ml)	5.3	16.7

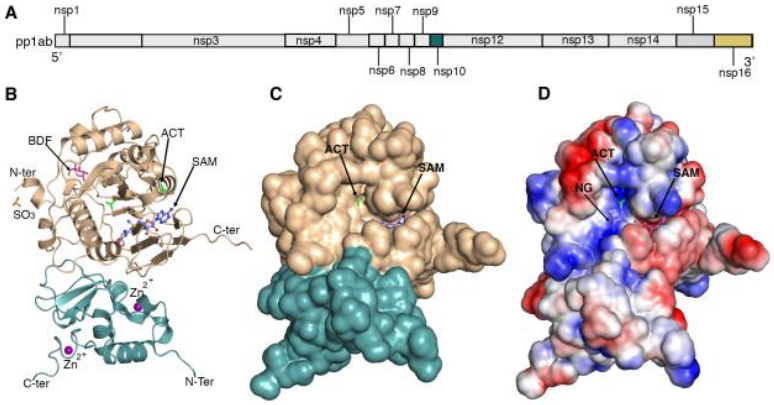

Figure 1. Overall structure of the nsp10-nsp16. A, Linear schematic of the orf1ab translation produce prior to nsp3 and nsp5 processing. B, Cartoon representation of the heterodimer of nsp16 (tan) in complex with nsp10 (teal). Ligands are sulfite (SO_3), β-D-fructopyranose, (BDF), acetate, (ACT), S-adenosyl-methionine (SAM), and Zn^{2+}. C, Solvent exposed surface, showing the SAM pocket and ACT. D, Surface charge showing the positively charged surface at the groove for nucleotide (NG) binding site and the negatively charged SAM binding pocket (C).

10. 不同动物中的 SARS-CoV-2 受体，ACE2

Broad and differential animal ACE2 receptor usage by SARS-CoV-2

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DOI：

编译者： 王玮

中文摘要：

COVID-19 已经造成了前所未有的全球公共卫生和经济危机。尽管蝙蝠和穿山甲被认为是天然的中间宿主，但 SARS-CoV-2 在人类中的起源和出现仍然是个谜。值得注意的是，与蝙蝠和穿山甲中发现的 SARS-CoV-2-like CoVs 相比，SARS-CoV-2 在其刺突蛋白中有一个多碱基的弗林裂解位点。SARS-CoV-2 以人 ACE2 为受体感染细胞。刺突蛋白的受体识别是决定冠状病毒宿主范围、组织嗜性和发病机制的主要因素。为了寻找 SARS-CoV-2 可能的宿主，该研究检测了 14 种哺乳动物 ACE2 的受体活性，发现来自多种动物的 ACE2 可以帮助 SARS-CoV-2 野生型或刺突蛋白中弗林裂解位点缺失的假慢病毒颗粒感染进入细胞（图一）。人/恒河猴和大鼠/小鼠的 ACE2 分别表现出最高和最低的受体活性。其余种类中，兔子和穿山甲 ACE2 与 SARS-CoV-2 刺突蛋白 S1 亚基能强烈结合，有效帮助假病毒感染。这些发现对了解潜在的自然宿主、人畜共患传播和动物模型的使用具有重要意义。

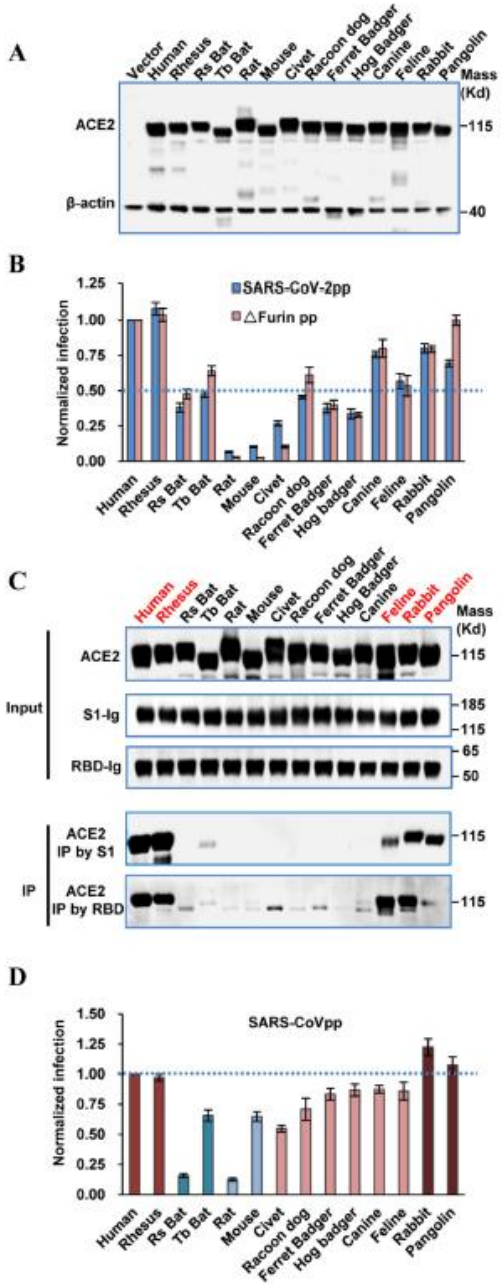

Fig. 3. Multiple ACE2 orthologues served as receptors for SARS-CoV-2. (A) Transient expression of ACE2 orthologs in 293T cells. The cell lysates were detected by western blot assay, using an anti-C9 monoclonal antibody. (B) HIV-Luc-based pseudotyped virus entry. 293T cells were transfected with ACE2s orthologs. At 48 h post transfection, the cells were infected by the pseudotyped virus of wildtype SARS-CoV-2 or mutant ΔFurin. At 48 h post infection, luciferase activity was measured and normalized to human ACE2, respectively. Error bars reveal the standard deviation of the means from four biological repeats. (C) IP assay. The upper panel showed the input of ACE2 protein with C9 tag, S1 and RBD with IgG tag. The lower panel showed the ACE2 pulled down by S1-Ig or RBD-Ig fusion protein.

图一 多种 ACE2 同源蛋白作为 SARS-CoV-2 的受体

Abstract:

The COVID-19 pandemic has caused an unprecedented global public health and economy crisis. The origin and emergence of its causal agent, SARS-CoV-2, in the human population remains mysterious, although bat and pangolin were proposed to be the natural reservoirs. Strikingly, comparing to the SARS-CoV-2-like CoVs identified in bats and pangolins, SARS-CoV-2 harbors a polybasic furin cleavage site in its spike (S) glycoprotein. SARS-CoV-2 uses human ACE2 as its receptor to infect cells. Receptor recognition by the S protein is the major determinant of host range, tissue tropism, and pathogenesis of coronaviruses. In an effort to search for the potential intermediate or amplifying animal hosts of SARS-CoV-

2, we examined receptor activity of ACE2 from 14 mammal species and found that ACE2 from multiple species can support the infectious entry of lentiviral particles pseudotyped with the wild-type or furin cleavage site deficient S protein of SARS-CoV-2. ACE2 of human/rhesus monkey and rat/mouse exhibited the highest and lowest receptor activity, respectively. Among the remaining species, ACE2 from rabbit and pangolin strongly bound to the S1 subunit of SARS-CoV-2 S protein and efficiently supported the pseudotyped virus infection. These findings have important implications for understanding potential natural reservoirs, zoonotic transmission, human-to-animal transmission, and use of animal models.