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 7 月 16 日疫情

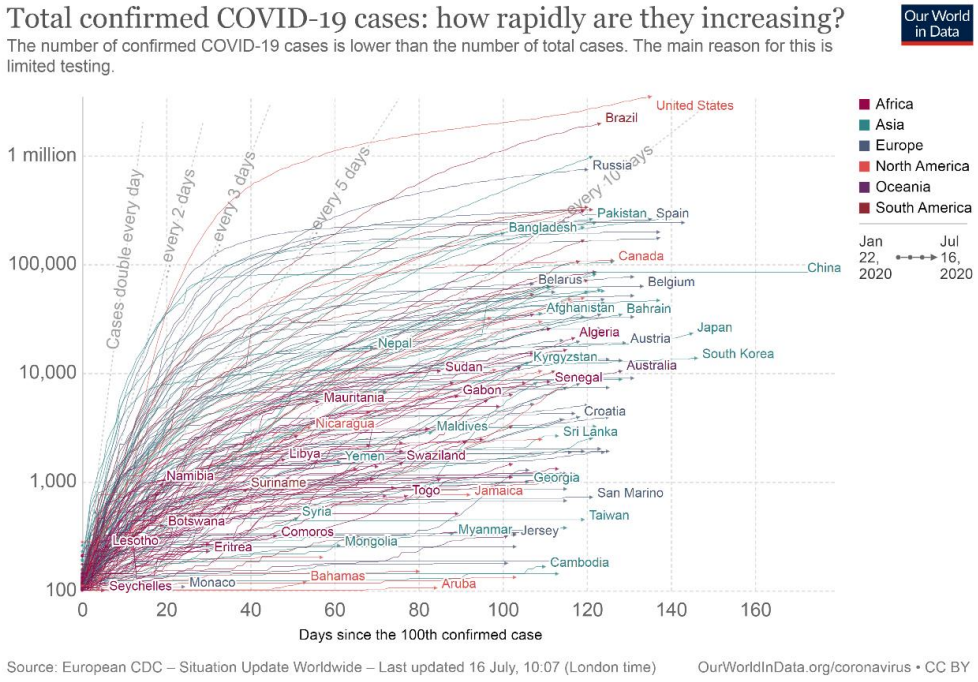
数据来源：WHO

发布时间：2020 年 7 月 16 日北京时间下午 4 点

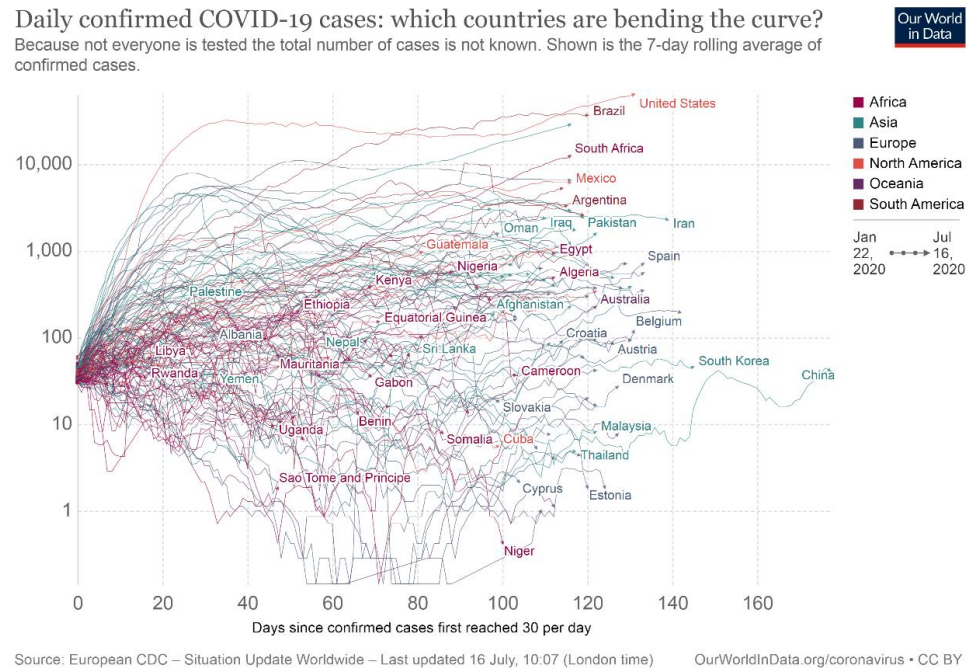
链接：https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

根据 WHO 提供的数据，2020 年 7 月 16 日全球累计确诊新型冠状病毒病人 **13378853** 例，当日新增确诊 **226181** 例，累计死亡 **580045** 例，当日新增死亡 5579。

中国累计确诊 85697 例，累计死亡 4651 例，当日新增确诊 20 例，新增死亡 2 例。



重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



重点国家每日新增确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）

全国新型冠状病毒肺炎新增确诊病例分布图（7 月 16 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 科学家呼吁将大流行的调查重点放在野生动物贸易上

Scientists call for pandemic investigations to focus on wildlife trade

来源：Nature

发布时间：2020-07-10

链接：https://www.nature.com/articles/d41586-020-02052-7

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通讯作者：-

通讯作者单位：-

DOI 或 PUBMED ID：10.1038/d41586-020-02052-7

编译者：宋张悦

中文摘要：

世界卫生组织（WHO）将于本周末派遣科学家前往中国，调查 COVID-19 疫情的源头。研究人员称，作为揭开冠状病毒大流行起源的努力的一部分，应该**对中国野生动物贸易进行彻查**。世界卫生组织总干事 Tedros Adhanom Ghebreyesus 在 7 月 7 日的新闻发布会上说:“任务的目标是增进对 COVID-19 动物宿主的了解,并确定疾病是如何在动物和人类之间传播的。”世界卫生组织应急项目主任 Michael Ryan 指出，武汉是一个很好的起点。

大多数研究人员都认为 SARS-CoV-2 病毒可能起源于马蹄蝙蝠，但它如何传播到人类仍然是个谜。这种病毒可能直接从蝙蝠跳到人类身上，随着时间的推移演变成目前的流行毒株，也可能通过中间动物传播。研究人员指出，野生动物贸易——在这种贸易中，许多动物彼此和人靠得很近——为病毒从一个物种扩散到另一个物种提供了完美的条件。

Abstract

The World Health Organization is sending scientists to China this weekend to investigate the origins of the COVID-19 outbreak. China’s wildlife trade

should be thoroughly investigated as part of efforts to uncover the origin of the coronavirus pandemic, say researchers.

3. 武汉 COVID-19 疫情的全面传播动态的重建

Reconstruction of the full transmission dynamics of COVID-19 in Wuhan

来源：Nature
发布时间：2020-07-16
链接：https://www.nature.com/articles/s41586-020-2554-8

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DOI 或 PUBMED ID：https://doi.org/10.1038/s41586-020-2554-8

编译者：宋张悦

中文摘要：

随着世界各国对遏制 COVID-19 大流行的干预措施的审查，可以通过研究中国武汉 SARS-CoV-2 的全面传播动态得出重要的经验教训，**在武汉，通过强有力的非药物干预抑制了当地的 COVID-19 疫情**。本文使用建模的方法，重建了 2020 年 1 月 1 日至 2020 年 3 月 8 日期间以事件和干预为特征的 5 个时期，基于 32,583 例实验室确诊病例的 COVID-19 全谱动态。考虑症状前传染性、时变确定率、传播率和人口流动，我们确定了**疫情的两个关键特征：高隐蔽性和高传播率**。我们估计，在 3 月 8 日之前，87%（下限 53%）的感染是未确诊的，可能包括无症状和轻微症状的病例；在疫情早期，基本繁殖数 R0 为 3.54(95%可信区间[CrI]: 3.40-3.67)，远高于 SARS 和 MERS。我们观察到，多管齐下的干预措施对控制疫情有相当大的积极作用，繁殖数量减少至 0.28(0.23-0.33)，预计截至 3 月 8 日，武汉总感染人数将减少 96.0%。我们进一步探讨了 14 天没有确珍感染后解除所有干预措施后复发的概率，根据未确诊感染率分别为 87%和 53%的模型，分别估计为 0.32 和 0.06，**强调了未确诊病例在改变干预策略中所构成的风险**。这些结果对继续监测和干预以最终控制 COVID-19 疫情具有重要的意义。

Abstract

As countries in the world review interventions for containing the COVID-19 pandemic, important lessons can be drawn by studying the full transmission dynamics of SARS-CoV-2 in Wuhan, China, where vigorous non-pharmaceutical interventions have suppressed the local COVID-19 outbreak[1]. Here, we use a modelling approach to reconstruct the full-spectrum dynamics of COVID-19 between January 1, 2020 and March 8, 2020 across five periods marked by events and interventions based on 32,583 laboratory-confirmed cases[1]. Accounting for presymptomatic infectiousness[2], time-varying ascertainment rates, transmission rates and population movements[3], we identify two key features of the outbreak: high covertness and high transmissibility. We estimate 87% (lower bound 53%) of the infections before March 8 were unascertained, potentially including asymptomatic and mild-symptomatic cases; and a basic reproduction number R_0 of 3.54 (95% credible interval [CrI]: 3.40-3.67) in the early outbreak, much higher than for SARS and MERS[4,5]. We observe that multi-pronged interventions had considerable positive effects on controlling the outbreak, decreasing the reproduction number to 0.28 (0.23-0.33) and by projection reducing the total

infections in Wuhan by 96.0% as of March 8. We furthermore explore the probability of resurgence following lifting of all interventions after 14 days of no ascertained infections, estimating it at 0.32 and 0.06 based on models with 87% and 53% unascertained infections, respectively, highlighting the risk posed by unascertained cases in changing intervention strategies. These results provide important implications for continuing surveillance and interventions to eventually contain COVID-19 outbreaks.

4. 我国献血者 SARS-CoV-2 抗体的流行情况

The prevalence of antibodies to SARS-CoV-2 among blood donors in China

来源：medRxiv

发布时间：2020-07-14

链接：https://www.medrxiv.org/content/10.1101/2020.07.13.20153106v1

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中文摘要：

我国献血者中 SARS-CoV-2 抗体的流行率较低，武汉市也是如此。根据我们的数据，SARS-CoV-2 在武汉捐献者中最早出现的时间应该不早于 2020 年 1 月。由于中国大部分人口在 COVID-19 大流行的早期没有受到感染，因此在疫苗普及之前，仍然需要采取有效的公共卫生措施来阻止病毒的传播。

Abstract:

The prevalence of antibodies to SARS-CoV-2 among blood donors in China was low, even in Wuhan city. According to our data, the earliest emergence of SARS-CoV-2 in Wuhan's donors should not earlier than January, 2020. As most of the population of China remained uninfected during the early wave of COVID-19 pandemic, effective public health measures are still certainly required to block viral spread before a vaccine is widely available.

5. 截至 7 月 17 日国家药监局已批准 44 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 7 月 17 日，国家药监局已批准 44 个新型冠状病毒检测产品，其中新冠病毒核酸检测试剂 23 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_20200717.xlsx”。

6. 基于细胞培养的 SARS-CoV-2 感染力检测以及 COVID-19 疫情期间对解除隔离的安全评估

Cell-based culture of SARS-CoV-2 informs infectivity and safe de-isolation assessments during COVID-19

链接：https://www.medrxiv.org/content/10.1101/2020.07.14.20153981v1

7. 轻度 COVID-19 病患者的胎盘 SARS-CoV-2 的研究

Placental SARS-CoV-2 in a patient with mild COVID-19 disease

链接：https://www.medrxiv.org/content/10.1101/2020.07.11.20149344v1

编译者：王玮

美国的研究者报告一例轻度 COVID-19 孕妇患者，并在其胎盘中发现了 SARS-CoV-2，新生儿的 COVID-19 为阴性。

8. 不同病情严重程度的 COVID-19 患者 B 细胞储备动态及交叉反应的出现

Dynamics of B-cell repertoires and emergence of cross-reactive responses in COVID-19 patients with different disease severity

来源：medRxiv

发布时间：2020-07-15

链接：https://www.medrxiv.org/content/10.1101/2020.07.13.20153114v1

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DOI 或 PUBMED ID：Preprint

编译者：雷颖

中文摘要：

COVID-19 患者表现出不同程度的疾病，从无症状到需要重症监护。虽然已经发现了一些抗 SAR-CoV-2 的单克隆抗体，但我们仍然缺乏对 COVID-19 患者 B 细胞受体(BCR)储备的整体景观的了解。文中作者对在感染期间多个时间点收集的 BCR 储备进行高通量测序，以表征在 19 例不同疾病严重程度的患者中针对 SARS-CoV-2 的 B 细胞反应的统计学和动态学特征。基于有原则的统计方法，他们确定了与不同疾病严重程度相关的 BCR 的差异序列特征。还确定了 34 个在患者中共有的显著扩增的罕见克隆系，作为对 SARS-CoV-2 的特定反应的候选。此外，他们还发现在一些患者中自然出现了对 SARS-CoV 和 SARS-CoV-2 具有交叉反应性的 BCR。总之，文中的结果为开发合理的治疗和疫苗来对抗 COVID-19 提供了重要的见解。

Abstract

COVID-19 patients show varying severity of the disease ranging from asymptomatic to requiring intensive care. Although a number of monoclonal antibodies against SARS-CoV-2 have been identified, we still lack an understanding of the overall landscape of B-cell receptor (BCR) repertoires in COVID-19 patients. Here, we used high-throughput sequencing of BCR repertoires collected over multiple time points during an infection to characterize statistical and dynamical signatures of the B-cell response to SARS-CoV-2 in 19 patients with different disease severities. Based on principled statistical approaches, we determined differential sequence features of BCRs associated with different disease severity. We identified 34 significantly expanded rare clonal lineages shared among patients as candidates for a specific response to SARS-CoV-2. Moreover, we identified natural emergence of a BCR with cross-reactivity to SARS-CoV and SARS-CoV-2 in a number of patients. Overall, our results provide important insights for development of rational therapies and vaccines against COVID-19.

9. 与成人 COVID-19 相比，MIS-C 儿童对 SARS-CoV2 的抗体反应不同

Antibody responses to SARS-CoV2 are distinct in children with MIS-C compared to adults with COVID-19
来源：medRxiv
发布时间：2020-7-14
链接：https://www.medrxiv.org/content/10.1101/2020.07.12.20151068v1
第一作者：Stuart P. Weisberg、Thomas Connors
通讯作者：Matteo Porotto、Donna L. Farber
通讯作者单位：美国纽约哥伦比亚大学
DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：
新型冠状病毒 SARS-CoV-2 引起的 COVID-19 的临床表现与年龄有关。虽然儿童在很大程度上免于遭受严重的呼吸道疾病困扰，但他们可能会出现与川崎病类似的 SARS-CoV-2 相关性多系统炎症综合症（MIS-C）。在这里，研究人员发现与严重 COVID-19 导致成人急性呼吸窘迫综合征（ARDS）的成年人以及从轻度疾病中恢复的成年人相比，MIS-C 儿童的抗体（Ab）反应不同。与 COVID 患者组相比，MIS-C 患者中抗 SARS-CoV-2 特异性抗体的广度和特异性降低；MIS-C 主要产生对 Spike（S）蛋白具有特异性的 IgG Abs，但对核衣壳（N）蛋白没有特异性，而 COVID-19 人群均具有抗 S IgG，IgM 和 IgA Abs 以及抗 N IgG Abs 。此外，与 COVID-19 队列相比，MIS-C 患者的中和活性降低，表明保护性血清学反应降低。这些结果表明，在患有严重疾病的儿童和成人中，感染过程和免疫反应不同，这可能会根据症状和年龄优化治疗方法。
Abstract:
Clinical manifestations of COVID-19 caused by the novel coronavirus SARS-CoV-2 are associated with age. While children are largely spared from severe respiratory disease, they can present with a SARS-CoV-2-associated multisystem inflammatory syndrome (MIS-C) similar to Kawasaki's disease. Here, we show distinct antibody (Ab) responses in children with MIS-C compared to adults with severe COVID-19 causing acute respiratory distress syndrome (ARDS), and those who recovered from mild disease. There was a reduced breadth and specificity of anti-SARS-CoV-2-specific antibodies in MIS-C patients compared to the COVID patient groups; MIS-C predominantly generated IgG Abs specific for the Spike (S) protein but not for the nucleocapsid (N) protein, while both COVID-19 cohorts had anti-S IgG, IgM and IgA Abs, as well as anti-N IgG Abs. Moreover, MIS-C patients had reduced neutralizing activity compared to COVID-19 cohorts, indicating a reduced protective serological response. These results suggest a distinct infection course and immune response in children and adults who develop severe disease, with implications for optimizing treatments based on symptom and age.

10. SARS-CoV-2 抗体依赖性增强的研究进展

A perspective on potential antibody-dependent enhancement of SARS-CoV-2
来源：Nature
发布时间：2020-07-13
链接：https://www.nature.com/articles/s41586-020-2538-8

第一作者：Ann M. Arvin
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DOI 或 PUBMED ID：https://doi.org/10.1038/s41586-020-2538-8
编译者：刘焕珍
中文摘要：
抗体依赖性疾病增强（ADE）的可能性是疫苗和抗体治疗发展的普遍关注点，因为抗体保护的机制在理论上有可能扩大病毒感染或引发免疫病理学。在 SARS-CoV-2 大流行的这一关键时刻，需要仔细审查与疾病 ADE 风险相关的观察结果。目前，无论是通过抗体、T 细胞或固有的宿主反应，临床发现、免疫学检测或生物标记物都无法区分任何严重的病毒感染和免疫增强疾病。体外系统和动物模型不能预测 ADE 发病的风险，部分原因是保护性和潜在的有害抗体介导机制是相同的，设计动物模型取决于了解抗病毒宿主反应如何在人体内变得有害。我们缺乏知识的影响是双重的。首先，迫切需要进行全面的研究，以确定 SARS-CoV-2 保护性免疫的临床相关性。其次，由于无论是疫苗接种还是抗体治疗后，我们都无法可靠地预测疾病的 ADE，因此，随着对 COVID-19 疾病的免疫干预的发展，必须依赖对人类安全性的仔细分析。

Abstract:
The possibility of antibody-dependent enhancement (ADE) of disease is a general concern for the development of vaccines and antibody therapies because the mechanisms that underlie antibody protection have the theoretical potential to amplify viral infections or trigger immunopathology. Observations relevant to the risks of ADE of disease require careful review at this critical point in the SARS-CoV-2 pandemic. At present, no clinical findings, immunologic assays or biomarkers are known to differentiate any severe viral infection from immune-enhanced disease, whether by antibodies, T cells or intrinsic host responses. In vitro systems and animal models do not predict the risk of ADE of disease, in part because protective and potentially detrimental antibody-mediated mechanisms are the same, and designing animal models depends on understanding how antiviral host responses may become harmful in people. The implications of our lack of knowledge are twofold. First, comprehensive studies are urgently needed to define clinical correlates of protective immunity against SARS-CoV-2. Second, since we cannot predict ADE of disease reliably after either vaccination or treatment with antibodies, regardless of what virus is the causative agent, it will be essential to depend on careful analysis of safety in humans as immune interventions for COVID-19 disease move forward.

11. 在 COVID-19,SARS 恢复病人和未感染人群中针对 SARS-CoV-2 的特异性 T 细胞免疫

SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls

简报 5 月 29 日第 27 条报道过该研究的预印本文章。
来源：Nature
发布时间：2020-07-15
链接：https://www.nature.com/articles/s41586-020-2550-z

12. I 型干扰素活性受损与重症 Covid-19 患者炎症反应加重相关

Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients

简报 4 月 24 日第 5 条报道过该研究的预印本文章。

来源：Science

发布时间：2020-07-15

链接：https://science.sciencemag.org/content/early/2020/07/10/science.abc6027

13. 对 COVID-19 患者的深层免疫分析揭示了患者的异质性和独特的免疫类型，及其对治疗干预的意义

Deep immune profiling of COVID-19 patients reveals distinct immunotypes with therapeutic implications

简报 5 月 29 日第 15 条报道过该研究的预印本文章。

来源：Science

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链接：https://science.sciencemag.org/content/early/2020/07/15/science.abc8511?rss=1

14. 低剂量全肺放射治疗 COVID-19 肺炎

Low-Dose Whole-Lung Radiation for COVID-19 Pneumonia

链接：https://www.medrxiv.org/content/10.1101/2020.07.11.20147793v1

15. 扩增 RNA 疫苗的研发

Amplifying RNA Vaccine Development

来源：N Engl J Med

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链接：

https://www.nejm.org/doi/full/10.1056/NEJMcibr2009737?query=featured_coronavirus

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中文摘要：

早期研究表明，DNA 和 RNA 疫苗都能诱导免疫反应。mRNA 疫苗的一个明显优点是，与 DNA 疫苗不同，它们不需要进入细胞核来表达抗原。相反，DNA 疫苗一旦进入细胞核，就会产生许多拷贝的 mRNA 分子，从而导致每个转染细胞产生更多的抗原。因此，人们感兴趣的是自扩增 RNA 疫苗，例如 Beissert 等人描述的疫苗策略，用以提高 mRNA 疫苗表达抗原的产率。自扩增 RNA 疫苗来源于甲型病毒的基因组骨架，其中编码病毒 RNA 复制机制的基因是完整的，但编码病毒结构蛋白的基因被编码疫苗抗原的转基因所取代。自扩增 RNA 疫苗可以质粒 DNA、病毒样 RNA 颗粒和体外转录 RNA 的形式传递，并能引起比 mRNA 更强的免疫应答。基于 DNA 质粒的自扩大 RNA 疫苗结合了更稳定的 DNA 核酸产物的优点，与更高水平的自扩大 RNA 疫苗的抗原表达相结合，在临床前模型中诱导比传统 DNA 疫苗更强的免疫应答。Beissert 等还描述了一种基于两个 RNA 载体的策略：一个保留复制酶编码基因，另一个编码抗原。

随着 Covid-19 大流行的出现，mRNA 疫苗是第一个进入临床试验的疫苗。核酸疫苗现在是解决这场大流行病危机的主要希望。自我扩增 RNA 疫苗，现在是反式扩增 RNA 疫苗，在体内提供扩增和持久生产抗原的能力，加上强大的固有免疫刺激特性，增加了这些能力，并可能提供可能需要的剂量保留（即获得相同的免疫反应与较小剂量的疫苗），以满足全球需求。

Abstract

Early studies showed that both DNA and RNA vaccines induced immune responses. A clear advantage of mRNA vaccines is that, unlike DNA vaccines, they do not need to enter the nucleus to express the antigen. Instead, once inside the nucleus, a DNA vaccine will produce many copies of mRNA molecules, resulting in the production of more antigen per transfected cell. Of interest, then, are self-amplifying RNA vaccines, such as those involved in the strategy described by Beissert et al. to increase the yield of antigen expressed by mRNA vaccines.

Self-amplifying RNA vaccines are derived from the genome backbone of an alphavirus in which the genes encoding the viral RNA replication machinery are intact but those encoding viral structural proteins are replaced with a transgene encoding the vaccine antigen. A self-amplifying RNA vaccine can be delivered in the form of plasmid DNA, viruslike RNA particles, and in vitro transcribed RNA and can elicit substantially stronger immune responses than mRNA. DNA plasmid–based self-amplifying RNA vaccines combine the advantages of a more stable DNA nucleic acid product with greater levels of antigen expression of self-amplifying RNA vaccines to elicit stronger immune responses in preclinical models than conventional DNA vaccines. Beissert et al. describe a strategy that is based on two RNA vectors — one retaining the replicase-encoding gene and the other encoding the antigen.

With the emergence of the Covid-19 pandemic, an mRNA vaccine was the first to enter clinical trials. Nucleic acid vaccines are now a major hope for solving this pandemic crisis. This comes as no surprise. From their earliest conception, nucleic acid vaccines were recognized as a possible solution for a rapid pandemic response. The need for only the sequence of a pathogen in order to generate the vaccine and its simplicity in manufacture have long been recognized as superpowers in nucleic acid vaccines with regard to the delivery of a rapid response to an emerging epidemic. The ability of self-amplifying RNA vaccines, and now trans-amplifying RNA vaccines, to provide amplified and durable production of antigen in vivo, coupled with potent inherent innate immune-stimulating properties, adds to these powers and may provide the dose-sparing (i.e., getting the same immune responses with smaller doses of vaccine) that will probably be needed to meet global demands. We can only hope that their deployment will render the Covid-19 pandemic crisis into a more manageable challenge, saving lives and decreasing morbidity.

16. 全人 IgG 与 SARS-CoV-2 S 蛋白的二价结合揭示了其有效中和的机制

Bivalent binding of a fully human IgG to the SARS-CoV-2 spike proteins reveals mechanisms of potent neutralization

来源：bioRxiv

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DOI 或 PUBMED ID：preprint
编译者：孔娟
中文摘要：
从天然组合抗体文库中可以筛选出不同种类的抗原特异性抗体，这些抗体不同于自然感染的宿主中的抗体。文中研究者从一个高度多样化的天然 Fab 文库中筛选得到 SARS-CoV-2 的中和抗体。抗体 5A6 能够有效阻断 S 蛋白受体结合域(RBD)与 ACE2 的结合，在细胞水平能够有效抑制 SARS-CoV-2 对 Vero E6 细胞的感染，并降低重组人鼻和支气管上皮模型中的病毒复制。5A6 在病毒表面占据较多的表位，并通过与 ACE2 相互作用界面上两个相邻 RBDs 末端的二价结合模式发挥其中和活性，一个在“上”位置，另一个在“下”位置，这解释了其优越的中和能力。此外，5A6 对临床分离的几种 S 蛋白突变株不敏感，包括比较世界范围流行的 D614G 突变。研究结果表明 5A6 可能是 COVID-19 的有效预防和治疗方法。
Abstract:
In vitro antibody selection against pathogens from naïve combinatorial libraries can yield various classes of antigen-specific binders that are distinct from those evolved from natural infection. Also, rapid neutralizing antibody discovery can be made possible by a strategy that selects for those interfering with pathogen and host interaction. Here we report the discovery of antibodies that neutralize SARS-CoV-2, the virus responsible for the COVID-19 pandemic, from a highly diverse naïve human Fab library. Lead antibody 5A6 blocks the receptor binding domain (RBD) of the viral spike from binding to the host receptor angiotensin converting enzyme 2 (ACE2), neutralizes SARS-CoV-2 infection of Vero E6 cells, and reduces viral replication in reconstituted human nasal and bronchial epithelium models. 5A6 has a high occupancy on the viral surface and exerts its neutralization activity via a bivalent binding mode to the tip of two neighbouring RBDs at the ACE2 interaction interface, one in the “up” and the other in the “down” position, explaining its superior neutralization capacity. Furthermore, 5A6 is insensitive to several spike mutations identified in clinical isolates, including the D614G mutant that has become dominant worldwide. Our results suggest that 5A6 could be an effective prophylactic and therapeutic treatment of COVID-19.

17. 针对 SARS-CoV-2 S 蛋白的多种人类单克隆抗体的快速分离和分析

Vanderbilt platform can rapidly ID neutralizing antibodies against SARS-CoV-2
Rapid isolation and profiling of a diverse panel of human monoclonal antibodies targeting the SARS-CoV-2 spike protein
来源：nature medicine
发布时间：2020-07-10
链接：https://www.nature.com/articles/s41591-020-0998-x

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DOI 或 PUBMED ID：https://doi.org/10.1038/s41591-020-0998-x
编译者：孔娟
中文摘要：
抗体是大多数 RNA 病毒免疫的主要决定因素，抗体的发现有望在重大流行病期间减少感染或疾病。新型冠状病毒 (SARS-CoV-2)已经引发了一场全球大流行，迄今已有数百万人感染，数十万人死亡。文中研究者使用了一个快速抗体发现平台来分离数百种抗 SARS-CoV-2 S 蛋白人单克隆抗体。研究者将这些单克隆抗体根据其对 S 蛋白亚结构域的反应性以及对 SARS-CoV 的交叉反应性分为五大类。这些单克隆抗体中有许多能抑制真正的 SARS-CoV-2 的感染，大多数中和单克隆抗体能识别病毒的受体结合域(RBD)。这项工作确定了 SARS-CoV-2 的易受攻击位点，并展示了先进抗体发现平台的高效和稳定性。
Abstract：
Antibodies are a principal determinant of immunity for most RNA viruses and have promise to reduce infection or disease during major epidemics. The novel coronavirus SARS-CoV-2 has caused a global pandemic with millions of infections and hundreds of thousands of deaths to date1,2. In response, we used a rapid antibody discovery platform to isolate hundreds of human monoclonal antibodies (mAbs) against the SARS-CoV-2 spike (S) protein. We stratify these mAbs into five major classes on the basis of their reactivity to subdomains of S protein as well as their cross-reactivity to SARS-CoV. Many of these mAbs inhibit infection of authentic SARS-CoV-2 virus, with most neutralizing mAbs recognizing the receptor-binding domain (RBD) of S. This work defines sites of vulnerability on SARS-CoV-2 S and demonstrates the speed and robustness of advanced antibody discovery platforms.

18. 调节 SARS-CoV-2 的转录环境，作为开发抗病毒化合物的有效方法

Modulating the transcriptional landscape of SARS-CoV-2 as an effective method for developing antiviral compounds
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链接：https://www.biorxiv.org/content/10.1101/2020.07.12.199687v1
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DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：
为了干扰 SARS-CoV-2 的生物学过程，研究人员致力于重建感染诱导的转录反应。利用 SARS-CoV-2 感染细胞的表达模式，在基因表达空间中确定了病毒感染所特定的区域，该区域与基于集成网络的细胞特征库中已知化合物的转录足迹成反比。在这里，研究人员证明了根据其对抗病毒诱导的转录环境的能力，成功鉴定出具有阻断 SARS-CoV-2 复制功效的化合物。发

现这些化合物有效地降低了病毒载量。RNA Seq 分析牵涉到胆固醇生物合成途径的诱导作为抑制的潜在机制，并建议靶向宿主生物学的这一方面可以显著降低 SARS-CoV-2 病毒载量。

Abstract:
To interfere with the biology of SARS-CoV-2, the virus responsible for the COVID-19 pandemic, we focused on restoring the transcriptional response induced by infection. Utilizing expression patterns of SARS-CoV-2-infected cells, we identified a region in gene expression space that was unique to virus infection and inversely proportional to the transcriptional footprint of known compounds characterized in the Library of Integrated Network-based Cellular Signatures. Here we demonstrate the successful identification of compounds that display efficacy in blocking SARS-CoV-2 replication based on their ability to counteract the virus-induced transcriptional landscape. These compounds were found to potently reduce viral load despite having no impact on viral entry or modulation of the host antiviral response in the absence of virus. RNA-Seq profiling implicated the induction of the cholesterol biosynthesis pathway as the underlying mechanism of inhibition and suggested that targeting this aspect of host biology may significantly reduce SARS-CoV-2 viral load.

19. 对速度的需求：在几周内从人类 SARS-CoV-2 样本到有效的保护性抗体

Need for Speed: From Human SARS-CoV-2 Samples to Protective and Efficacious Antibodies in Weeks

来源：Cell

发布时间：2020-07-09

链接：https://www.cell.com/cell/fulltext/S0092-8674(20)30748-0

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DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2020.06.017

编译者：刘焕珍

中文摘要：

SARS-CoV-2 的出现推动了全球范围内以前所未有的速度来研究医学对策。在本期《细胞》杂志上，曹等人从康复捐献者身上鉴定出数千种 SARS-CoV-2 中和抗体。作者提高了我们对冠状病毒刺突糖蛋白免疫的理解，并详细介绍了快速识别和鉴定保护性单克隆抗体的新途径。

Abstract:
The emergence of SARS-CoV-2 has driven a global research effort to identify medical countermeasures at an unprecedented pace. In this issue of Cell, Cao et al. identify thousands of SARS-CoV-2 neutralizing antibodies from convalescent donors. The authors improve our understanding of immunity against the coronavirus spike glycoprotein and detail novel pathways to rapidly identify and characterize protective monoclonal antibodies.

20. 响应 SARS-CoV-2 的共同抗体的结构分析

Structural basis of a shared antibody response to SARS-CoV-2

来源：Science
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链接：https://science.sciencemag.org/content/early/2020/07/10/science.abd2321
第一作者：Meng Yuan
通讯作者：Ian A. Wilson
通讯作者单位：Scripps Institute
DOI：10.1126/science.abd2321
编译：蒋立春
中文摘要：
从分子层面理解响应 SARS-CoV-2 的中和抗体可以加速疫苗设计以及药物开发。作者们分析了 294 个不同的 SARS-CoV-2 的抗体，发现 IGHV3-53 是被最频繁用到的靶向刺突蛋白的受体结合域（RBD）的 IGHV 基因，编码了其中约 10%的抗体。研究者们讲带和不带 Fab CR3022 的两个 IGHV3-53 的中和抗体和靶向刺突蛋白的受体结合域（RBD）进行了共结晶，并得到了 2.33 to 3.20 Å
精度的结构。这些结构显示胚系残基主导了 ACE2 结合位点的识别。IGHV3-53 编码抗体含有 CDR H3 环的异常短变体，但同时允许抗体轻链的多样性。这些 IGHV3-53 抗体只通过了很少的亲和力成熟就获得了高效价，是有设计疫苗的非常有潜力的选择。对这些结构模式以及结合模型的了解可以帮助科学家们设计可以引发类似中和抗体反应的抗原。

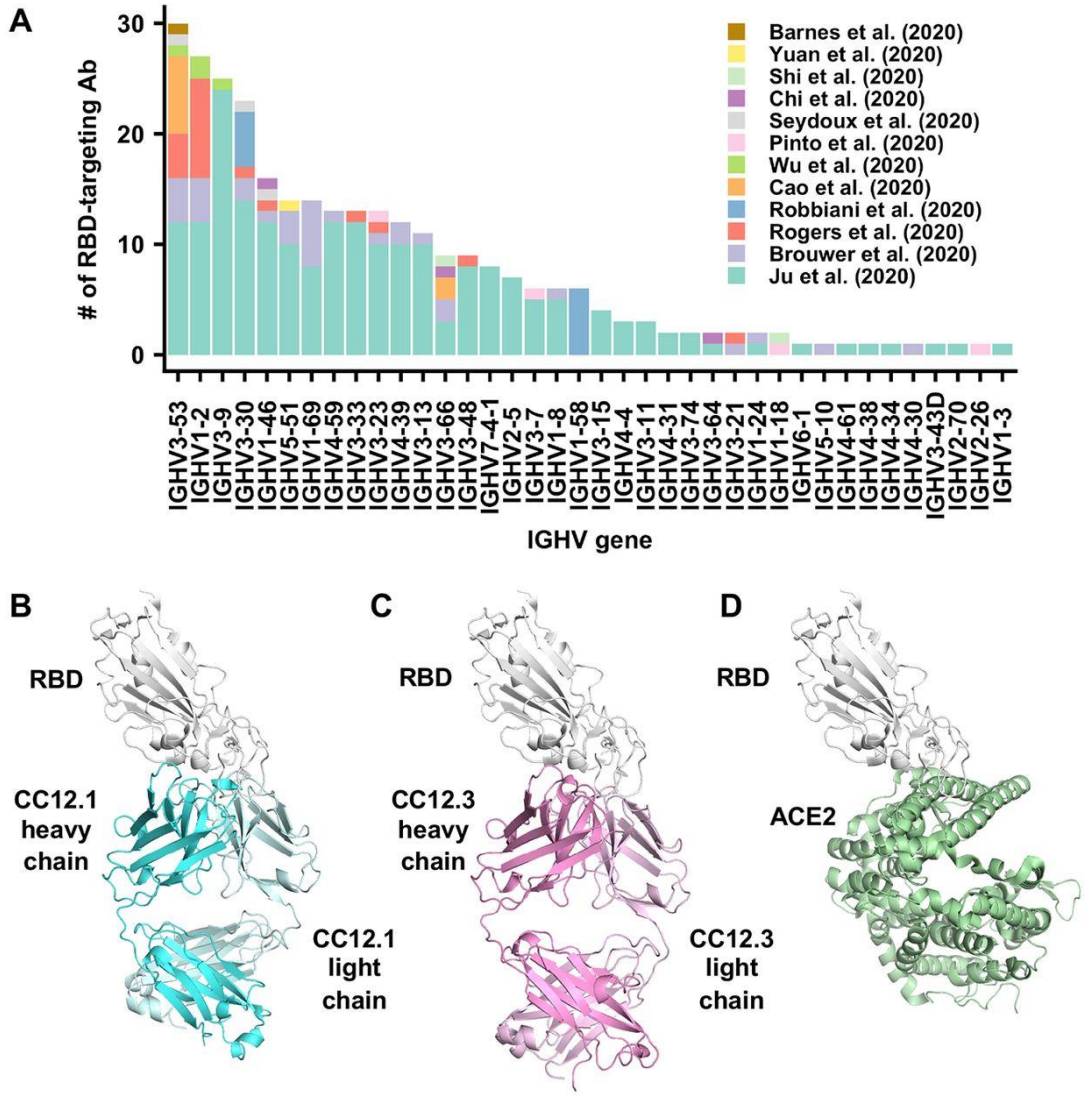

Fig. 1 Structures of two IGHV3-53 antibodies.

(A) The distribution of IGHV gene usage is shown for a total of 294 RBD-targeting antibodies (17–28). (B and C) Crystal structures of (B) CC12.1 in complex with SARS-CoV-2 RBD, (C) CC12.3 with SARS-CoV-2 RBD, and (D) human ACE2 with SARS-CoV-2 RBD (PDB 6MOJ) (12).

Abstract:

Molecular understanding of neutralizing antibody responses to SARS-CoV-2 could accelerate vaccine design and drug discovery. We analyzed 294 anti-SARS-CoV-2 antibodies and found that IGHV3-53 is the most frequently used IGHV gene for targeting the receptor-binding domain (RBD) of the spike protein. Co-crystal structures of two IGHV3-53 neutralizing antibodies with RBD, with or without Fab CR3022, at 2.33 to 3.20 Å resolution revealed that the germline-encoded residues dominate recognition of the ACE2 binding site. This binding mode limits the IGHV3-53 antibodies to short CDR H3 loops, but accommodates light-chain diversity. These IGHV3-53 antibodies show minimal affinity maturation and high potency, which is promising for vaccine design. Knowledge of these structural motifs and

binding mode should facilitate design of antigens that elicit this type of neutralizing response.

21. Gilead 提供了关于研究抗病毒药物瑞德西韦治疗 COVID-19 的更多数据

Gilead Presents Additional Data on Investigational Antiviral Remdesivir for the Treatment of COVID-19

来源：Gilead

发布时间：2020-07-10

链接：https://www.gilead.com/news-and-press/press-room/press-releases/2020/7/gilead-presents-additional-data-on-investigational-antiviral-remdesivir-for-the-treatment-of-covid-19

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中文摘要：

吉列科学公司（Nasdaq:GILD）今天宣布了关于瑞德西韦的更多数据，这是一种治疗 COVID-19 的抗病毒研究药物，增加了关于瑞德西韦治疗结果的现有知识体系。在这项分析中，瑞德西韦与临床恢复的改善和死亡率降低 62%有关，这是一个需要在前瞻性临床试验中证实的重要发现。

分析表明，与标准治疗相比，瑞德西韦治疗可显著改善临床恢复，降低死亡率 62%。对比分析的结果显示，74.4%的瑞德西韦治疗的患者在第 14 天康复，而接受标准护理的患者为 59.0%；康复定义为临床状态的改善（基于 7 点序贯量表）。在分析中，第 14 天接受瑞德西韦治疗的患者的死亡率为 7.6%，而未服用瑞德西韦的患者的死亡率为 12.5%（调整后的比值比为 0.38，95%可信区间为 0.22-0.68，p=0.001）。

在互联网 COVID-19 会议上提出的关于瑞德西韦安全性和有效性的其他新数据特征亚组分析，包括在美国治疗的患者的种族和种族，与改善临床状态相关的全球基线特征，以及同时使用羟氯喹。在体外数据显示氯喹以剂量依赖的方式抑制瑞德西韦的抗病毒活性后，Gilead 对同时使用瑞德西韦和羟氯喹治疗的患者与接受瑞德西韦治疗的患者的临床结果进行了分析同时服用羟氯喹。通过 14 天的中位随访，与未接受羟氯喹治疗的患者相比，同时接受羟氯喹治疗的患者的康复率和可能性更低（57%对 69%，协变量调整 HR[95%CI]0.61[0.45,0.83]，p=0.002）。在 14 天的分析窗口中，同时使用羟氯喹与死亡率增加无关。分析还显示，合并羟氯喹组的患者发生不良事件的比率总体较高。调整基线变量后，3-4 级不良事件的差异显著。

一项对 77 名使用瑞德西韦的儿童患者进行的分析表明，到第 28 天，绝大多数患者的临床状况有所改善，73%的患者出院。到第 28 天，12%的人仍在住院治疗，但仍在环境空气中，4%的人已经死亡。在 39 名基线时需要有创机械通气的患儿中，80%的危重病人康复了；在不需要有创通气的 38 名患儿中，87%康复了。在 86 名接受瑞德西韦治疗的孕妇和产后妇女（中位年龄为 33 岁）中，96%的孕妇和 89%的产后妇女的氧支持水平有所改善。在基线检查时病情较重的孕妇和产后妇女的临床恢复率同样高，分别为 93%和 89%。基线时未接受有创性氧支持的孕妇恢复的中位时间最短（5 天），基线时接受有创通气的孕妇和产后妇女恢复的中位时间相似（13 天）。没有发现新的安全信号；最常见的不良事件是由于潜在的疾病，大多数实验室异常是 1-2 级。

Abstract:
Gilead Sciences, Inc. (Nasdaq: GILD) today announced additional data on remdesivir, an investigational antiviral for the treatment of COVID-19, adding to the available body of knowledge on treatment outcomes with remdesivir. In this analysis, remdesivir was associated with an improvement in clinical recovery and a 62 percent reduction in the risk of mortality compared with standard of care - an important finding that requires confirmation in prospective clinical trials.
The analysis demonstrated that remdesivir treatment was associated with significantly improved clinical recovery and a 62 percent reduction in the risk of mortality compared to standard of care. Findings from the comparative analysis showed that 74.4 percent of remdesivir-treated patients recovered by Day 14 versus 59.0 percent of patients receiving standard of care; recovery was defined as improvement in clinical status based on a 7-point ordinal scale. The mortality rate for patients treated with remdesivir in the analysis was 7.6 percent at Day 14 compared with 12.5 percent among patients not taking remdesivir (adjusted odds ratio 0.38, 95% confidence interval 0.22-0.68, p=0.001).
Additional new data on the safety and efficacy of remdesivir presented at the Virtual COVID-19 Conference feature subgroup analyses, including race and ethnicity of patients treated in the United States, and global baseline characteristics associated with improved clinical status, and concomitant use of hydroxychloroquine. Following the availability of in vitro data demonstrating chloroquine inhibits the antiviral activity of remdesivir in a dose-dependent manner, Gilead conducted an analysis of clinical outcomes with patients who were treated with both remdesivir and hydroxychloroquine concomitantly, versus patients who were treated with remdesivir and who did not receive concomitant hydroxychloroquine. Through a median follow-up of 14 days, the rates and likelihood of recovery were lower in patients who received concomitant hydroxychloroquine compared with patients treated with remdesivir who did not receive hydroxychloroquine (57 percent vs. 69 percent, covariate-adjusted HR [95% CI] 0.61 [0.45, 0.83], p=0.002). Concomitant hydroxychloroquine use was not associated with increased mortality in the 14-day analysis window. The analysis also showed that patients in the concomitant hydroxychloroquine group experienced overall higher rates of adverse events. After adjusting for baseline variables, this difference was significant for Grade 3-4 adverse events.
An analysis of 77 pediatric patients treated with remdesivir in the compassionate use program demonstrated that the vast majority improved in clinical status by Day 28, with 73 percent discharged from the hospital. By Day 28, 12 percent remained hospitalized but on ambient air and four percent had died. Of the 39 pediatric patients who required invasive mechanical ventilation at baseline, 80 percent of these critically ill patients recovered; of the 38 patients not requiring invasive ventilation, 87 percent recovered. Among the 86 pregnant and postpartum women treated with remdesivir in the compassionate use program (median age of 33), 96 percent of pregnant and 89 percent of postpartum women achieved improvement in oxygen support levels. Pregnant and postpartum women who had more

severe illness at baseline achieved similarly high rates of clinical recovery, at 93 percent and 89 percent, respectively. Pregnant women not on invasive oxygen support at baseline had the shortest median time to recovery (5 days), and both pregnant and postpartum women on invasive ventilation at baseline had similar median times to recovery (13 days). No new safety signals were identified; the most common AEs were due to underlying disease and most laboratory abnormalities were Grades 1–2.

22. SARS-CoV-2 mRNA 疫苗初步报道

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

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文章链接：https://www.nejm.org/doi/pdf/10.1056/NEJMoa2022483?articleTools=true

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编译者：雷颖

中文摘要：

背景：严重急性呼吸综合征冠状病毒 2(SARS-CoV-2)于 2019 年底出现，并在全球范围内传播，促使国际社会努力加快疫苗的研制。候选疫苗 mRNA-1273 编码稳定的 SARS-CoV-2 刺突蛋白。

方法：我们进行了临床一期，剂量爬坡开放标签试验，包括 45 名健康成年人，18 至 55 岁，他们接受了两次疫苗接种，间隔 28 天，mRNA-1273 的剂量为 25μg、100μg 或 250μg。每个剂量组有 15 名参与者。

结果：第一次接种后，剂量越高，抗体反应越高（第 29 天酶联免疫吸附试验抗 S-2P 抗体几何平均滴度[GMT]，25μg 组 40,227，100μg 组 109,209，250μg 组 213,526）。第二次接种后，滴度增加（第 57 天 GMT 分别为 299,751、782,719 和 1,192,154）。在第二次接种后，在所有被评估的参与者中，用两种方法检测血清中和活性，其值通常类似于对照组恢复期血清标本分布的上半部分。在超过一半的参与者中发生的不良事件包括疲劳、寒战、头痛、肌痛和注射部位的疼痛。在第二次接种后，全身性不良事件更常见，特别是剂量最高的情况下，250μg 剂量组的三名参与者（21%）报告了一个或多个严重不良事件。

结论：在所有参与者中，mRNA-1273 疫苗诱导了抗 SARS-CoV-2 免疫反应，没有发现限制试验的安全性问题。这些发现支持了这种疫苗的进一步发展。(由国家过敏和传染病研究所及其他机构资助；mRNA-1273 临床试验编号 NCT04283461)。

Abstract

BACKGROUND

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in late 2019 and spread globally, prompting an international effort to accelerate development of a vaccine. The candidate vaccine mRNA-1273 encodes the stabilized prefusion SARS-CoV-2 spike protein.

METHODS

We conducted a phase 1, dose-escalation, open-label trial including 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart,

with mRNA-1273 in a dose of 25 μg, 100 μg, or 250 μg. There were 15 participants in each dose group.
RESULTS
After the first vaccination, antibody responses were higher with higher dose (day 29 enzyme-linked immunosorbent assay anti-S-2P antibody geometric mean titer [GMT], 40,227 in the 25-μg group, 109,209 in the 100-μg group, and 213,526 in the 250-μg group). After the second vaccination, the titers increased (day 57 GMT, 299,751, 782,719, and 1,192,154, respectively). After the second vaccination, serum neutralizing activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens. Solicited adverse events that occurred in more than half the participants included fatigue, chills, headache, myalgia, and pain at the injection site. Systemic adverse events were more common after the second vaccination, particularly with the highest dose, and three participants (21%) in the 250-μg dose group reported one or more severe adverse events.
CONCLUSIONS
The mRNA-1273 vaccine induced anti-SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. These findings support further development of this vaccine. (Funded by the National Institute of Allergy and Infectious Diseases and others; mRNA-1273 ClinicalTrials.gov number, NCT04283461).

23. SARS-CoV-2 用网格蛋白介导的内吞进入细胞

SARS-CoV-2 uses clathrin-mediated endocytosis to gain access into cells
来源：biorxiv
发布时间：2020-07-16
链接：https://www.biorxiv.org/content/10.1101/2020.07.13.201509v2
第一作者：Armin Bayati,
通讯作者：Peter S McPherson
通讯作者单位：McGill University, Canada
编译：蒋立春
中文摘要：
SARS-CoV-2 用刺突糖蛋白和细胞表面进行接触发动病毒的外膜和细胞膜的融合，使得病毒 RNA 可以转到细胞质。研究者们用刺突糖蛋白和装载有假病毒的刺突糖蛋白来确定 SARS-CoV-2 在结合到质膜后怎么快速地进行内吞。通过化学抑制剂以及功能缺失的方法，研究者们展示了 SARS-CoV-2 通过网格蛋白介导的内吞进入到细胞。这些实验结果显示 SARS-CoV-2 可能是先通过和细胞质膜接触，然后很快地进入到内吞系统的腔内。这强烈提示病毒膜的融合发生在内含体的管腔膜。这个发现对于开发降低或者抑制感染的化学药物有重要启示作用。
Abstract:
With more than 13 million cases and 570,000 deaths, and with the resulting social upheaval, the COVID-19 pandemic presents one of the greatest challenges ever to the scientific community. It is thus vital to fully understand the biology of

SARS-CoV-2, the causative agent of COVID-19. SARS-CoV-2 uses the spike glycoprotein to interact with the cell surface and to drive fusion of the viral membrane with cellular membranes, thus allowing transfer of viral RNA to the cytosol. Here we use purified spike glycoprotein protein and lentivirus pseudotyped with spike glycoprotein to determine that SARS-CoV-2 undergoes rapid endocytosis following binding to the plasma membrane. Using chemical inhibitors and loss of function approaches, we demonstrate that this cellular entry is through clathrin-mediated endocytosis. Thus, it appears that SARS-CoV-2 first engages the plasma membrane, then rapidly enters the lumen of the endosomal system, strongly suggesting that fusion of the viral membrane occurs with the lumenal membrane of endosomes. This discovery has important implications for the development of chemical probes to reduce or block infection.

24. SARS-CoV-2 的感染依赖于细胞表面的硫酸肝素和 ACE2

SARS-CoV-2 Infection Depends on Cellular Heparan Sulfate and ACE2

来源：biorxiv

发布时间：2020-07-14

链接：https://www.biorxiv.org/content/10.1101/2020.07.14.201616v1

第一作者：Thomas Mandel Clausen

通讯作者：Jeffrey D.Esko

通讯作者单位：UCLA

编译：蒋立春

中文摘要：

这个研究表明 SARS-CoV-2 的刺突蛋白通过其受体结合域和细胞表面的硫酸肝素和 ACE2 相互作用。分子对接研究提示在 ACE2 的结合域边上有一个可能的肝素/硫酸肝素结合位点。在体外实验种，ACE2 和肝素是互相独立地结合到刺突蛋白的细外域。用肝素作为模板可以产生一个三聚复合体。和纯化但阿比组会实验的结果想法，刺突蛋白结合到细胞上的硫酸肝素和 ACE2 是相互依赖的。普通肝素、非抗凝肝素，肝素裂解酶处理，纯化的肺部硫酸肝素可以高效地阻碍刺突蛋白的结合，装载有刺突蛋白的假病毒以及 SARS-CoV-2 病毒感染细胞。这些发现支持 SARS-CoV-2 的病毒的结合和感染过程中包括了和硫酸肝素以及 ACE2 一起形成一个复合物的模型。通过调控硫酸肝素或者使用外源肝素来抑制病毒的结合可能为开发新的抗病毒方案提供了契机。

Abstract:

We show that SARS-CoV-2 spike protein interacts with cell surface heparan sulfate and angiotensin converting enzyme 2 (ACE2) through its Receptor Binding Domain. Docking studies suggest a putative heparin/heparan sulfate-binding site adjacent to the domain that binds to ACE2. In vitro, binding of ACE2 and heparin to spike protein ectodomains occurs independently and a ternary complex can be generated using heparin as a template. Contrary to studies with purified components, spike protein binding to heparan sulfate and ACE2 on cells occurs codependently. Unfractionated heparin, non-anticoagulant heparin, treatment with heparin lyases, and purified lung heparan sulfate potently block spike protein binding and infection by spike protein-pseudotyped virus and SARS-CoV-2 virus. These findings

support a model for SARS-CoV-2 infection in which viral attachment and infection involves formation of a complex between heparan sulfate and ACE2. Manipulation of heparan sulfate or inhibition of viral adhesion by exogenous heparin may represent new therapeutic opportunities.

25. 被 SARS-CoV-2 感染细胞形成合胞体

Syncytia formation by SARS-CoV-2 infected cells

链接：https://www.biorxiv.org/content/10.1101/2020.07.14.202028v1

26. SARS-CoV-2 刺突蛋白 S1 蛋白跨越血脑屏障：动力学、分布、机制、以及 APoE 基因型、性别和炎症反应对 S1 蛋白跨血脑屏障的影响

The S1 protein of SARS-CoV-2 crosses the blood-brain barrier: Kinetics, distribution, mechanisms, and influence of ApoE genotype, sex, and inflammation

链接:https://www.biorxiv.org/content/10.1101/2020.07.15.205229v1

27. SARS-CoV-2 spike ectodomain 蛋白对低温灵敏

Cold sensitivity of the SARS-CoV-2 spike ectodomain

来源：bioRxiv

发布时间：2020-07-12

链接： https://www.biorxiv.org/content/10.1101/2020.07.12.199588v1

第一作者：Robert J Edwards

通讯作者：Robert J Edwards；Priyamvada Acharya

通讯作者单位：杜克大学

DOI 或 PUBMED ID：Preprint

编译者：杨欢

中文简介：

在这篇短文中，作者报道了稳定的 SARS-CoV-2 spike ectodomain construct 对低温敏感。SARS-CoV-2 spike ectodomain construct 目前广泛用于免疫原设计中。当在 22 或 37 度下保存 1 周时，刺突蛋白在负染色电子显微镜（negative stain electron microscopy）下显示出排列整齐的三聚体峰， 但在 4 度下储存可将刺突蛋白三聚体的比例降低至<10%，同时还降低了蛋白的热稳定性，增强了 ACE-2 受体结合位点的暴露。在 37 度下短暂孵育后，冷藏样品可恢复形态良好的构象。

Highlights：

• SARS-CoV-2 S ectodomain construct, widely used for vaccine studies, exhibits cold sensitivity.

• Negative stain electron microscopy shows disintegration of spike structure upon storage at 4 ° C.

• Differential scanning calorimetry measurements confirm destabilization by cold.

• Cold storage alters antigenicity of SARS-CoV-2 spike.

• Brief incubation at 37 ° C restored spike integrity after cold-storage.

28. 利用 1051 名 COVID-19 患者的数据构建出 SARS-CoV-2 Spike 蛋白的线性表位特征全貌

Linear epitope landscape of SARS-CoV-2 Spike protein constructed from 1,051 COVID-19 patients

来源：medRxiv
发布时间：2020-07-14
链接：https://www.medrxiv.org/content/10.1101/2020.07.13.20152587v1
第一作者：Yang Li, Ming-liang Ma, Qing Lei, Feng Wang
通讯作者：Xionglin Fan[2], Sheng-ce Tao[1]
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1 Shanghai Center for Systems Biomedicine, Key Laboratory of Systems Biomedicine (Ministry of Education), Shanghai Jiao Tong University, Shanghai, China
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DOI 或 PUBMED ID：
编译者：宋珂
中文摘要：

用于治疗和预防 COVID-19 的中和型抗体和疫苗的需求十分迫切。为了能够精准开发抗体和疫苗，关键的一点是使用系统性的方法，了解 SARS-CoV-2 Spike 蛋白中的哪一部分具有高度的免疫原性。本文中，作者使用多肽芯片分析了 1051 名 COVID-19 患者血清中的 IgG 反应，建立了 Spike 蛋白的线性表位特征全貌。作者发现了两个线性表位丰富的区域，一个是 CTD 区域，另一个是靠近 S2' 切割位点和融合肽的区域。出乎意料的是，作者发现 RBD 区域的线性表位却比较少。作者共确定了 19 条具有免疫原性的多肽，其中 3 条来自 RBD 区域的多肽的免疫原性中等，另外 16 条来自 Spike 蛋白其他区域的多肽的免疫原性则比较强。这些多肽可以作为系统性地精准开发 COVID-19 抗体和疫苗的基础。

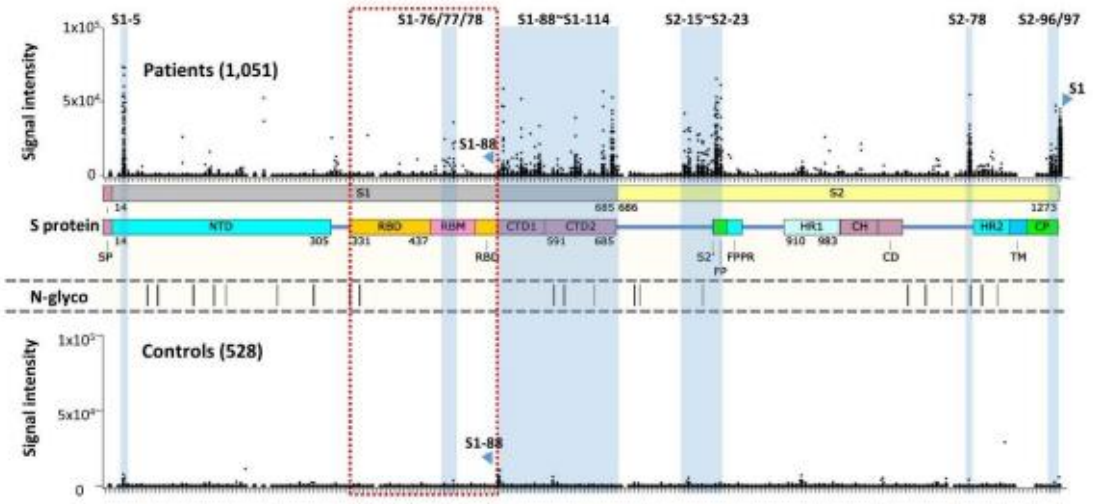

Figure 1. The IgG linear epitope landscape of SARS-CoV-2 Spike protein. The signal intensities of 1,051 COVID-19 sera against 197 peptides were obtained by using the peptide microarray. The peptides are listed in X-axis and aligned to the corresponding locations on Spike protein. As a control, the signal intensities of S1 protein were also presented. The missing spots are peptides either could not be synthesized or failed for BSA conjugation (see **Table S2** for details). A cohort of 528 controls sera were also analyzed on the microarray. In addition, the known N-glycosylation sites (N-glyco) were aligned with Spike protein. The peptides or regions with significant binding were marked blue. Peptide S1-88 was specifically labeled because significant bindings were also observed for the controls. SP: signaling peptide; NTD: N-terminal domain; RBD: receptor biding domain; RBM: receptor binding motif; CTD1:

C-terminal domain 1; CTD2: C-terminal domain 2; S2': protease cleavage site; FP: fusion peptide; FPPR: fusion peptide proximal region; HR1: heptad repeat 1; HR2: heptad repeat 2; CH: center helix; CD: connector domain; TM: trans-membrane; CP: cytoplasmic.

Abstract:

Neutralization antibodies and vaccines for treating COVID-19 are desperately needed. For precise development of antibodies and vaccines, the key is to understand which part of SARS-CoV-2 Spike protein is highly immunogenic on a systematic way. We generate a linear epitope landscape of Spike protein by analyzing serum IgG response of 1,051 COVID-19 patients with a peptide microarray. We reveal two regions that rich of linear epitopes, i.e., CTD and a region close to the S2' cleavage site and fusion peptide. Unexpectedly, we find RBD is lack of linear epitope. Besides 3 moderate immunogenic peptides from RBD, 16 highly immunogenic peptides from other regions of Spike protein are determined. These peptides could serve as the base for precise development of antibodies and vaccines for COVID-19 on a systematic level.

29. SARS-CoV-2 RNA 在感染细胞中的直接 RNA 与蛋白质相互作用图谱

A direct RNA-protein interaction atlas of the SARS-CoV-2 RNA in infected human cells

来源：biorxiv

发布时间：2020-07-15

链接：https://www.biorxiv.org/content/10.1101/2020.07.15.204404v1

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DOI 或 PUBMED ID：Preprint

编译者：王玮

中文摘要：

SARS-CoV-2 感染对全球人类健康构成了威胁，也是前所未有的研究挑战。其中最紧迫的任务是详细了解分子间相互作用，这些相互作用促进病毒复制或有助于受感染细胞的宿主防御机制。SARS-CoV-2 细胞因子协作进行病毒翻译和基因组复制，但直接与病毒 RNA 相互作用的宿主细胞蛋白质组的综合图谱尚未阐明。该研究使用 RNA 反义纯化和质谱（RAP-MS）来获得一个无偏的定量图谱，该图谱描述了被感染的人类细胞中直接与 SARS-CoV-2 RNA 结合的蛋白质组。并发现了冠状病毒复制所需的已知宿主因子、RNA 代谢调节因子和宿主防御途径，以及 SARS-CoV-2 直接结合物中的数十个潜在药物靶点。该研究进一步整合 SARS-CoV-2 RNA 相互作用组与病毒感染诱导的蛋白质组动力学，将相互作用蛋白组与 SARS-CoV-2 感染的生物学联系起来。RAP-MS 验证发现 CNBP 是促炎细胞因子的调节因子，直接与 SARS-CoV-2 RNA 结合。证明干扰素诱导的蛋白 RYDEN 抑制 SARS-CoV-2 核糖体移码，并证明抑制 SARS-CoV-2 结合蛋白能够操纵病毒复制。SARS-CoV-2 RNA 相互作用组为研究 SARS-CoV-2 感染提供了一个前所未有的分子视角，可以系统地分析宿主依赖因子和宿主防御策略，这是设计新的治疗策略的重要前提。

Abstract:
SARS-CoV-2 infections pose a global threat to human health and an unprecedented research challenge. Among the most urgent tasks is obtaining a detailed understanding of the molecular interactions that facilitate viral replication or contribute to host defense mechanisms in infected cells. While SARS-CoV-2 co-opts cellular factors for viral translation and genome replication, a comprehensive map of the host cell proteome in direct contact with viral RNA has not been elucidated. Here, we use RNA antisense purification and mass spectrometry (RAP-MS) to obtain an unbiased and quantitative picture of the human proteome that directly binds the SARS-CoV-2 RNA in infected human cells. We discover known host factors required for coronavirus replication, regulators of RNA metabolism and host defense pathways, along with dozens of potential drug targets among direct SARS-CoV-2 binders. We further integrate the SARS-CoV-2 RNA interactome with proteome dynamics induced by viral infection, linking interactome proteins to the emerging biology of SARS-CoV-2 infections. Validating RAP-MS, we show that CNBP, a regulator of proinflammatory cytokines, directly engages the SARS-CoV-2 RNA. Supporting the functional relevance of identified interactors, we show that the interferon-induced protein RYDEN suppresses SARS-CoV-2 ribosomal frameshifting and demonstrate that inhibition of SARS-CoV-2-bound proteins is sufficient to manipulate viral replication. The SARS-CoV-2 RNA interactome provides an unprecedented molecular perspective on SARS-CoV-2 infections and enables the systematic dissection of host dependency factors and host defense strategies, a crucial prerequisite for designing novel therapeutic strategies.

30. 单细胞分析揭示 COVID-19 患者肺前体细胞的功能

Single-cell analysis reveals the function of lung progenitor cells in COVID-19 patients

链接：https://www.biorxiv.org/content/10.1101/2020.07.13.200188v1.full.pdf

编译者：王玮

来自上海东方医院的研究者通过对 COVID-19 患者支气管肺泡灌洗液（BALF）的单细胞 RNA 测序（scRNA-Seq）揭示了不同的肺前体细胞如何协同工作来预防和补充严重 SARS-CoV-2 感染后肺泡丢失的机制。

31. 重症 COVID-19 患者中抗 Anti-SARS-CoV-2 IgG 促进巨噬细胞的过度炎症反应

Anti-SARS-CoV-2 IgG from severely ill COVID-19 patients promotes macrophage hyper-inflammatory responses

链接：https://www.biorxiv.org/content/10.1101/2020.07.13.190140v1

编译者：孔娟

研究表示来自 COVID-19 重症患者血清的抗 S 蛋白抗体诱导人类巨噬细胞的超炎症反应，随后破坏肺内皮屏障完整性并诱导微血管血栓形成。这种过度炎症能力与抗体 Fc 尾部的糖基化变化有关。此外，通过使用福他替尼的活性成分可以在体外特异性地抑制抗 S 蛋白抗体诱导的过度炎症反应。

32. 生物医药公司关于 COVID-19 的最新进展

Biopharma Update on the Novel Coronavirus: July 13

来源:Biospace

发布时间：2020-07-13

链接：https://www.biospace.com/article/biopharma-update-on-the-novel-coronavirus-july-13/

美国 FDA 已经批准了 173 个紧急授权使用的检测，包括 144 个分子检测，27 个抗体检测和 2 个抗原检测。

FDA 为 pfizer 和 biontech 的两个 mrna 疫苗候选开通了快速审批通道。

Equilium 宣布一项在印度进行的临床试验中针对 CD6-ALCAM 通路的 itolizumab 单克隆抗体药物可以显著降低住院病人的死亡率.

ExeGi Pharma 宣布了一项采用细菌治疗 COVID-19 的临床试验结果。在这组 70 个病人的试验中，高剂量的由 8 个细菌株组成的细菌治疗可以有效缓解 COVID-19。

Bellerophon 制药公司关于内吸一氧化氮治疗 COVID-19 的三期临床试验完成了第一例病人的给药。

Avacta 集团开始了和 Integumen 公司的合作，评估最近研发出来的可以结合 SARS-CoV-2 刺突蛋白的 Affimer 试剂检测废水中 SARS-CoV-2 的能力，为 COVID-19 的爆发提供每个局部地区的实时预警。

君实生物完成了 SARS-CoV-2 中和性单抗的临床一期病人招募。同时君实会启动一项该抗体在高风险人群中的临床试验以检测该抗体的预防作用。

Altimmune 公司和阿拉巴马大学宣布鼻腔给药的 COVID-19 疫苗 AdCOVID 在临床前试验中取得阳性结果。