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 6 月 18 日疫情

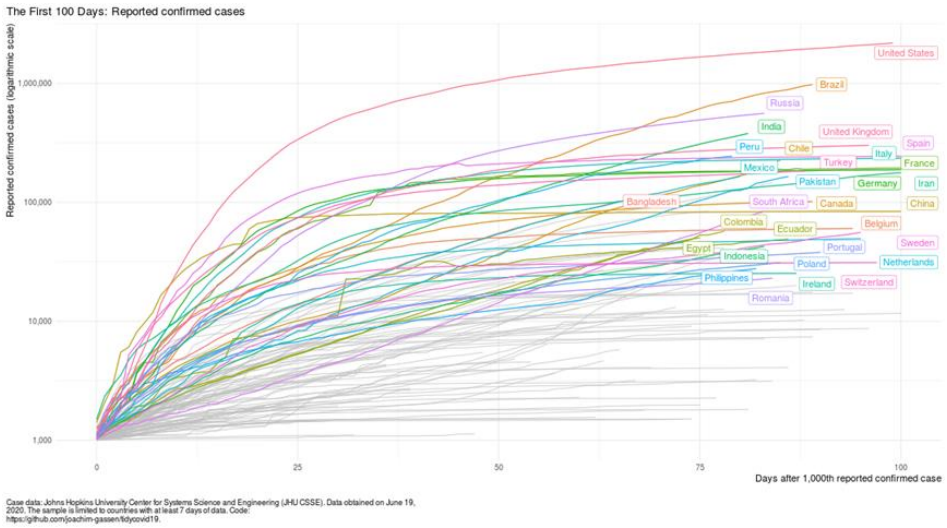
数据来源：WHO

发布时间：2020 年 6 月 18 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 6 月 18 日全球累计确诊新型冠状病毒病人 8242999 例，当日新增确诊 181232 例，累计死亡 445535 例，当日新增死亡 5245。

中国累计确诊 84903 例，累计死亡 4645 例，当日新增确诊 36 例，新增死亡 0 例。



重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止 6 月 19 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 25 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

根据中国新闻网的消息，6 月 11 日，我国北京市新发地批发市场发生聚集性疫情。截至 6 月 18 日 24 时，北京市自 6 月 11 日以来累计报告确诊病例 183 例，尚在观察的无症状感染者 15 例。

中国疾病预防控制中心 19 日发布消息称，该中心 18 日晚通过“新型冠状病毒国家科技资源服务系统”正式发布 2020 年 6 月北京新发地批发市场新冠疫情及病毒基因组序列数据。

2. 武汉地区 SARS-CoV-2 IgG 抗体的流行与产生抗 SARS-CoV-2 长效保护性抗体的关系

Prevalence of IgG antibodies to SARS-CoV-2 in Wuhan - implications for the ability to produce long-lasting protective antibodies against SARS-CoV-2

来源：medRxiv

发布时间：2020-06-16

链接：https://www.medrxiv.org/content/10.1101/2020.06.13.20130252v1

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中文摘要：

背景：感染 SARS-CoV-2 的人是否会对 SARS-CoV-2 产生长期免疫，并在感染得到解决后保留长期的保护性抗体尚待确定。本研究旨在探讨武汉地区 4 组人群中 SARS-CoV-2 抗体的检测结果。

方法：包括 2020 年 2 月 29 日至 2020 年 4 月 29 日对 SARS-CoV-2 进行 COVID-19 IgM/IgG 和 RT-PCR 检测的 4 组患者：来自乐山医院、武汉大学中南医院和武汉市第七医院的 1470 例 COVID-19 住院患者，3832 名未经 COVID-19 诊断的医护人员、19555 名普通工人和 1616 名其他住院患者（N=26473）。症状发作后<21 天接受 IgM /IgG 检测的 COVID-19 患者被排除在外。

结果：COVID-19 患者的 IgG 流行率为 89.8%（95%CI 88.2-91.3%），医护人员为 4.0%（95%CI 3.4-4.7%），一般工作者为 4.6%（95%CI 4.3-4.9%），其他患者为 1.0%（与 COVID-19 患者比较，p 均<0.001）。随着年龄的增长，医护人员和普通工人的 IgG 流行率显著增加。SARS-CoV-2 的 IgM 抗体在 COVID-19 患者中的流行率为 31.4%，在医护人员中的流行率为 1.5%，在普通工人中的流行率为 1.3%，在其他患者中的流行率为 0.2%。

结论：很少有医疗服务提供者有抗 SARS-CoV-2 的 IgG 抗体，尽管其中相当一部分人感染了该病毒。在 SARS-CoV-2 感染后，人们不太可能产生针对该病毒的长期保护性抗体。

Abstract:

Background: It is to be determined whether people infected with SARS-CoV-2 will develop long-term immunity against SARS-CoV-2 and retain long-lasting protective antibodies after the infection is resolved. This study was to explore to explore the outcomes of IgG antibodies to SARS-CoV-2 in four groups of individuals in Wuhan, China.

Methods: We included the following four groups of individuals who received both COVID-19 IgM/IgG tests and RT-PCR tests for SARS-CoV-2 from February 29, 2020 to April 29, 2020: 1470 hospitalized patients with COVID-19 from Leishenshan Hospital, Zhongnan Hospital of Wuhan University, and Wuhan No. 7 Hospital, 3832 healthcare providers without COVID-19 diagnosis, 19555 general workers, and 1616 other patients to be admitted to the hospital (N=26473). COVID-19 patients who received IgM/IgG tests <21 days after symptom onset were excluded.

Results: IgG prevalence was 89.8% (95% CI 88.2-91.3%) in COVID-19 patients, 4.0% (95% CI 3.4-4.7%) in healthcare providers, 4.6 (95% CI 4.3-4.9 %) in general workers, and 1.0% in other patients (p all <0.001 for comparisons with COVID-19 patients). IgG prevalence increased significantly by age among healthcare workers

and general workers. Prevalence of IgM antibodies to SARS-CoV-2 was 31.4% in COVID-19 patients, 1.5% in healthcare providers, 1.3% in general workers, and 0.2% in other patients. Conclusions: Very few healthcare providers had IgG antibodies to SARS-CoV-2, though a significant proportion of them had been infected with the virus. After SARS-CoV-2 infection, people are unlikely to produce long-lasting protective antibodies against this virus.

3. 截至 6 月 19 日国家药监局已批准 43 个新型冠状病毒检测产品

来源链接：http://www.nmpa.gov.cn/WS04/CL2583/

截至 2020 年 6 月 19 日，国家药监局已批准 43 个新型冠状病毒检测产品，其中新冠病毒核酸检测试剂 22 个，抗体检测试剂 21 个。详见参考文件：“国家药监局新型冠状病毒检测试剂注册信息_20200619.xlsx”。

4. 在纳米等离子体平台上高精度多重 SARS-CoV-2 抗体检测方法及唾液检测能力

High-Accuracy Multiplexed SARS-CoV-2 Antibody Assay with Avidity and Saliva Capability on a Nano-Plasmonic Platform

来源：biorxiv

发布时间：2020.06.17

文章链接：https://www.biorxiv.org/content/10.1101/2020.06.16.155580v1

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DOI：https://doi.org/10.1101/2020.06.16.155580

编译者：张怡

中文摘要：

SARS-CoV-2 病毒的爆发和迅速传播已经导致了一场可怕的全球大流行，迄今已有数百万人感染，约 40 万人死亡。对 COVID-19 抗体的高精度检测是抗击疫情不可或缺的一部分。在此，我们在近红外纳米等离子体金(pGOLD)平台上开发了针对人血清和唾液中 SARS-CoV-2 刺突蛋白（S1 亚基和受体结合区域 RBD）的双抗体检测。通过检测近 600 份血清样本，pGOLD COVID-19 检测，IgG 和 IgM 的特异性达到 99.78%，在发病 14 天后收集的血清中灵敏度为 100%，对其他疾病的交叉反应性为零。Two-plex 相关分析显示，血清 IgM 与 RBD 的结合高于与 S1 的结合。检测了 IgG 抗体对多种抗原的亲和力，揭示了 COVID-19 患者抗体的成熟情况，为区分近期感染和远程感染以及识别 SARS-CoV-2 再次感染提供了一个强有力的工具。同样重要的是，**由于分析灵敏度高，pGOLD COVID-19 检测方法在人唾液中检测了微量抗体，首次对 SARS-CoV-2 抗体进行了无创检测**。

Abstract

The outbreak and rapid spread of SARS-CoV-2 virus has led to a dire global pandemic with millions of people infected and ~ 400,000 deaths thus far. Highly accurate detection of antibodies for COVID-19 is an indispensable part of the effort to combat the pandemic. Here we developed two-plex antibody detection against SARS-CoV-2 spike protein (the S1 subunit and receptor binding domain RBD) in human serum and saliva on a near-infrared nano-plasmonic gold (pGOLD) platform. By testing nearly 600 serum samples, pGOLD COVID-19 assay achieved ~ 99.78 % specificity for detecting both IgG and IgM with 100 % sensitivity in sera

collected > 14 days post disease symptom onset, with zero cross-reactivity to other diseases. Two-plex correlation analysis revealed higher binding of serum IgM to RBD than to S1. IgG antibody avidity toward multiple antigens were measured, shedding light on antibody maturation in COVID-19 patients and affording a powerful tool for differentiating recent from remote infections and identifying re-infection by SARS-CoV-2. Just as important, due to high analytical sensitivity, the pGOLD COVID-19 assay detected minute amounts of antibodies in human saliva, offering the first non-invasive detection of SARS-CoV-2 antibodies.

5. 利用数字蛋白质芯片对 COVID-19 细胞因子风暴的监测

A Digital Protein Microarray for COVID-19 Cytokine Storm Monitoring

来源：medrxiv

发布时间：2020-06-17

链接：https://www.medrxiv.org/content/10.1101/2020.06.15.20131870v1.full.pdf

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DOI 或 PUBMED ID：preprint

编译者：孔娟

中文摘要：

有研究表明细胞因子风暴会导致 COVID-19 的严重发病率，但快速细胞因子检测并不常用于监测危重患者。研究者报告了一个基于机器学习的数字蛋白质微阵列平台的临床应用，该平台用于对密歇根大学医院 ICU 收治的重症 COVID-19 患者细胞因子进行快速多重定量。该平台包括两个低成本模块:(1)一个半自动流体分配/混合模块，可在生物安全柜内操作，以最大限度地减少技术人员暴露于病毒感染的风险；(2)一个 12-12-15 英寸的紧凑型荧光光学扫描仪，用于潜在的床边读数。该平台能够在临床实践中进行每日细胞因子分析，具有高灵敏度(< 0.4 pg/mL)、分析间重复性(~10%CV)和 10 分钟分析孵育的近实时操作。使用该平台进行的细胞因子谱测试结果分显示能够观察到接受托珠单抗治疗(IL-6 抑制剂)后 IL-6 的明显升高，同时在所有重症 COVID-19 患者中存在显著的细胞因子谱变异，并发现 IL-6 与临床生物标志物(如铁蛋白和 CRP)之间的弱相关性。研究数据显示，患者对 COVID-19 抗炎治疗的反应存在较大的个体间差异，这再次证明了快速细胞因子检测指导下的个性化策略的必要性。

Abstract:

Despite widespread concern for cytokine storms leading to severe morbidity in COVID-19, rapid cytokine assays are not routinely available for monitoring critically ill patients. We report the clinical application of a machine learning-based digital protein microarray platform for rapid multiplex quantification of cytokines from critically ill COVID-19 patients admitted to the intensive care unit (ICU) at the University of Michigan Hospital. The platform comprises two lowcost modules: (i) a semi-automated fluidic dispensing/mixing module that can be operated inside a biosafety cabinet to minimize the exposure of technician to the virus infection and (ii) a 12-12-15 inch compact fluorescence optical scanner for the potential near-bedside readout. The platform enabled daily cytokine analysis in clinical practice with high sensitivity (<0.4pg/mL),

inter-assay repeatability (~10% CV), and near-real-time operation with a 10min assay incubation. A cytokine profiling test with the platform allowed us to observe clear interleukin -6 (IL-6) elevations after receiving tocilizumab (IL-6 inhibitor) while significant cytokine profile variability exists across all critically ill COVID-19 patients and to discover a weak correlation between IL-6 to clinical biomarkers, such as Ferritin and CRP. Our data revealed large subject-to-subject variability in a patient's response to anti-inflammatory treatment for COVID-19, reaffirming the need for a personalized strategy guided by rapid cytokine assays.

6. COVID-19 患者的味觉和嗅觉障碍：在中国发生的显著特征

Self-reported taste and smell disorders in patients with COVID-19: distinct features in China

编译:王玮

链接: https://www.medrxiv.org/content/10.1101/2020.06.12.20128298v1

来自华中科技大学同济医学院附属同济医院等单位的研究团队随访了 1172 名 COVID-19 患者，分析发现，10 名住院患者中会出现 1 名患者嗅觉丧失，5 名患者会出现 1 名患者味觉丧失，且与 COVID-19 的严重程度有关。多数患者在 2 周内嗅觉和味觉功能恢复正常。

编者注:在欧美国家 COVID-19 患者中大概率发生味觉和嗅觉障碍,在国内患者中较为少见。

SARS-CoV2 导致嗅觉损害的机理研究

编译：蒋立春

7. 嗅觉上皮中天然免疫信号通路降低气味受体水平：模拟 COVID-19 病人中暂时的失去嗅觉

Innate immune signaling in the olfactory epithelium reduces odorant receptor levels: modeling transient smell loss in COVID-19 patients

链接:https://www.medrxiv.org/content/10.1101/2020.06.14.20131128v1

8. SARS-CoV-感染金色仓鼠中嗅觉上皮的大量暂时受损和支持细胞（而是不嗅觉神经元）的感染相关

Massive transient damage of the olfactory epithelium associated with infection of sustentacular cells by SARS-CoV-2 in golden Syrian hamsters

链接:https://www.biorxiv.org/content/10.1101/2020.06.16.151704v1

9. COVID-19 的外泌体 microRNAs 驱动血栓形成

Exosomal microRNAs Drive Thrombosis in COVID-19

编译:王玮

链接: https://www.medrxiv.org/content/10.1101/2020.06.16.20133256v1

来自美国 Montefiore University Hospital 等单位的研究团队，将 26 位 COVID-19 患者纳入研究,根据入院时的血清 D-二聚体水平将人群分为两组,发现与低 D-二聚体组相比，高 D-二聚体组患者的外泌体 miR-424 显著上调，而外泌体 miR-103a、miR-145 和 miR-885 显著下调（$p<0.0001$）。

10. SARS-CoV-2 中和抗体反应在重症患者中更强

SARS-CoV-2 Neutralizing Antibody Responses Are More Robust in Patients with Severe Disease

链接：https://www.biorxiv.org/content/10.1101/2020.06.13.150250v1

编译者：孔娟

研究者对 35 名感染 SARS-CoV-2 后约 1 个月的血浆进行了中和抗体检测，结果发现重症患者血浆中抗 SARS-CoV-2 假病毒和活病毒的平均抗体中和滴度相比非重症患者分别高约 5 倍和约 7 倍，这些发现对那些寻求血浆疗法、分离中和性单克隆抗体和免疫决定因素的人具有重要意义。

11. 严重而非轻度 COVID-19 患者中 SARS-CoV-2 特异性 T 细胞和 B 细胞的分化反应

Divergent SARS-CoV-2-specific T and B cell responses in severe but not mild COVID-19

链接：https://www.biorxiv.org/content/10.1101/2020.05.11.088674v1

编译者：张鹏伟

荷兰阿姆斯特丹大学研究团队发现与临床轻度的患者相比危重患者的 $CD4^+$T 细胞反应有质的损害，这些患者的特异性 IgG 抗体反应非常强烈。观察到的不同的 T 细胞和 B 细胞反应可能表明危重的 COVID-19 患者的免疫反应失调。

12. 重症 Covid-19 与呼吸衰竭的全基因组关联研究

Genomewide Association Study of Severe Covid-19 with Respiratory Failure

来源：NEJM

发布时间：2020-06-17

链接：https://www.nejm.org/doi/full/10.1056/NEJMoa2020283?query=featured_home

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DOI 或 PUBMED ID：10.1056/NEJMoa2020283

编译者：宋张悦

中文摘要：

本研究在欧洲 SARS-CoV-2 大流行的意大利和西班牙的 7 家医院进行了一项涉及 1980 名 Covid-19 和重症（定义为呼吸衰竭）患者的全基因组关联研究。本研究在 Covid-19 呼吸衰竭患者中发现了一个 3p21.31 基因簇作为遗传易感性位点，并证实可能与 ABO 血型系统有关。6 月 5 日的简报第 21 条已经报道过该文的预印本。

13. 多水平的蛋白组学研究揭示干预宿主的治疗 SARS-CoV-2 and SARS-CoV 感染的策略

Multi-level proteomics reveals host-perturbation strategies of SARS-CoV-2 and

SARS-CoV
编译：蒋立春
德国慕尼黑工业大学的研究们从转录组、蛋白质组、泛素化组、以及磷酸化蛋白质等方面研究了 SARS-CoV-2 和 SARS-CoV 对一个人肺来源细胞的影响。从网络水平揭示了 SARS-CoV-2 and SARS-CoV 感染的分子机理以及可能的有效干预方法，作者也展示了根据该分析鉴定出激酶抑制剂以及基质金属蛋白酶抑制剂 SARS-CoV-2 的抗病毒作用。
链接:https://www.biorxiv.org/content/10.1101/2020.06.17.156455v1

14. 重症 COVID-19 病人中有更强的中和抗体反应
哥伦比亚大学何大一团队研究了 35 个 COVID-19 病人感染一个月之后的体内抗体，发现重症病人中中和抗体滴度高于普通病人的 5~7 倍。
SARS-CoV-2 Neutralizing Antibody Responses Are More Robust in Patients with Severe Disease
链接:https://www.biorxiv.org/content/10.1101/2020.06.13.150250v1

15. COVID-19 病人中内皮细胞功能损害以及内皮细胞屏障破坏
荷兰的科学家通过比较 48 个 COVID-19 病人和 10 个正常人血浆成分，发现 COVID-19 病人血浆中硫酸肝素和肝素酶水平显著提高。作者也讨论了的血浆中肝素酶和病症严重程度的关系以及临床中低分子量肝素的疗效。
Increased plasma heparanase activity in COVID-19 patients
链接:https://www.medrxiv.org/content/10.1101/2020.06.12.20129304v1

美国天普大学的研究者们发现 SARS-CoV-2 的刺突蛋白可以改变体外培养的模拟人血脑屏障的模型的屏障功能
The SARS-CoV-2 spike protein alters barrier function in 2D static and 3D microfluidic in vitro models of the human blood–brain barrier
链接:https://www.biorxiv.org/content/10.1101/2020.06.15.150912v1

16. 时间轴免疫分析表明 COVID-19 病人具有迥异的发病机制
Longitudinal immune profiling reveals distinct features of COVID-19 pathogenesis
英国曼彻斯特大学的研究者们对 73 个 COVID-19 病人从入院开始进行了免疫细胞和血清中的蛋白的多时间点检测。时间轴数据分析表明病人在入院时候呈现非常高的中性粒细胞/T 细胞比如以及非正常的单核细胞活化。在预后良好的病人中这两个指标都恢复了。
链接:https://www.medrxiv.org/content/10.1101/2020.06.13.20127605v1

17. 新加坡免疫学合作网络（Singapore Immunology Network） 研究表明不成熟的中性粒细胞/VD2 T 细胞比例可以作为重症 COVID-19 病人早诊的标志物
Whole blood immunophenotyping uncovers immature neutrophil-to-VD2 T-cell ratio as an early prognostic marker for severe COVID-19
链接:https://www.biorxiv.org/content/10.1101/2020.06.11.147389v1

18. 西湖大学郭天南团队用蛋白质组技术，发现 COVID-19 病程延长的病人中特征性的发生 Treg 细胞介导的免疫抑制现象
Proteomics Uncovers Immunosuppression in COVID-19 Patients with Long Disease

Course
链接:https://www.medrxiv.org/content/10.1101/2020.06.14.20131078v1

19. 由原型病原体制备而开启的 SARS-CoV-2 mRNA 疫苗研发

SARS-CoV-2 mRNA Vaccine Development Enabled by Prototype Pathogen Preparedness
来源：bioRxiv
发布时间：2020-06-11
链接：https://www.biorxiv.org/content/10.1101/2020.06.11.145920v1
第一作者：Kizzmekia S. Corbett
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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.06.11.145920
编译者：刘焕珍
中文摘要：
需要 SARS-CoV-2 疫苗来控制全球 COVID-19 公共卫生危机。原子水平的结构指导了融合前稳定突变的应用，该突变可改善 β 冠状病毒刺突蛋白的表达和免疫原性。使用这种确定的免疫原设计，SARS-CoV-2 序列的释放立即触发了快速生产表达融合前稳定的 SARS-CoV-2 刺突三聚体（mRNA-1273）的 mRNA 疫苗。我们发现在没有免疫病理学证据的情况下，mRNA-1273 可以诱导小鼠的肺和鼻中有效的中和抗体和 CD8 T 细胞反应，并且可以保护小鼠免受 SARS-CoV-2 感染。目前，mRNA-1273 正处于 2 期临床试验中，并朝着 3 期功效评估的方向发展。
Abstract:
A SARS-CoV-2 vaccine is needed to control the global COVID-19 public health crisis. Atomic level structures directed the application of prefusion-stabilizing mutations that improved expression and immunogenicity of betacoronavirus spike proteins. Using this established immunogen design, the release of SARS-CoV-2 sequences triggered immediate rapid manufacturing of an mRNA vaccine expressing the prefusion-stabilized SARS-CoV-2 spike trimer (mRNA-1273). Here, we show that mRNA-1273 induces both potent neutralizing antibody and CD8 T cell responses and protects against SARS-CoV-2 infection in lungs and noses of mice without evidence of immunopathology. mRNA-1273 is currently in a Phase 2 clinical trial with a trajectory towards Phase 3 efficacy evaluation.

20. 法国、德国、意大利以及荷兰 4 个欧洲国家向阿斯利康公司（AZ）锁定了牛津疫苗的使用权

链接:https://www.biocentury.com/article/305455?editionId=ckbhancgg2xb7016845vvt1ry&editionType=daily
Four EU countries secure access to Oxford vaccine as AZ’s dose commitments exceed 2B
根据 biocentury6 月 17 日的报道，医药公司阿斯利康 AZ 承诺生产 20 亿剂针对 SARS-CoV-2 的疫苗。法国、德国、意大利以及荷兰 4 个欧洲国家向 AZ 锁定了疫苗的使用权。该疫苗是 AZ 从牛津大学获得授权的重组腺病毒疫苗 ChAdOx1(AZ 代号为 AZD1222).牛津大学正在

招募 10 万位成年人志愿者进行疫苗的 II/III 期临床试验. 该疫苗的大规模生产马上开始，公众最早有望于年底可以接种到该疫苗。

21. 我国研制的全球首个新冠灭活疫苗所有受试者全部产生抗体，将在中国和巴西进行三期临床试验

根据梅斯医学 6 月 16 的综合报道

链接:https://www.medsci.cn/article/show_article.do?id=fbd7196012cd

我国研制的全球首个新冠灭活疫苗在 1120 位 18-59 的志愿者中的 I/II 临床试验结果的揭盲。根据报道疫苗接种后安全、有效，接种疫苗组受试者均产生高滴度抗体，18-59 岁组中剂量按照 0,14 天和 0,21 天程序接种两剂后中和抗体阳转率达 97.6%，按照 0,28 天程序接种两剂中和抗体阳转率达 100%。

根据梅斯医学同日的另一则报告

链接:https://www.medsci.cn/article/show_article.do?id=c3f3196013e0

，针对该疫苗的三期临床试验将在中国和巴西进行

科兴生物新冠病毒疫苗初步显示安全有效！三期临床试验将在中国和巴西进行

22. 结合人源化小鼠和恢复期人血清的 SARS-CoV-2 抗体鸡尾酒的研究

Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail

链接：https://science.sciencemag.org/content/early/2020/06/15/science.abd0827

编译者：张丽双

美国纽约 Regeneron Pharmaceuticals 公司结合人源化小鼠和恢复期患者这两种平行和高通量方法得到抗 SARS-CoV-2 spike 蛋白的人源化中和抗体组合，减少可能在应答中出现的病毒逃逸突变的可能性。

23. 抗 SARS-CoV-2 spike 蛋白的抗体鸡尾酒防止了使用单个抗体造成的快速突变逃逸

Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies

链接：https://science.sciencemag.org/content/early/2020/06/15/science.abd0831

编译者：张丽双

美国纽约 Regeneron Pharmaceuticals 公司发现单个抗体在体外传代中会造成快速的突变逃逸，而采用抗 SARS-CoV-2 spike 蛋白的非竞争性的抗体鸡尾酒可以防止这种突变逃逸。

24. 人单克隆抗体广泛中和 SARS 相关病毒

Broad neutralization of SARS-related viruses by human monoclonal antibodies

链接：https://science.sciencemag.org/content/early/2020/06/15/science.abc7424

编译者：张丽双

美国 Adimab 公司从一个恢复期 SARS 患者供体筛选到几种可广泛中和 SARS-CoV、SARS-CoV-2 和蝙蝠 SARS 样病毒 WIV1 的中和抗体，这些中和抗体通过阻断受体结合和诱导 S1 脱落，介导交叉保护。

25. 从 COVID-19 患者中分离出强的近种系 SARS-CoV-2 中和抗体

Longitudinal isolation of potent near-germline SARS-CoV-2-neutralizing antibodies from COVID-19 patients

链接：https://www.biorxiv.org/content/10.1101/2020.05.11.088674v1
编译者：张鹏伟
德国科隆大学研究团队证明 SARS-CoV-2 中和抗体很容易从不同的前体库中产生，促进了在接种疫苗后迅速诱导保护性免疫反应的希望。

26. 分离有效的 SARS-CoV-2 中和抗体在小动物模型中可防止疾病

Isolation of potent SARS-CoV-2 neutralizing antibodies and protection from disease in a small animal model
链接：https://science.sciencemag.org/content/early/2020/06/15/science.abc7520
编译者：孔娟
研究者从筛选出的 1800 多种抗体中分离出有效的针对 RBD 和非 RBD 表位 S 蛋白的中和抗体，并在 SARS-CoV-2 仓鼠模型中表现出较好的保护作用。

27. 来自 COVID-19 患者的强力中和抗体确定了多个易感靶标

Potent neutralizing antibodies from COVID-19 patients define multiple targets of vulnerability
链接：https://science.sciencemag.org/content/early/2020/06/15/science.abc5902
编译者：孔娟
研究者从恢复期 COVID-19 患者血清中分离出几种单克隆抗体，其中一种在 0.007 微克/毫升的浓度下能够有效地抑制 SARS-CoV-2 的感染。竞争试验和电镜研究表明 SARS-CoV-2 S 蛋白含有多个不同的抗原位点，包括几个受体结合域(RBD)表位以及非 RBD 表位，这些发现疫苗设计提供一定的指导。
文章分类：药物研发

28. 一个热稳定关闭的 SARS-CoV-2 刺突蛋白三聚体

A thermostable, closed, SARS-CoV-2 spike protein trimer.
来源：biorxiv
发布时间：2020-06-17
链接：https://www.biorxiv.org/content/10.1101/2020.06.15.152835v1
第一作者：Xiaoli Xiong，John A.G. Briggs
通讯作者：Xiaoli Xiong，John A.G. Briggs
通讯作者单位：英国 MRC Laboratory of Molecular Biology
编译者：蒋立春
中文摘要：
SARS-CoV-2 的刺突 S 蛋白介导了病毒结合受体以及进入细胞的过程，是免疫系统的主要目标。S 蛋白有相当大的构象灵活性。它从关闭到开放构象变化暴露出受体结合位点，其后的预融合构象到融合后构象介导了病毒和细胞膜的融合。S 蛋白衍生物是疫苗候选物、诊断分析试剂、以及研究 SARS-CoV-2 的生物学和免疫学研究工具的构成成分。该研究对 S 蛋白进行突变，设计出了热稳的、交联的保持在预融合状态的 S 蛋白三聚体。研究者们对发生了交联以及没有交联的蛋白的结构进行研究，鉴定出 S 蛋白三聚体的迥异的两种关闭状态。作者们展示了这个设计的热稳定关闭态的 S 蛋白三具体可以用于血清学检测。该蛋白可以作为血清学检测、病毒学研究的试剂，也可以作为免疫原。
The spike (S) protein of SARS-CoV-2 mediates receptor binding and cell entry and is the dominant target of the immune system. S exhibits substantial

conformational flexibility. It transitions from closed to open conformations to expose its receptor binding site, and subsequently from prefusion to postfusion conformations to mediate fusion of viral and cellular membranes. S protein derivatives are components of vaccine candidates and diagnostic assays, as well as tools for research into the biology and immunology of SARS-CoV-2. Here we have designed mutations in S which allow production of thermostable, crosslinked, S protein trimers that are trapped in the closed, pre-fusion, state. We have determined the structures of crosslinked and non-crosslinked proteins, identifying two distinct closed conformations of the S trimer. We demonstrate that the designed, thermostable, closed S trimer can be used in serological assays. This protein has potential applications as a reagent for serology, virology and as an immunogen.

29. 冠状病毒的突破：地塞米松是首个可挽救生命的药物

Coronavirus breakthrough: dexamethasone is first drug shown to save lives

来源：nature(新闻稿)

发布时间：2020-06-16

链接：https://www.nature.com/articles/d41586-020-01824-5

第一作者：Heidi Ledford

通讯作者：Heidi Ledford

通讯作者单位：

DOI 或 PUBMED ID：10.1038/d41586-020-01824-5

编译者：刘焕珍

中文摘要：

英国一项随机对照临床试验发现，一种廉价且常用的类固醇可以挽救 COVID-19 重病患者的生命。地塞米松是首个被证明能减少冠状病毒患者死亡的药物。在这项试验中，因冠状病毒感染而使用呼吸机的患者死亡人数减少了约三分之一。地塞米松对需要呼吸机治疗的危重病人的作用最为显著，将仅需输氧但未使用呼吸机的患者死亡率降低了 20%，不过，地塞米松对轻症患者几乎没有效果。

Abstract:

An inexpensive and commonly used steroid can save the lives of people seriously ill with COVID-19, a randomized, controlled clinical trial in the United Kingdom has found. The drug, called dexamethasone, is the first shown to reduce deaths from the coronavirus that has killed more than 430,000 people globally. In the trial, it cut deaths by about one-third in patients who were on ventilators because of coronavirus infection. The study enrolled 2,100 participants who received dexamethasone at a low or moderate dose of six milligrams per day for ten days, and compared how they fared against about 4,300 people who received standard care for coronavirus infection. The effect of dexamethasone was most striking among critically ill patients on ventilators. Those who were receiving oxygen therapy but were not on ventilators also saw improvement: their risk of dying was reduced by 20%. The steroid had no effect on people with mild cases of COVID-19 — those not receiving oxygen or ventilation.

30. GLUCOCOVID：甲基强的松龙治疗成人重症 COVID-19 肺炎的对照研究

GLUCOCOVID: A controlled trial of methylprednisolone in adults hospitalized with COVID-19 pneumonia

链接：https://www.medrxiv.org/content/10.1101/2020.06.17.20133579v1

编译者：张丽双

西班牙一家医院的临床试验结果显示，短期使用甲基强的松龙可改善重症 COVID-19 肺炎的临床预后，降低进入 ICU、需要 NIV 或死亡的风险。

31. mavrilimumab 联合 GM-CSF 阻断治疗 COVID-19 肺炎和系统性炎症：一项单中心前瞻性队列研究

GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study

来源：the lancet

发布时间：2020-06-16

链接：https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30170-3/fulltext

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DOI 或 PUBMED ID：10.1016/S2665-9913(20)30170-3

编译者：宋张悦

中文摘要：

背景：COVID-19 肺炎和全身性炎症患者的死亡率很高。本研究的目的是检测马夫利列单抗(mavrilimumab)，一种粒细胞-巨噬细胞集落刺激因子(GM-CSF)受体的单克隆抗体，是否能改善 COVID-19 肺炎和系统性炎症患者的临床结局。

方法：这项单中心前瞻性队列研究纳入了 18 岁及以上、在意大利米兰圣拉斐尔医院(San Raffaele Hospital)住院的 COVID-19 严重肺炎、缺氧和全身炎症的患者。在当时医院给予的标准治疗中，患者接受单次静脉注射(6 毫克/公斤)mavrilimumab。对照组由在同一家医院接受标准治疗的具有相似基线特征的同期患者组成。主要结局是临床改善的时间(定义为临床状况 7 分制中 2 分或 2 分以上的改善)。其他结局包括患者达到临床改善的比例、生存率、无机械通气生存率和退热时间。每天监测不良事件。

发现：在 2020 年 3 月 17 日至 4 月 15 日期间，13 例非机械通气患者(中位年龄 57 岁[IQR 52-58]， 12 名[92%]男性)接受了 mavrilimumab 治疗；对照组 26 例患者(中位年龄 60 岁[IQR 53-67]， 17 名[65%]男性)接受了标准治疗。随访 28 天，mavrilimumab 组无死亡病例，对照组死亡 7 例(27%)(p=0.086)。在 28 天时，mavrilimumab 组和对照组 17 例(65%)患者均有临床好转(p=0.030)，mavrilimumab 的改善较对照组早(平均改善 8 天[IQR 5-11] vs 19 天[11 至>28]， p=0·0001)。到第 28 天，mavrilimumab 组有 1 例(8%)进展为机械通气，对照组有 9 例(35%)进展为机械通气或死亡(p=0·14)。到第 14 天，mavrilimumab 组 11 例发热患者中有 10 例(91%)退烧，对照组 18 例发热患者中有 11 例(61%)退烧(p=0.18)：与对照组相比，接受 mavrilimumab 治疗者退热更快(中位退烧时间为 1 天[IQR 1-2]vs 7 天[3 至>14]， p=0.0093)。Mavrilimumab 耐受性良好，没有输注反应。对照组中有 3 例(12%)出现感染并发症。

解释：与标准治疗相比，**在非机械通气的 COVID-19 重症肺炎和系统性炎症患者中，**

Mavrilimumab 治疗可改善临床结局。治疗耐受性良好。疗效的确认需要进一步的受控试验。

Abstract:

Background: Mortality in patients with COVID-19 pneumonia and systemic hyperinflammation is high. We aimed to examine whether mavrilimumab, an anti-granulocyte–macrophage colony-stimulating factor receptor-α monoclonal antibody, added to standard management, improves clinical outcomes in patients with COVID-19 pneumonia and systemic hyperinflammation.

Methods: This single-centre prospective cohort study included patients aged 18 years or older who were admitted to San Raffaele Hospital (Milan, Italy) with severe COVID-19 pneumonia, hypoxia, and systemic hyperinflammation. Patients received a single intravenous dose (6 mg/kg) of mavrilimumab added to standard care given by the hospital at the time. The control group consisted of contemporaneous patients with similar baseline characteristics who received standard care at the same hospital. The main outcome was time to clinical improvement (defined as improvement of two or more points on the seven-point ordinal scale of clinical status). Other outcomes included proportion of patients achieving clinical improvement, survival, mechanical ventilation-free survival, and time to fever resolution. Adverse events were monitored daily.

Findings: Between March 17 and April 15, 2020, 13 non-mechanically ventilated patients (median age 57 years [IQR 52–58], 12 [92%] men) received mavrilimumab and 26 patients (median age 60 [IQR 53–67], 17 [65%] men) in the control group received standard care. During the 28-day follow-up, no patients in the mavrilimumab group died, and seven (27%) patients in the control group died (p=0·086). At day 28, all patients in the mavrilimumab group and 17 (65%) patients in the control group showed clinical improvement (p=0·030), with earlier improvement in the mavrilimumab than in the control group (mean time to improvement 8 days [IQR 5 to 11] vs 19 days [11 to >28], p=0·0001). By day 28, one (8%) patient in the mavrilimumab group progressed to mechanical ventilation compared with nine (35%) patients in the control group who progressed to mechanical ventilation or died (p=0·14). By day 14, fever resolved in ten (91%) of 11 febrile patients in the mavrilimumab group, compared with 11 (61%) of 18 febrile patients in the control group (p=0·18); fever resolution was faster in mavrilimumab recipients versus controls (median time to resolution 1 day [IQR 1 to 2] vs 7 days [3 to >14], p=0·0093). Mavrilimumab was well tolerated, with no infusion reactions. Three (12%) patients in the control group developed infectious complications.

Interpretation: Mavrilimumab treatment was associated with improved clinical outcomes compared with standard care in non-mechanically ventilated patients with severe COVID-19 pneumonia and systemic hyperinflammation. Treatment was well tolerated. Confirmation of efficacy requires controlled testing.

32. 具有 Spike 蛋白天然突变的 SARS-CoV-2 病毒变体表现出不同的细胞侵入能力

Naturally mutated spike proteins of SARS-CoV-2 variants show differential

levels of cell entry

来源：bioRxiv
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编译者：宋珂

中文摘要：

造成 COVID-19 疫情的病原体 SARS-CoV-2 病毒，在人群内持续传播的过程中不断发生突变。此类突变会在 Spike（S）蛋白上发生，S 蛋白能够与 ACE2 受体结合并被 TMPRSS2 裂解。然而，尚不清楚 S 蛋白的突变是否会影响 SARS-CoV-2 病毒的感染能力。本文中作者发现，携带天然突变的 S 蛋白可以借由 ACE2 和 TMPRSS2 的影响，增强或减弱侵入细胞的能力。SARS-CoV-2 S 假慢病毒侵入细胞的能力总体上比 SARS-CoV S 更低。在所有 S 蛋白的突变中，携带 D614G 突变的病毒显示出最高的侵入细胞能力。通过对 S 蛋白的结构分析解释了这一现象的原因。尽管如此，携带 D614G 突变的病毒仍可以被原型病毒的抗血清中和。总而言之，现有数据表明 S 蛋白的 D614G 突变增强了病毒的感染能力，但同时保持了对中和抗体的的敏感性。

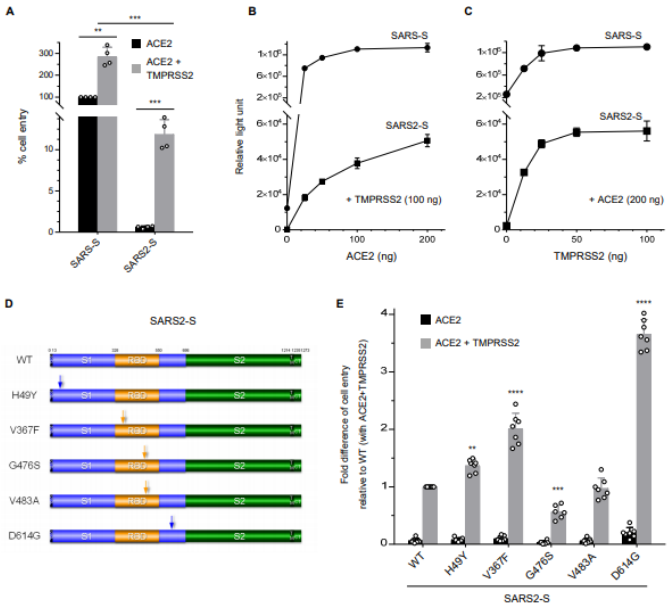

Figure 1. The SARS-CoV-2 S protein has significantly low cell entry activity, with a strong dependency on TMPRSS2, and its variant proteins display differential levels of entry activity. (A) Viruses were prepared by transfection of 293T cells with the HiBiT-tagged lentiviral packaging plasmid, the firefly luciferase-reporter lentiviral transfer plasmid, and either a SARS-CoV S (SARS-S) or SARS-CoV-2 S (SARS2-S) expression plasmid. Viral supernatants were subjected to HiBiT assays, and S-pseudotyped viruses normalized by HiBiT activity were used for infection of 293T cells expressing the host receptor ACE2 alone (black) or coexpressing TMPRSS2 (gray). Cell entry was determined by firefly luciferase activity in cell lysates. Data from four experiments are shown as a percentage of cell entry of

SARS-S-pseudotyped viruses into 293T cells expressing ACE2 only (mean ± s.d., n = 3 technical replicates). The p value was calculated using two-tailed paired Student's t-test, **p < 0.005, ***p < 0.001. (B, C) The effect of ACE2 or TMPRSS2 expression levels on cell entry activity. 293T cells were transfected with a high and constant level of an expression plasmid encoding ACE2 together with increasing levels of a TMPRSS2 expression plasmid (B), and vice versa (C). Transfected cells were infected with lentiviruses pseudotyped with either SARS-S (circle) or SARS2-S (square), as described in A. Data shown are representative of three independent experiments (mean ± s.d., n = 3 technical replicates). (D) Schematic illustration of the prototype (wild-type, WT) and globally spread variant SARS2-S proteins. Numbers indicate amino acid positions. The signal peptide (SP), transmembrane domain (TM), cytoplasmic tail (CT), S1 subunit (S1), S2 subunit (S2), and receptor-binding domain (RBD) are indicated. The positions of mutations are indicated by arrows. (E) Functional comparison of the entry activity of WT and mutant SARS2-S proteins. Different S-pseudotyped viruses were prepared as described in A and used for infection of 293T cells expressing the host receptor ACE2 alone (black) or coexpressing TMPRSS2 (gray). Cell entry was determined by firefly luciferase activity in cell lysates. Data are shown as the fold difference of cell entry relative to that of WT into 293T cells coexpressing ACE2 and TMPRSS2 (mean± s.d. from six to seven independent experiments with three technical replicates); **p < 0.005, ***p < 0.001, ****p < 0.0001 compared with WT using one-way ANOVA with Dunnett's multiple comparison test.

Abstract:
The causative agent of the coronavirus disease 2019 (COVID-19) pandemic, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is steadily mutating during continuous transmission among humans. Such mutations can occur in the spike (S) protein that binds to the angiotensin-converting enzyme-2 (ACE2) receptor and is cleaved by transmembrane protease serine 2 (TMPRSS2). However, whether S mutations affect SARS-CoV-2 infectivity remains unknown. Here, we show that naturally occurring S mutations can reduce or enhance cell entry via ACE2 and TMPRSS2. A SARS-CoV-2 S-pseudotyped lentivirus exhibits substantially lower entry than SARS-CoV S. Among S variants, the D614G mutant shows the highest viral entry, as supported by structural observations. Nevertheless, the D614G mutant remains susceptible to neutralization by antisera against prototypic viruses. Taken together, these data indicate that the D614G mutation enhances viral infectivity while maintaining neutralization susceptibility.

33. SARS-CoV-2 中 Spike 蛋白的 D614G 突变增强了病毒对多型人类细胞的传染能力

The D614G mutation in SARS-CoV-2 Spike increases transduction of multiple human cell types

来源：bioRxiv

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中文摘要：

近期出现了一种 SARS-CoV-2 病毒的新型分离株，该毒株的 Spike 蛋白存在一个点突变 D614G，且流行性迅速超过了其他毒株。这种 Spike 蛋白的变体是全球 SARS-CoV-2 基因组中最普遍的进化枝（A2a）的典型特征。通过系统基因组学数据分析，多个研究组认为 D614G 突变可能会提高病毒的转播能力，从而造成正向选择。但另一些研究组则声称，当前已有的证据还不足以证明发生了正向选择。而且，在 A2a 进化分支中，Spike 蛋白的 D614G 突变与 ORF1b 蛋白的 P314L 突变存在连锁不平衡，因此很难单独从种群遗传学角度分辨出 Spike D614G 突变的功能意义。本文中，作者对人密码子优化的 Spike 蛋白进行定点突变，引入 D614G 突变。同时使用该突变体和野生型 D614 Spike 蛋白合成 SARS-CoV-2 假慢病毒颗粒（S 病毒）。作者发现，在包括人肺上皮细胞在内的多种细胞系中，携带 D614G 突变的 S 病毒在感染细胞的效率上比野生型 S 病毒高 8 倍。这为 Spike 蛋白中的 D614G 突变提高了病毒感染人类细胞的能力提供了功能性证据。作者还进一步发现，携带 D614G 突变的蛋白在体外和人体细胞中对切割更具抵抗能力，这也许能为病毒传染能力的增强提供一种机理解释。鉴于目前正在开发或进行临床试验的几款疫苗均基于最初的（D614）Spike 序列，以上结果对提高这些疫苗在防御近期流行的 SARS-CoV-2 病毒分离株中的功效具有重要意义。

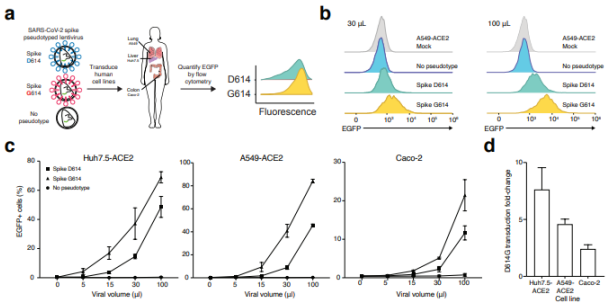

Figure 2. SARS-CoV-2 Spike D614G pseudotyped lentivirus results in increased transduction of human lung, liver and colon cell lines. (a) Schematic of EGFP lentivirus pseudotyped with SARS-CoV2 Spike proteins (or no pseudotype) and readout of EGFP fluorescence by flow cytometry. (b) Flow cytometry of A549-ACE2 cells at 3 days post-transduction with 30 or 100 uL SARS-CoV-2 spike pseudotyped lentivirus. (c) Percent of EGFP+ cells at 3 days post-transduction with the indicated volume of virus and pseudotype in human liver Huh7.5-ACE2 cells, lung A549-ACE2 cells, and colon Caco-2 cells (n = 3 replicates, error bars are s.e.m.). (d) The maximum fold-change in viral transduction in each cell line of G614 Spike as compared to D614 Spike (error bars are s.e.m.).

Abstract:

Recently, a novel isolate of the SARS-CoV-2 virus carrying a point mutation in the Spike protein (D614G) has emerged and rapidly surpassed others in prevalence, including the original SARS-CoV-2 isolate from Wuhan, China. This Spike variant is a defining feature of the most prevalent clade (A2a) of SARS-CoV-2 genomes worldwide. Using phylogenomic data, several groups have proposed that the D614G variant may confer increased transmissibility leading to positive selection, while others have claimed that currently available evidence does not support positive selection. Furthermore, in the A2a clade, this mutation is in linkage disequilibrium with a ORF1b protein variant (P314L), making it difficult to

discern the functional significance of the Spike D614G mutation from population genetics alone. Here, we perform site-directed mutagenesis on a human codon-optimized spike protein to introduce the D614G variant and produce SARS-CoV-2-pseudotyped lentiviral particles (S-Virus) with this variant and with D614 Spike. We show that in multiple cell lines, including human lung epithelial cells, that S-Virus carrying the D614G mutation is up to 8-fold more effective at transducing cells than wild-type S-Virus. This provides functional evidence that the D614G mutation in the Spike protein increases transduction of human cells. Further we show that the G614 variant is more resistant to cleavage in vitro and in human cells, which may suggest a possible mechanism for the increased transduction. Given that several vaccines in development and in clinical trials are based on the initial (D614) Spike sequence, this result has important implications for the efficacy of these vaccines in protecting against this recent and highly-prevalent SARS-CoV-2 isolate.

34. SARS-CoV-2 病毒中 Spike 蛋白的 D614G 突变可减少 S1 脱落并提高病毒传染能力

The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity

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中文摘要：

随着时间推移，SARS-CoV-2 病毒中 Spike 蛋白（S）存在 D614G 突变的分离毒株成为主要类型，说明这种突变增强了病毒的传播能力。本文中，作者比较了 S 蛋白 614 残基位置分别为天冬氨酸（S^{D614}）和甘氨酸（S^{G614}）时的功能性质。作者发现，针对表达 ACE2 的细胞，S^{G614} 型假逆转录病毒的感染能力明显高于 S^{D614} 型病毒。这种更强的感染能力与 S 蛋白中更少的 S1 结构域脱落有关，也与 S 蛋白能更好地组装成假病毒颗粒有关。在由 SARS-CoV-2 病毒的 M 蛋白，N 蛋白，E 蛋白和 S 蛋白合成的类病毒颗粒中，也得到了相似的结果。然而，S^{G614} 型病毒与 ACE2 的结合能力并未高于 S^{D614} 型病毒。而且，康复病人的血浆对包含这两类 S 蛋白的假病毒的中和效率也差异不大。以上结果表明，S^{G614} 型病毒比 S^{D614} 更稳定，这也与流行病学数据中 S^{G614} 型病毒的传播效率更高相一致。

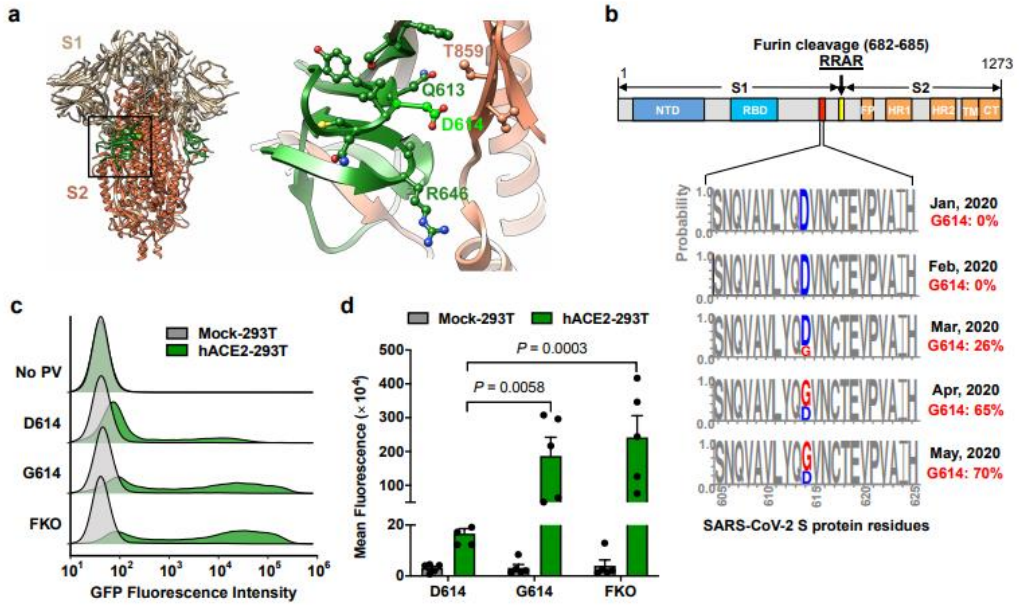

Figure 1. The D614G mutation is associated with enhanced infectivity. Cryo-EM structure of S1 (grey) and S2 (orange) heterodimer (PBD 6VXX). The residues 581-676, a C-terminal region of the S1 domain involved in S2 interaction, is shown in green. Aspartic acid 614 is shown in light green. The area indicated with a black square is presented magnified at the right. Residues within 5.5 Å of D614 are shown in a ball-and-stick representation. b, A representation of the SARS-CoV-2 Sprotein (upper panel) and D/G variation at the residue 614 presented in logo plots at different time points between January 1st and May 30th, 2020 (lower panel). Total number of sequences analyzed: 17 in January, 33 in February, 293 in March, 1511 in April, and 2544 in May. NTD: N-terminal domain, RBD: Receptor-binding domain, FP: Fusion peptide, HR1 and HR2: Heptad-repeat region 1 and 2, respectively, TM: Transmembrane region, CT: Cytoplasmic tail. c,d, Mock- and hACE2-293T cells on 96-well plates were infected with MLV PV (5 x 108 vector genome per well) expressing GFP and pseudotyped with the indicated viral glycoprotein and analyzed 24 h later. Representative histograms (c) or mean ± SEM (d) of five experiments conducted using two independent PV preparations are shown. Each dot in (d) indicates an average value of a duplicated experiment. Significant differences were analyzed by two-way ANOVA with Sidak multiple comparisons test. PV titers are presented in Extended Data Fig. 1. FKO: Furincleavage knockout mutant.

Abstract:

SARS coronavirus 2 (SARS-CoV-2) isolates encoding a D614G mutation in the viral spike (S) protein predominate over time in locales where it is found, implying that this change enhances viral transmission. We therefore compared the functional properties of the S proteins with aspartic acid (S^{D614}) and glycine (S^{G614}) at residue 614. We observed that retroviruses pseudotyped with S^{G614} infected ACE2-expressing cells markedly more efficiently than those with S^{D614}. This greater infectivity was correlated with less S1 shedding and greater incorporation of the S protein into the pseudovirion. Similar results were obtained using the virus-like particles produced with SARS-CoV-2 M, N, E, and S proteins. However, S^{G614} did not bind ACE2 more efficiently than S^{D614}, and the pseudoviruses containing

these S proteins were neutralized with comparable efficiencies by convalescent plasma. These results show S^{G614} is more stable than S^{D614}, consistent with epidemiological data suggesting that viruses with S^{G614} transmit more efficiently.

35. 单细胞筛选宠物、畜禽和野生动物的 SARS-CoV-2 靶细胞

Single-cell screening of SARS-CoV-2 target cells in pets, livestock, poultry and wildlife

链接：https://www.biorxiv.org/content/10.1101/2020.06.13.149690v1

来自深圳华大基因等单位的研究团队为宠物、家畜、家禽和野生动物中的 11 个代表物种构建了单细胞图谱，并发现猫体内 SARS-CoV-2 靶细胞的比例明显高于调查的其他物种，在家猪的多种细胞类型中检测到 SARS-CoV-2 靶细胞。此外，该研究还筛选了 144 种病毒受体的表达模式，得到了一个完整的病毒靶细胞图谱。

36. SARS-CoV-2 刺突蛋白对哺乳动物 ACE2 蛋白具有广泛的宿主倾向性

The SARS-CoV-2 Spike protein has a broad tropism for mammalian ACE2 proteins

链接：https://www.biorxiv.org/content/10.1101/2020.06.17.156471v1

编译者：刘焕珍

除人 ACE2 外，SARS-CoV-2 的 S 蛋白对哺乳动物 ACE2 受体具有广泛的宿主倾向性。22 个不同宿主中，狗，猫和兔子的 ACE2 蛋白最适合 SARS-CoV-2，而蝙蝠和鸟的 ACE2 蛋白则是使用效率最低的受体。

37. 不同物种的 ACE2 介导 SARS-CoV-2 进入细胞

Cell entry of SARS-CoV-2 conferred by angiotensin-converting enzyme 2 (ACE2) of different species

链接:https://www.biorxiv.org/content/10.1101/2020.06.15.153916v1

编译:蒋立春

哈尔滨兽医研究所和广州医科大学的研究者们研究了 11 种不同物种的 ACE2 介导 SARS-CoV-2 进入不易感细胞的能力。研究者们发现中华菊头蝠，家猫，狗猪，山羊特别是马来穿山甲的 ACE2 可以介导 SARS-CoV-2 进入不易感的细胞。

38. 禽类对 SARS-CoV-2 和 MERS-CoV 不易感

Lack of susceptibility of poultry to SARS-CoV-2 and MERS-CoV

链接:https://www.biorxiv.org/content/10.1101/2020.06.16.154658v1

编译：蒋立春

美国禽类研究中心的研究人员用 SARS-CoV-2 和 MERS-CoV 对多种禽类进行了感染实验，发现禽类对 SARS-CoV-2 和 MERS-CoV 不易感。

Chickens, turkeys, ducks, quail and geese were challenged with SARS-CoV-2 or MERS-CoV. No disease was observed, no virus replication was detected and antibodies were not detected in serum. Neither virus replicated in embryonating chickens eggs. Poultry are unlikely to serve a role in the maintenance of either virus.

39. 全基因组 CRISPR 筛选揭示调控 SARS-CoV-2 感染的宿主基因

Genome-wide CRISPR screen reveals host genes that regulate SARS-CoV-2 infection

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发布时间：2020-06-17
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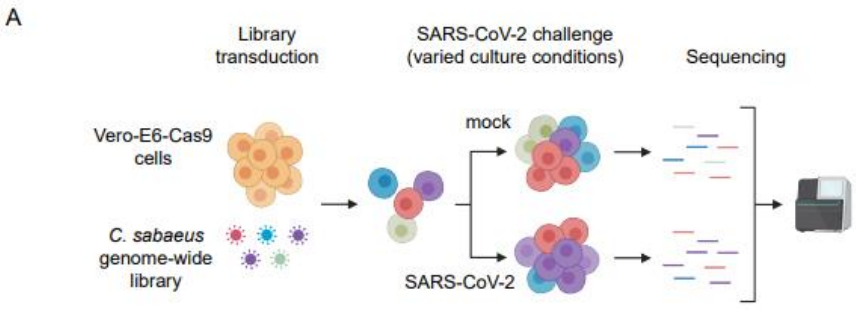
通讯作者：John G. Doench , Craig B. Wilen
通讯作者单位： Broad institute, 耶鲁大学
编译者：蒋立春

中文摘要：

鉴定出 SARS-CoV-2 感染必需的宿主基因可以帮助我们理解 COVID-19 的发病机制，以及找到全新的药物靶点。该文中作者进行了全基因组的 CRISPR 筛选。该筛选成功鉴定出了包括受体 ACE2 和蛋白酶 Cathepsin L 等已知的对 SARS-CoV-2 感染必需的宿主因子。此外，该研究还发现了新的促进病毒感染的基因和通路包括 SWI/SNF 染色体重构复合物以及 TGF-B 信号通路里的关键成分。抑制这些通路的小分子可以阻止 SARS-CoV-2 引起的细胞死亡。该研究同事揭示报警蛋白 HMGB1 对 SARS-CoV-2 的复制起到关键作用。而与之相反，失去组蛋白 H3.3 的伴侣复合物会让细胞更容易死于病毒感染。

Identification of host genes essential for SARS-CoV-2 infection may reveal novel therapeutic targets and inform our understanding of COVID-19 pathogenesis. Here we performed a genome-wide CRISPR screen with SARS-CoV-2 and identified known SARS-CoV-2 host factors including the receptor ACE2 and protease Cathepsin L. We additionally discovered novel pro-viral genes and pathways including the SWI/SNF chromatin remodeling complex and key components of the TGF-β signaling pathway. Small molecule inhibitors of these pathways prevented SARS-CoV-2-induced cell death. We also revealed that the alarmin HMGB1 is critical for SARS-CoV-2 replication. In contrast, loss of the histone H3.3 chaperone complex sensitized cells to virus-induced death. Together this study reveals potential therapeutic targets for SARS-CoV-2 and highlights host genes that may regulate COVID-19 pathogenesis.

Figure 1



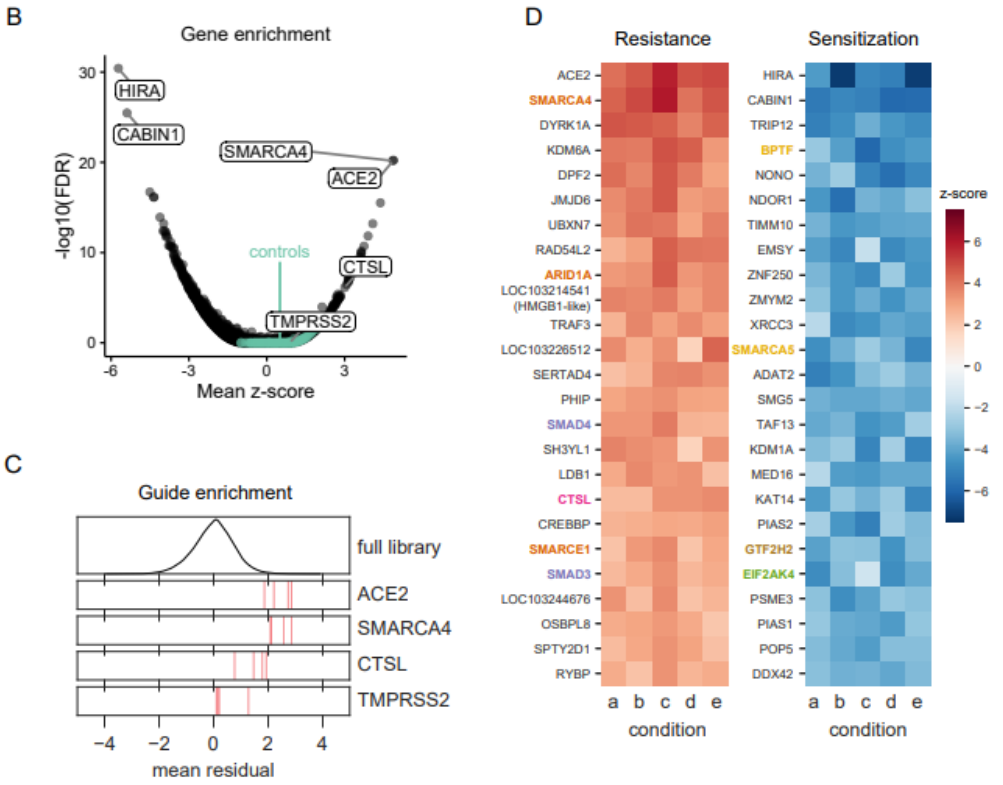


Fig. 1. Genome-wide CRISPR screen identifies genes critical for SARS-CoV-2-induced cell death. (A) Schematic of pooled screen. Vero-E6 cells expressing Cas9 were transduced with the genome-wide C. sabaeus library via lentivirus. The transduced cell population then either received a mock treatment or was challenged with SARS-CoV-2 under various culture conditions. Surviving cells from each condition were isolated and the sgRNA sequences were amplified by PCR and sequenced. (B) Volcano plot showing top genes conferring resistance and sensitivity to SARS-CoV-2. The gene-level z-score and -log10(FDR) were both calculated using the mean of the five Cas9-v2 conditions. Non-targeting control sgRNAs were randomly grouped into sets of 4 to serve as “dummy” genes and are shown in green. (C) Performance of individual guide RNAs targeting ACE2, SMARCA4, CTSL, and TMPRSS2. The mean residual across the five Cas9-v2 conditions is plotted for the full library (top) and for the 4 guide RNAs targeting each gene. (D) Heatmaps of the top 25 gene hits for resistance and sensitivity, ranked by mean z-score in the Cas9-v2 conditions. Genes that are included in one of the gene sets labeled in (Fig 2A) are colored accordingly. Condition a: Cas9v2 D5 2.5e6 Hi-MOI; b: Cas9v2 D5 5e6 Hi-MOI; c: Cas9v2 D2 5e6 Hi-MOI; d: Cas9v2 D10 5e6 Hi-MOI; e: Cas9v2 D5 2.5e6 Lo-MOI.

40. SARS-CoV-2 的核衣壳蛋白和 RNA 一起发生相分离的现象

编译：蒋立春

北卡罗来纳大学教堂山分校研究团队发现了特定的病毒 RNA 驱动了 SARS-CoV-2 的核衣壳蛋白发生相分离的现象

Specific viral RNA drives the SARS CoV-2 nucleocapsid to phase separate

链接:https://www.biorxiv.org/content/10.1101/2020.06.11.147199v1

华盛顿大学团队的研究表明 SARS-CoV-2 的核衣壳蛋白结构是动态无序的、和 RNA 一起会发生相分离

The SARS-CoV-2 nucleocapsid protein is dynamic, disordered, and phase separates with RNA

链接:https://www.biorxiv.org/content/10.1101/2020.06.17.158121v1

41. 比较分析冠状病毒的基因组 RNA 结构揭示 SARS 样冠状病毒的 RNA 结构保守性

Comparative analysis of coronavirus genomic RNA structure reveals conservation in SARS-like coronaviruses

链接:https://www.biorxiv.org/content/10.1101/2020.06.15.153197v1

42. SARS-CoV-2 的 3a 离子通道在脂质纳米盘中的冷冻电镜结构

Cryo-EM structure of the SARS-CoV-2 3a ion channel in lipid nanodiscs

链接:https://www.biorxiv.org/content/10.1101/2020.06.17.156554v1

43. SARS-CoV-2 的刺突蛋白的冷冻电镜中意外的包含结合游离脂肪酸的口袋

Unexpected free fatty acid binding pocket in the cryo-EM structure of SARS-CoV-2 spike protein

链接:https://www.biorxiv.org/content/10.1101/2020.06.18.158584v1

44. SARS-CoV-2 主要蛋白酶与紫草素的复合物晶体结构

Crystal structure of SARS-CoV-2 main protease in complex with a Chinese herb inhibitor shikonin

链接: https://www.biorxiv.org/content/10.1101/2020.06.16.155812v1

编译：王玮

来自赣南医学院等单位的研究团队报道了 SARS-CoV-2 主要蛋白酶在 2.45 埃分辨率下的晶体结构，并发现催化二元化合物的 His41-Cys145 的构象发生了剧烈的变化，紫草素与共价抑制剂的结合方式不同。

45. COVID-19 更新：FDA 撤销氯喹和羟氯喹的紧急使用授权

Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Chloroquine and Hydroxychloroquine

链接：https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-chloroquine-and

编译者：雷颖

2020 年 6 月 15 日美国食品和药物管理局（FDA）撤销了磷酸氯喹和硫酸羟氯喹的紧急使用授权（EUA），不再允许在无法进行临床试验或参加临床试验不可行的情况下，将捐赠给美国国家战略储备库的磷酸氯喹和硫酸羟氯喹用于治疗住院的 COVID-19 患者。根据对 EUA 的持续分析和最近的科学数据，FDA 确定氯喹和羟氯喹不太可能对 EUA 中授权用途的 COVID-19 治疗有效。另外，鉴于持续的严重心脏不良事件和其他潜在的严重副作用，氯喹和羟氯喹的已知和潜在益处不再超过授权使用的已知和潜在风险。这是签发 EUA 的法定标准。因此在与 FDA 磋商后，美国卫生和公共服务部的生物医学高级研究与开发局（BARDA）给 FDA 发了一封信，基于最新科学数据要求撤销磷酸氯喹和硫酸羟氯喹的 EUA。

46. 大型研究使羟氯喹的希望黯淡

Big studies dim hopes for hydroxychloroquine

链接：https://science.sciencemag.org/content/368/6496/1166

编译者：雷颖

羟氯喹及其姊妹药物氯喹已被用于抗击疟疾和其他疾病。自实验表明它们可能对抗 SARS-CoV-2 以来，全球已进行了数百次临床试验。科学家们正在尝试不同剂量，单独或与抗生素阿奇霉素、抗病毒化合物法匹拉韦或其他药物联合使用；以及患有轻度或重度疾病的患者，医护人员，孕妇和艾滋病毒携带者等。文中列举了多项羟氯喹的临床试验，包括英国牛津大学的迄今为止规模最大的康复试验(Recovery)、明尼苏达大学双城分校的暴露后预防(PEP)试验、西班牙巴塞罗那进行的大型 PEP 试验、曼谷玛希顿大学的暴露前预防(PrEP)试验等，但大部分的研究结果令人失望。