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. 2021 年 1 月 28 日疫情

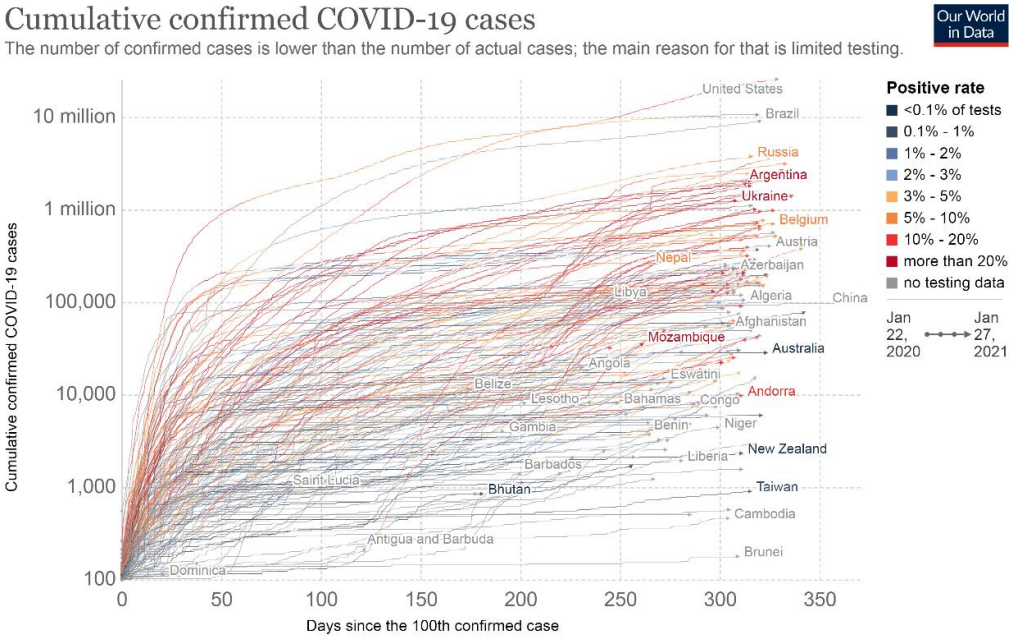
数据来源：WHO

发布时间：2021 年 1 月 28 日北京时间下午 4 点

链接：https://covid19.who.int/

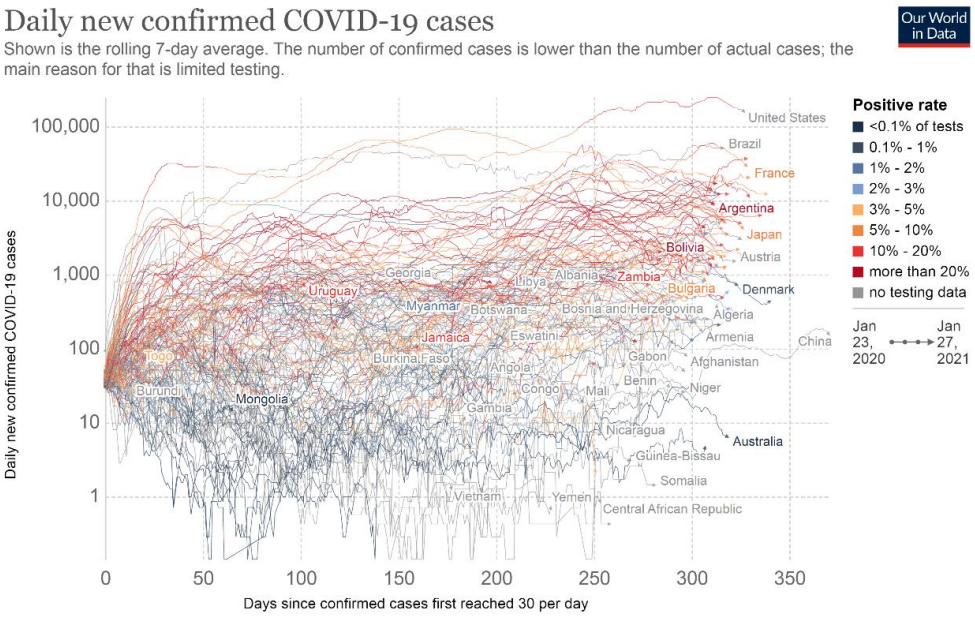
根据 WHO 提供的数据，2021 年 1 月 28 日全球累计确诊新型冠状病毒病人 **100,455,529** 例，当日新增确诊 **562,001** 例，累计死亡 **2,166,440** 例，当日新增死亡 **16,061**。

中国累计确诊 100,548 例，累计死亡 4,818 例，当日新增确诊 117 例，新增死亡 2 例。



Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 29 January, 00:03 (London time), Official data collated by Our World in Data – Last updated 27 January, 13:40 (London time)
CC BY

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



Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 29 January, 00:03 (London time), Official data collated by Our World in Data – Last updated 27 January, 13:40 (London time)
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重点国家每日新增确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）

全国新型冠状病毒肺炎新增确诊病例分布图（1 月 28 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 我国河北疫情时间序列图

发布时间：2021-01-29

来源：https://news.qq.com/zt2020/page/feiyan.htm#/area?pool=hebei

3. 礼来和 AbCellera 合作开发的 COVID-19 单克隆抗体可以在不依赖集中输液中心的情况下进行大规模静脉注射

Lilly, AbCellera mAb could enable broad deployment for COVID without taxing infusion centers

来源：biocentury

发布时间：2021-01-22

链接：https://www.biocentury.com/article/633653

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编译者：刘焕珍

中文摘要：

一项流动的 III 期预防研究显示，来自 AbCellera 和 Lilly 的 COVID-19 单克隆抗体 Bamlanimab 减少了疗养院居民和工作人员的症状。这研究结果强调可以采用不依赖集中输液中心的情况下进行大规模部署静脉注射单抗的策略。该试验将休闲车改装成移动式研究单位，并使用拖车将所有临床试验用品运送给志愿者。Bamlanimab 应该保持对源自英国的新菌株 501Y.V1 的完全活性，但是它对南非 501Y.V2 变种的效力可能较低。在接受预防性 Bamlanimab 单抗治疗的居民中，没有 COVID 归因的死亡，而安慰剂组有 4 例死亡。针对 501Y V1 变种，发言人说，Bamlanimab 在含有突变的蛋白的假病毒检测系统中 “保持了完全中和能力”，该突变与英国变异体的快速传播有关。礼来并没有透露它正在采取什么措施来解决逃逸突变。

Abstract:

A mobile Phase III prevention study showing a COVID-19 mAb from AbCellera and Lilly reduced symptomatic cases in nursing home residents and staff highlights a strategy that could enable mass deployment without relying on centralized infusion centers. The trial converted recreational vehicles into mobile research units and used bamlanivimab should maintain full activity against the new strain 501Y.V1 originating in the U.K., but that it may be less potent against the South African variant 501Y.V2. There were no COVID-attributed deaths among residents who received prophylactic bamlanivimab versus four in the placebo group. Against the 501Y.V1 variant, the spokesperson said bamlanivimab “maintains full neutralization” in a pseudovirus assay using spike proteins bearing mutations implicated in the rapid spread of the U.K. variant. Lilly did not disclose what, if any, steps it is taking to address escape mutations.

4. 根据年龄和血清状态制定的模型化新冠肺炎疫苗接种优先化策略

Model-informed COVID-19 vaccine prioritization strategies by age and serostatus

来源：Science

发布时间：2021-01-21

链接：https://science.sciencemag.org/content/early/2021/01/21/science.abe6959

第一作者：Kate M. Bubar

通讯作者：Kate M. Bubar

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DOI: 10.1126/science.abe6959

编译者：孔娟

中文摘要：

SARS-CoV-2 疫苗的初始供应有限，这就提出了如何对可用剂量进行优先排序的问题。文中研究者使用了一种基于模型的方法来量化新冠肺炎疫苗优先策略对累积发病率、死亡率和寿命损失的影响。文中比较了五种年龄分层的优先策略。优先接种 20-49 岁成人能够高效阻断传播，最大程度地降低了累积发病率。但在大多数情况下，当优先接种 60 岁以上成人的疫苗时，死亡率和丧失的生命年数可以降至最低。使用个体水平血清学检测将剂量重新定向至血清阴性个体提高了每种剂量的边际影响，同时有可能减少 COVID-19 影响中存在的不平等现象。虽然最大影响优先级策略在各国、传播率、疫苗接种推广速度以及对自然获得的免疫力的估计方面基本一致，该框架可用于比较不同背景下优先化战略的影响。

Abstract:

Limited initial supply of SARS-CoV-2 vaccine raises the question of how to prioritize available doses. Here, we used a mathematical model to compare five age-stratified prioritization strategies. A highly effective transmission-blocking vaccine prioritized to adults ages 20-49 years minimized cumulative incidence, but mortality and years of life lost were minimized in most scenarios when the vaccine was prioritized to adults over 60 years old. Use of individual-level serological tests to redirect doses to seronegative individuals improved the marginal impact of each dose while potentially reducing existing inequities in COVID-19 impact. While maximum impact prioritization strategies were broadly consistent across countries, transmission rates, vaccination rollout speeds, and estimates of naturally acquired immunity, this framework can be used to compare impacts of prioritization strategies across contexts.

5. 1 月 22 日快迅：CDC 更新了有关 COVID 疫苗剂量的建议；以及更多疫苗相关信息

Jan. 22 Quick Takes: CDC updates advice on COVID vaccine dosing; plus more vaccines for COVAX

来源：Biocentury

发布时间：2021-1-23

链接：https://www.biocentury.com/article/633679

作者：DANIELLE GOLOVIN 和 JEFF CRANMER（执行编辑）

编译者：雷颖

中文摘要：

美国疾病预防控制中心说，第二剂 CovID-19 疫苗是由 Moderna Inc.（NASDAQ：MRNA）以及合作伙伴 BioNTech SE（NASDAQ：BNTX）和 Pfizer Inc.（NYSE：PFE）共同使用，可以在第一剂给药后的六周内使用。据 CDC 称，先前的建议是辉瑞和 BioNTech 的 Comirnaty 为三周，而 Moderna 产品为四周。该机构还指出，mRNA 疫苗不能彼此互换，也不能与其他 COVID-19 疫苗互换。另外，BioNTech 和 辉瑞公司将以非盈利的价格向 COVAX 提供多达 4000 万剂的 Comirnaty 剂量。首批交付产品将于本季度交付给 COVAX，这是一项全球合作伙伴关系，旨在使至少 20％的中低收入国家人口能够获得 COVID-19 疫苗。

Baseclick GmbH 使用来自加利福尼亚太平洋生物科学公司（NASDAQ：PACB）的测序方法，开发了用于 SARS-CoV-2 的 Click Tech 单株突变扫描试剂盒，以鉴定病毒基因组中与传染性、疾病进展和免疫原性相关的突变。该方法可以确定可能成为新的优势株的病毒群体中的小突变，并跟踪整个病程中 COVID-19 患者中的所有 SARS-CoV-2 突变。

Abstract

CDC said the second dose of COVID-19 vaccines from Moderna Inc. (NASDAQ:MRNA)

and partners BioNTech SE (NASDAQ:BNTX) and Pfizer Inc. (NYSE:PFE) can be administered up to six weeks after the first dose. The prior recommendation had been three weeks for Comirnaty from Pfizer and BioNTech and four weeks for the Moderna product, according to CDC. The agency also noted that the mRNA vaccines are not interchangeable with each other or with other COVID-19 vaccines.

Separately, BioNTech and Pfizer will supply COVAX with up to 40 million doses this year of Comirnaty at a not-for-profit price. The first deliveries are due this quarter to COVAX, a global partnership that aims to make it possible for at least 20% of the population of low- and middle-income countries to have access to COVID-19 vaccines.

Using a sequencing method from Pacific Biosciences of California Inc. (NASDAQ:PACB), baseclick GmbH developed its Click Tech Single Strain Mutation Mapping Kit for SARS-CoV-2 to identify mutations in the virus' genome section responsible for infectivity, disease progression and immunogenicity. The method can determine minor occurring mutations in virus populations that may become new dominant strains, as well as track all SARS-CoV-2 mutations within a COVID-19 patient over the course of the disease.

6. mRNA 疫苗诱导 SARS-CoV-2 抗体及传播中的变异

mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants

来源：bioRxiv

发布时间：2021-1-19

链接：https://www.biorxiv.org/content/10.1101/2021.01.15.426911v1

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编译者：张鹏伟

中文摘要：

在这里，我们报告了 20 名接受 Moderna（mRNA-1273）或 Pfizer-BioNTech（BNT162b2）疫苗的志愿者的抗体和记忆 B 细胞反应。与先前的报道一致，在第二次疫苗注射后 8 周，志愿者表现出高水平的 IgM 和 IgG 抗 SARS-CoV-2 spike 蛋白、受体结合域（RBD）结合滴度。此外，血浆中和活性和 RBD 特异性记忆 B 细胞的相对数量与自然感染后恢复的个体相当。然而，对编码 E484K 或 N501Y 或 K417N:E484K:N501Y 组合的 SARS-CoV-2 变异体的活性降低了一个小但显著的幅度。与这些发现一致，疫苗诱导的单克隆抗体（mab）能有效地中和 SARS-CoV-2，靶向许多不同的 RBD 表位，与从感染供体分离的 mab 相同。与 S 三聚体复合的单克隆抗体的结构分析表明，疫苗和病毒编码的 S 采用相似的构象诱导等效的抗 RBD 抗体。然而，在 17 种最有效的单抗中，有 14 种单抗的中和作用被 K417N、E484K 或 N501Y 突变减少或消除。值得注意的是，当重组水泡性口炎病毒（rVSV）/SARS-CoV-2s 在疫苗诱导的单克隆抗体存在下培养时，选择了相同的突变。综上所述，这些结果表明，临床使用的单克隆抗体应针对新出现的变异进行检测，并且可能需要定期更新 mRNA 疫苗，以避免潜在的临床疗效损失。

Abstract:

To date severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has infected nearly 100 million individuals resulting in over two million deaths. Many vaccines are being deployed to prevent coronavirus disease-2019 (COVID-19) including two novel mRNA-based vaccines. These vaccines elicit neutralizing antibodies and appear to be safe and effective, but the precise nature of the elicited antibodies is not known. Here we report on the antibody and memory B cell responses in a cohort of 20 volunteers who received either the Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines. Consistent with prior reports, 8 weeks after the second vaccine injection volunteers showed high levels of IgM, and IgG anti-SARS-CoV-2 spike protein (S), receptor binding domain (RBD) binding titers. Moreover, the plasma neutralizing activity, and the relative numbers of RBD-specific memory B cells were equivalent to individuals who recovered from natural infection. However, activity against SARS-CoV-2 variants encoding E484K or N501Y or the K417N:E484K:N501Y combination was reduced by a small but significant margin. Consistent with these findings, vaccine-elicited monoclonal antibodies (mAbs) potently neutralize SARS-CoV-2, targeting a number of different RBD epitopes epitopes in common with mAbs isolated from infected donors. Structural analyses of mAbs complexed with S trimer suggest that vaccine- and virus-encoded S adopts similar conformations to induce equivalent anti-RBD antibodies. However, neutralization by 14 of the 17 most potent mAbs tested was reduced or abolished by either K417N, or E484K, or N501Y mutations. Notably, the same mutations were selected when recombinant vesicular stomatitis virus (rVSV)/SARS-CoV-2 S was cultured in the presence of the vaccine elicited mAbs. Taken together the results suggest that the monoclonal antibodies in clinical use should be tested against newly arising variants, and that mRNA vaccines may need to be updated periodically to avoid potential loss of clinical efficacy.

7. 新冠疫苗 mRNA-1273 可诱导针对 SARS-CoV-2 病毒变异株 spike 突变体的中和性抗体

mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants

来源：BioRxiv

发布时间：2021-01-18

链接：https://www.biorxiv.org/content/10.1101/2021.01.25.427948v1

第一作者：Kai Wu

通讯作者：Darin K.Edwards

通讯作者单位：ModernaTX,Inc.

DOI 或 PUBMED ID：https://doi.org/10.1101/2021.01.25.427948

编译者：姜连连

中文摘要：

引起严重呼吸道疾病的新冠病毒肆虐全球，已导致全世界超过 200 万人死亡。Moderna 的 mRNA 疫苗在III期临床取得约 94%的有效保护性且获得紧急使用授权。近来，英国(B.1.1.7)和南非(B.1.351)流行的 SARS-CoV-2 病毒变异株在 spike 蛋白上出现突变，导致在假病毒中和实验中康复病人血清对之中和性较低并对特定的单抗无结合性。因此，用水疱型口炎病毒和慢病毒假病毒表达几株 spike 变异蛋白对 mRNA-1273 疫苗免疫的人类或灵长类血清进

行中和能力分析。所有检测血清对英国分离株的中和效价没有显著影响，但对南非流行的变异株的中和效价降低。临床受试者的血清用口炎病毒表达 D614G spike 蛋白检测中和滴度为 1/1852。口炎水泡假病毒表达的 K417N-E484K-N501Y-D614G 突变 spike 蛋白和表达全部突变的南非株，与 D614G 突变 spike 蛋白中和效价相比，受试者血清对两种 spike 蛋白突变中和效价分别降低 2.7 和 6.4 倍。最重要的是受试者血清对口炎病毒表达的南非突变体的中和效价都为 1/290，具备完全中和病毒能力。同样地，30ug 和 100ug 的 mRNA-1273 免疫的灵长动物血清对假病毒的中和效价分别为 1/323 和 1/404，与单点突变体相比，南非突变株的中和效价降低了 5-10 倍。英国株和南非株均有特异性单点突变，且对假病毒检测的中和效价影响相似。尽管在观察病例中，免疫后血清对南非变异株的中和效价均为 1/300。总之，以上数据说明 mRNA-1273 疫苗免疫后的受试者虽然血清中和效价降低但仍能显著中和南非变异株。

Abstract:

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the causative infection of a global pandemic that has led to more than 2 million deaths worldwide. The Moderna mRNA-1273 vaccine has demonstrated ~94% efficacy in a Phase 3 study and has been approved under Emergency Use Authorization. The emergence of SARS-CoV-2 variants with mutations in the spike protein, most recently circulating isolates from the United Kingdom (B.1.1.7)and Republic of South Africa(B.1.351), has led to lower neutralization from convalescent serum by pseudovirus neutralization assays and resistance to certain monoclonal antibodies. Here, using two orthogonal VSV and lentivirus PsVN assays expressing spike variants, we assessed the neutralizing capacity of sera from human subjects or non-human primates that received mRNA-1273. No significant impact on neutralization against the UK variant was detected in either case, however reduced neutralization was measured against the mutations present in SA. Geometric mean titer (GMT) of human sera from clinical trial participants in VSV PsVN assay using D614G spike was 1/1852. VSV pseudoviruses with spike containing K417N-E484K-N501Y-D614G and full B.1.351 mutations resulted in 2.7 and 6.4-fold GMT reduction, respectively, when compared to the D614G VSV pseudovirus. Importantly, the VSV PsVN GMT of these human sera to the full B.1.351 spike variant was still 1/290, with all evaluated sera able to fully neutralize. Similarly, sera from NHPs immunized with 30 or 100 μg of mRNA-1273 had VSV PsVN GMTs of ~ 1/323 or 1/404, respectively, against the full B.1.351 spike variant with a ~ 5 to 10-fold reduction compared to D614G. Individual mutations that are characteristic of the B.1.1.7 and B.1.351 variants had a similar impact on neutralization when tested in VSV or in lentivirus PsVN assays. Despite the observed decreases, the GMT of VSV PsVN titers in human vaccinee sera against the B.1.351 variant remained at ~1/300. Taken together these data demonstrate reduced but still significant neutralization against the full B.1.351 variant following mRNA-1273 vaccination.

8. 根据 Novavax 官网信息，该公司的 COVID-19 疫苗在英国进行的三期临床试验中显示出 89.3%的有效性，而且对最新的英国和南非病毒株有效

Novavax COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial

来源：Novavax
发布时间：2021-01-28
链 接 ： https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3
要点：
这是首个展示对英国和南非两种突变株都有临床保护效果的疫苗
在英国 3 期临床试验显示出 89.3%的保护率， 同时有超过 50%是目前占优势的英国突变株
在南非的临床 2b 试验显示有超过 90%为南非突变株
Highlight:
First to Demonstrate Clinical Efficacy Against COVID-19 and Both UK and South Africa Variants
Strong efficacy in Phase 3 UK trial with over 50% of cases attributable to the now-predominant UK variant and the remainder attributable to COVID-19 virus
Clinical efficacy demonstrated in Phase 2b South Africa trial with over 90% of sequenced cases attributable to prevalent South Africa escape variant
编者注：
Novavax 是一家位于美国马里兰的公司，这次 COVID-19 疫苗采用的是重组蛋白结合纳米颗粒技术。

9. 强生单剂新冠疫苗达到 3 期临床主要终点，下周递交 EUA 申请

来源：药明康德公众号
发布时间：2021-01-30
链接：https://mp.weixin.qq.com/s/CYqc3nt1yBeEPDQb-Ww4uQ
摘要：
今日，强生（Johnson & Johnson）公司宣布了其新冠在研疫苗 Ad26.COV2.S 在 3 期临床试验 ENSEMBLE 中获得的顶线效力和安全性结果。这一结果是基于在 43783 名参与者中积累的 468 名出现症状的 COVID-19 患者。试验结果表明，这一新冠疫苗在单次接种 28 天之后，对中度和重度 COVID-19 的预防能力达到 66%。同时它预防重度疾病的效力达到 85%，并且完全预防 COVID-19 相关的住院和死亡。
试验结果同时显示，这款疫苗对在南非最初发现的新冠突变病毒株也具有保护能力。

10. 对逃避用于治疗 COVID-19 的抗体的病毒突变的前瞻性图谱绘制

Prospective mapping of viral mutations that escape antibodies used to treat COVID-19
来源：Science
发布时间：2021-01-25
链接：https://science.sciencemag.org/content/early/2021/01/22/science.abf9302
第一作者：Tyler N. Starr, Allison J. Greaney
通讯作者：Jesse D. Bloom
通讯作者单位：Basic Sciences and Computational Biology, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA
DOI 或 PUBMED ID：10.1126/science.abf9302
编译者：宋张悦
中文摘要：

抗体是治疗 SARS-CoV-2 的一种潜在方法，但病毒进化逃逸的风险仍不清楚。在这里，我们绘制了 SARS-CoV-2 受体结合域（RBD）的所有突变如何影响 REGN-COV2 抗体鸡尾酒（再生元公司（Regeneron）开发）和 LY-CoV016 抗体（礼来公司开发的）的结合。这些完整的图谱揭示了一个完全逃逸 REGN-COV2 鸡尾酒抗体的单氨基酸突变，该鸡尾酒由两个靶向不同结构表位的抗体组成（REGN10933 和 REGN10987）。该图谱还确定了在接受 REGN-COV2 治疗的持续感染患者中以及在体外病毒逃逸选择期间选择的病毒突变。最后，该图谱揭示，现在流行的 SARS-CoV-2 毒株中已经存在逃避单个抗体的突变。总的来说，这些完整的逃逸图谱能够解释病毒监测期间观察到的突变的后果。

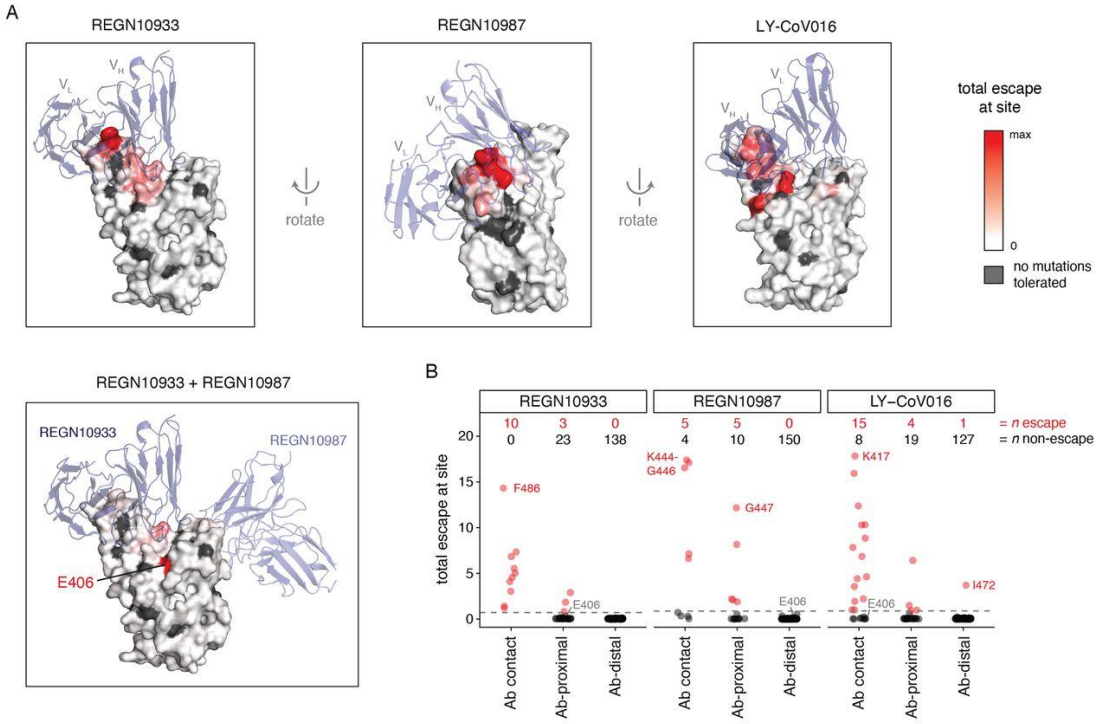

Fig. 4 Structural context of escape mutations.

(A) Escape maps projected on antibody-bound RBD structures. [REGN10933 and REGN10987: PDB 6XDG (11); LY-CoV016: PDB 7C01 (13)]. Antibody heavy- and light-chain variable domains are shown as blue cartoons, and the RBD surface is colored to indicate how strongly mutations at that site mediate escape (white indicates no escape, red indicates strongest escape site for that antibody/cocktail). Sites where no mutations are functionally tolerated are colored gray. (B) For each antibody, sites were classified as direct antibody contacts (non-hydrogen atoms within 4 Å of antibody), antibody-proximal (4–8 Å), or antibody-distal (>8 Å). Each point indicates a site, classified as escape (red) or non-escape (black). The dashed gray line indicates the cutoff used to classify sites as escape or non-escape (see Methods for details). Red and black numbers indicate how many sites in each category are escape or non-escape sites, respectively. Interactive visualizations are at https://jbloomlab.github.io/SARS-CoV-2-RBD_MAP_clinical_Abs/ and hypothesized mechanisms of escape and additional structural details for labeled points are shown in fig. S6.

Abstract:

Antibodies are a potential therapy for SARS-CoV-2, but the risk of the virus evolving to escape them remains unclear. Here we map how all mutations to SARS-CoV-2's receptor-binding domain (RBD) affect binding by the antibodies in the REGN-COV2 cocktail and the antibody LY-CoV016. These complete maps uncover a single amino-acid mutation that fully escapes the REGN-COV2 cocktail, which consists of two antibodies targeting distinct structural epitopes. The maps also identify viral mutations that are selected in a persistently infected patient treated with REGN-COV2, as well as during in vitro viral escape selections. Finally, the maps reveal that mutations escaping the individual antibodies are already present in circulating SARS-CoV-2 strains. Overall, these complete escape maps enable interpretation of the consequences of mutations observed during viral surveillance.

11. 正在流行的 SARS-CoV-2 Spike 蛋白 N439K 突变体在逃避抗体介导的免疫响应同时保持了病毒的适应性

Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity

来源：cell

发布时间：2021-01-28

链接：https://www.cell.com/cell/fulltext/S0092-8674(21)00080-5

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DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2021.01.037

编译者：宋张悦

中文摘要：

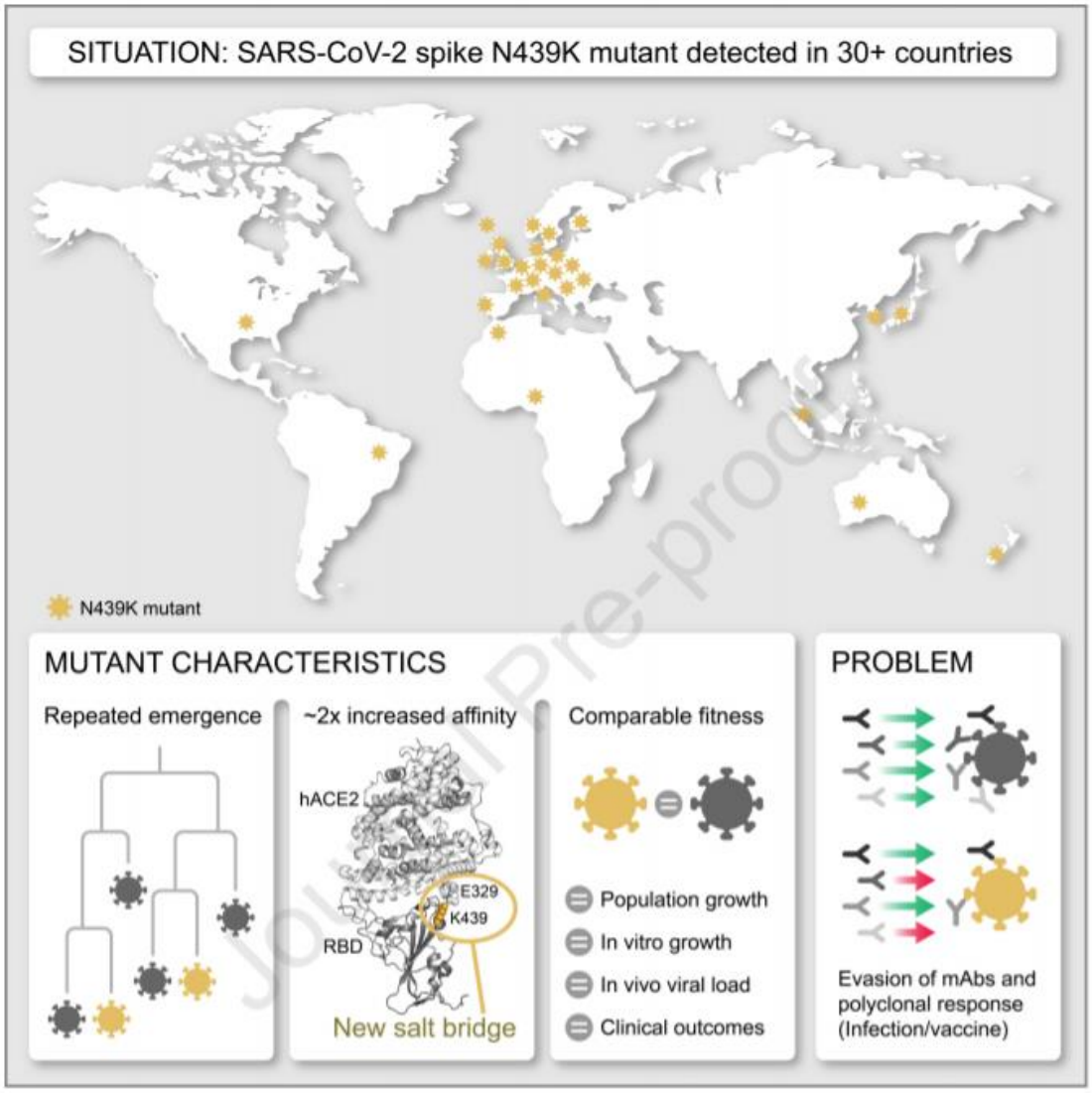
•受体结合基序(RBM)是 SARS-CoV-2 的一个高度可变区域

•RBM 的 N439K 突变在多个谱系中独立出现

•N439K 增加了 spike 对 hACE2 的亲和力;病毒的适应性和疾病没有改变

•N439K 对几个单克隆抗体具有抗性，逃避了一些多克隆反应

简报第 79 期（2020 年 11 月 7 日-11 月 13 日周报）第 15 篇文章，报道过该研究的预印本。



Abstract:

Highlights

- The receptor-binding motif (RBM) is a highly variable region of SARS-CoV-2 spike
- RBM mutation N439K has emerged independently in multiple lineages
- N439K increases spike affinity for hACE2; viral fitness and disease are unchanged
- N439K confers resistance to several mAbs and escapes some polyclonal responses

12. SARS-CoV-2 变异株 B.1.351 和 B.1.1.7 对抗体中和能力的耐药性增强

Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization

来源：bioRxiv

发布时间：2021-01-26

链接：https://www.biorxiv.org/content/10.1101/2021.01.25.428137v2

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DOI 或 PUBMED ID：
编译者：宋珂
中文摘要：

Covid-19 疫情造成了全球性的破坏，但其病原体 SARS-CoV-2 病毒却仍在肆虐。结束这次疫情的希望取决于开发有效的处置措施。单一以及联合单克隆抗体(mAb)疗法已获得紧急使用授权，而且更多的抗体也正在研发中。此外，多种疫苗方案已显示出良好的前景，其中两种疫苗对 Covid-19 的保护效果可以达到大约 95%。然而，以上这些处置措施针对的是 2019 年出现的初期 SARS-CoV-2 病毒。而此后病毒发生了相当多的进化，包括具有 D614G 突变的变异株已成为主要的流行株。不过，仅含有 D614G 突变的病毒并未表现出特异的抗原性。而近期在英国和南非出现的新的 SARS-CoV-2 变种 B.1.1.7 和 B.1.351 则十分令人担忧。因为据称这两种新的病毒变种更易于传播，而且其 spike 蛋白具有大量的突变。本文中，作者报道称 B.1.1.7 变异株难以被大多数识别 spike 蛋白 N 端结构域(NTD)的单克隆抗体中和，同时对一些识别受体结合结构域(RBD)的单克隆抗体也具有相当的耐药性。保守而言，B.1.1.7 对恢复期患者血浆的抗性大约是未突变病毒的 3 倍，对疫苗接种者血清的抗性大约是 2 倍。对 B.1.351 变异株的研究结果则更令人担忧，因为该变体不仅无法被大多数识别 NTD 的单克隆抗体中和，而且也无法被多个识别 RBD 的单一单克隆抗体中和，这在很大程度上是由于 E484K 突变造成的。尽管一些单克隆抗体的组合仍然保持了中和活性。此外，B.1.351 的抗性明显更强，其对恢复期患者血浆的抗性大约是未突变病毒的 11-33 倍，对疫苗接种者血清的抗性大约是 6.5-8.6 倍。B.1.351 和其他具有类似 spike 蛋白突变的病毒变异株为使用单抗治疗带来了新的挑战，并威胁到现有疫苗的保护效果。

Abstract:

The Covid-19 pandemic has ravaged the globe, and its causative agent, SARS-CoV-2, continues to rage. Prospects of ending this pandemic rest on the development of effective interventions. Single and combination monoclonal antibody (mAb) therapeutics have received emergency use authorization, with more in the pipeline. Furthermore, multiple vaccine constructs have shown promise, including two with ~95% protective efficacy against Covid-19. However, these interventions were directed toward the initial SARS-CoV-2 that emerged in 2019. Considerable viral evolution has occurred since, including variants with a D614G mutation that have become dominant. Viruses with this mutation alone do not appear to be antigenically distinct, however. Recent emergence of new SARS-CoV-2 variants B.1.1.7 in the UK and B.1.351 in South Africa is of concern because of their purported ease of transmission and extensive mutations in the spike protein. We now report that B.1.1.7 is refractory to neutralization by most mAbs to the N-terminal domain (NTD) of spike and relatively resistant to a number of mAbs to the receptor-binding domain (RBD). It is modestly more resistant to convalescent plasma (~3 fold) and vaccinee sera (~2 fold). Findings on B.1.351 are more worrisome in that this variant is not only refractory to neutralization by most NTD mAbs but also by multiple individual mAbs to the receptor-binding motif on RBD, largely due to an E484K mutation, although some mAb combinations retain activity. Moreover, B.1.351 is markedly more resistant to neutralization by

convalescent plasma (~11-33 fold) and vaccinee sera (~6.5-8.6 fold). B.1.351 and emergent variants with similar spike mutations present new challenges for mAb therapy and threaten the protective efficacy of current vaccines.

13. 双组份 spike 蛋白纳米颗粒疫苗能够保护猕猴抵御 SARS-CoV-2 病毒感染

Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection

来源：Cell

发布时间：2021-01-25

链接：https://www.cell.com/cell/fulltext/S0092-8674(21)00078-7#comments-heading

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DOI 或 PUBMED ID：10.1016/j.cell.2021.01.035

编译者：宋珂

亮点

- 双组分蛋白纳米颗粒能够表达 SARS-CoV-2 Spike 蛋白的多个副本
- Spike 蛋白纳米颗粒在体外表现出增强同源 B 细胞活化的作用
- 为小鼠、兔子和食蟹猴接种疫苗，可诱导其产生有效的中和作用
- 疫苗可保护猕猴抵御大剂量 SARS-CoV-2 病毒的感染挑战

中文摘要：

SARS-CoV-2 疫情持续对个人生活、全球医疗体系和经济造成破坏。因此，对一种能够预防病毒感染、传播和发病的疫苗的需求十分迫切。本文中，作者合成了一种基于蛋白的双组分纳米颗粒疫苗，其能够表达 SARS-CoV-2 spike 蛋白的多个副本。免疫研究表明，该疫苗可以诱导小鼠、兔和食蟹猴产生有效的抗体中和响应。疫苗诱导的免疫力能够保护猕猴抵御高剂量的病毒感染挑战。在猕猴的上、下呼吸道中，病毒感染和复制的能力明显下降。此类纳米颗粒是一种很有希望的遏制 SARS-CoV-2 疫情的候选疫苗。

Highlights

- Two-component protein nanoparticles display multiple copies of the SARS-CoV-2 Spike
- Spike protein nanoparticles enhance cognate B cell activation in vitro
- Vaccination induces potent neutralization in mice, rabbits and cynomolgus macaques
- Vaccination protects macaques against a high-dose SARS-CoV-2 challenge

Abstract:

The SARS-CoV-2 pandemic is continuing to disrupt personal lives, global healthcare systems and economies. Hence, there is an urgent need for a vaccine that prevents viral infection, transmission and disease. Here, we present a two-

component protein-based nanoparticle vaccine that displays multiple copies of the SARS-CoV-2 spike protein. Immunization studies show that this vaccine induces potent neutralizing antibody responses in mice, rabbits and cynomolgus macaques. The vaccine-induced immunity protected macaques against a high dose challenge, resulting in strongly reduced viral infection and replication in upper and lower airways. These nanoparticles are a promising vaccine candidate to curtail the SARS-CoV-2 pandemic.

14. 对早期 SARS-CoV-2 病毒株系采取的针对宿主的治疗方案对突变株 B.1.1.7 仍有效

Host-directed therapies against early-lineage SARS-CoV-2 retain efficacy against B.1.1.7 variant

来源：biorxiv

发表时间：2021-01-24

链接：https://www.biorxiv.org/content/10.1101/2021.01.24.427991v1

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通讯作者：Nevan J. Krogan

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编译：蒋立春

中文摘要：

最近一个新的 SARS-CoV-2 病毒突变株 B.1.1.7，首次在英国被发现并正在扩散到多个其他国家。该毒株的出现加剧了公共卫生安全担忧，同时使得疫苗和治疗方案是否仍对该病毒株有效成为了急需要回答的问题。我们和其他研究人员之前发现针对宿主主导的治疗可以有效治疗病毒感染。针对宿主的药物更加不容易发生抗药性，因为宿主基因相比病毒基因更不容易发生突变，是非常有前景的用于对抗新发病毒突变的治疗方案。这篇研究中，首次对 B.1.1.7 的全长病毒进行了研究。作者们发现在人的肠道细胞系和肺上皮细胞系中，两个针对宿主的药物，plitidepsin (aplidin; 一致翻译延长因子 eEF1A) 和 ralimetinib (抑制 p38 激酶通路)，以及瑞德西韦这三种药，对于早期的 SARS-CoV-2 株系和 B.1.1.7 突变体有相仿的抗病毒活性。作者们发现 plitidepsin 对两种株系的病毒抗病毒活性都高出瑞德西韦一个数量级。该研究表明持续开发针对宿主的治疗方案来应对现在以及将来的冠状病毒突变株的爆发有着重要意义。

Abstract:

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in millions of deaths worldwide and massive societal and economic burden. Recently, a new variant of SARS-CoV-2, known as B.1.1.7, was first detected in the United Kingdom and is spreading in several other countries, heightening public health concern and raising questions as to the resulting effectiveness of vaccines and therapeutic interventions. We and others previously identified host-directed therapies with antiviral efficacy against SARS-CoV-2 infection. Less prone to the development of therapy resistance, host-directed drugs represent promising therapeutic options to combat emerging viral variants as host genes possess a lower propensity to mutate compared to viral genes. Here, in the first study of the full-length B.1.1.7 variant virus, we find two host-directed drugs, plitidepsin (aplidin; inhibits translation

elongation factor eEF1A) and ralimetinib (inhibits p38 MAP kinase cascade), as well as remdesivir, to possess similar antiviral activity against both the early-lineage SARS-CoV-2 and the B.1.1.7 variant, evaluated in both human gastrointestinal and lung epithelial cell lines.We find that plitidepsin is over an order of magnitude more potent than remdesivir against both viruses. These results highlight the importance of continued development of host-directed therapeutics to combat current and future coronavirus variant outbreaks.

15. 海洋来源的首创抗癌药物 Plitidepsin 可以通过靶向宿主蛋白 eEF1A 有效抑制 SARS-CoV-2

Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A

来源：science

发表时间：2021-01-25

链接：https://science.sciencemag.org/content/early/2021/01/22/science.abf4058

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通讯作者：Adolfo García-Sastre

通讯作者单位： Icahn School of Medicine at Mount Sinai, New York, NY, USA.

编译：蒋立春

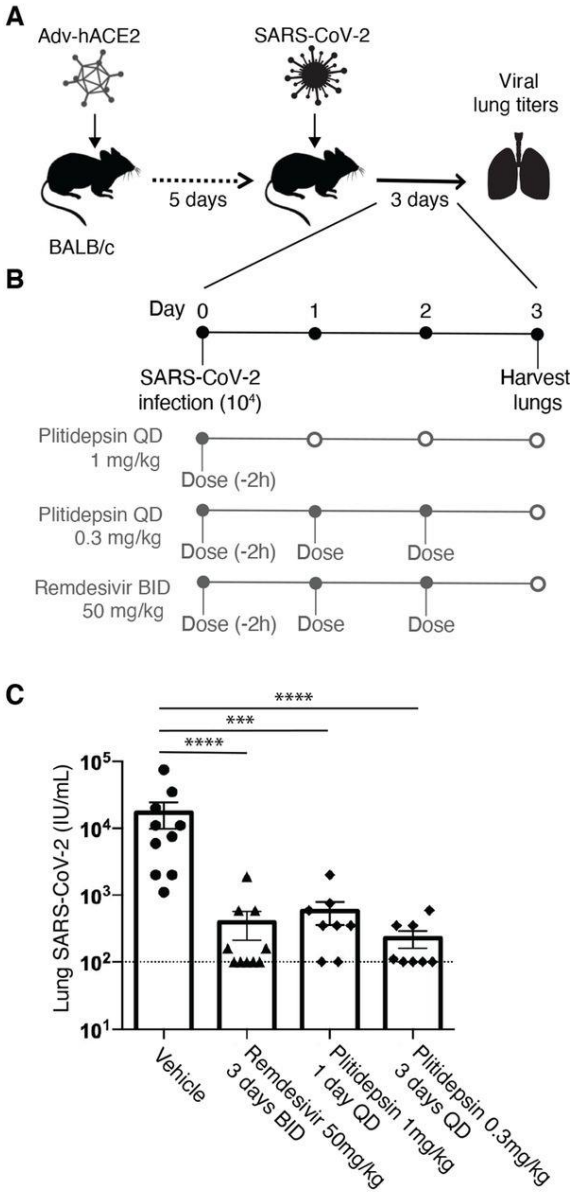
中文摘要：

SARS-CoV-2 病毒蛋白和真核生物翻译机器相互作用，抑制翻译过程可以起到有力的抗病毒效果。这项工作中，作者报道了作为孤儿药物上市的 plitidepsin (aplidin)在体外系统中抗 SARS-CoV-2 的活性是瑞德西韦的 27.5 倍（IC90=0.88nM），且在体外培养细胞中毒性有限。通过对一个药物抵抗突变株的研究，作者们发现 plitidepsin 的抗病毒活性是通过抑制一个已知的药物靶点 eEF1A 实现的。作者们在两种 SARS-CoV-2 感染的小鼠模型中发现在体内实验中，plitidepsin 的预防性治疗可以将肺部病毒的复制降低两个数量级。

Abstract:

SARS-CoV-2 viral proteins interact with the eukaryotic translation machinery and inhibitors of translation have potent antiviral effects. Here we report that the drug plitidepsin (aplidin), which has limited clinical approval, possesses antiviral activity (IC90 = 0.88 nM) 27.5-fold more potent than remdesivir against SARS-CoV-2 in vitro, with limited toxicity in cell culture.

Through the use of a drug resistant mutant, we show that the antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A. We demonstrate the in vivo efficacy of plitidepsin treatment in two mouse models of SARS-CoV-2 infection with a reduction of viral replication in the lungs by two orders of magnitude using prophylactic treatment. Our results indicate that plitidepsin is a promising therapeutic candidate for COVID-19.



编者注：

plitidepsin 是一种海洋来源的首创（first-in-class）抗癌药物，最初是从一种原索动物——地中海海鞘（Aplidiumalbicans）中获得的，能够特异性地与真核翻译延长因子 1A2（eEF1A2）结合，并靶向该蛋白的非典型作用，通过细胞凋亡（程序性死亡）导致肿瘤细胞死亡。目前，该药物正处于临床开发用于多种血液学肿瘤的治疗，包括治疗复发性或难治性 MM 的组合研究，以及治疗复发性或难治性血管免疫母细胞性 T 细胞淋巴瘤的 II 期研究。在美国和欧盟，plitidepsin 均被授予了孤儿药资格。（https://med.sina.com/article_detail_103_2_57408.html，新浪医药）

16. 工程化人单克隆抗体对 SARS-like 病毒具有广泛而有效的抗病毒作用

Broad and potent activity against SARS-like viruses by an engineered human monoclonal antibody

来源：science

发布时间：2021-1-25

链接：https://science.sciencemag.org/content/early/2021/01/22/science.abf4830
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DOI 或 PUBMED ID：10.1126/science.abf4830
编译者：王玮
中文摘要：
冠状病毒（cov）人畜共患，说明积极的应对措施是非常必要的。该研究采用定向进化的方法设计了三种 SARS-CoV-2 抗体，以增强中和广度和效力。其中一个亲和成熟变异体 ADG-2 对一大类 sarbecovirus 的受体结合域（RBDs）具有很强的结合活性，并能高效地中和具有代表性的流行性 sarbecovirus。结构和生化研究表明，ADG-2 利用不同的方法来识别与受体结合位点重叠的高度保守的表位。在 SARS 和 COVID-19 的免疫活性小鼠模型中，预防性地给予 ADG-2 对呼吸负荷、肺部病毒复制和肺部病理提供了完全的保护。总之，ADG-2 是一种很有前途的广谱的抗 clade 1 sarbecoviruses 的候选药物。
Abstract:
The recurrent zoonotic spillover of coronaviruses (CoVs) into the human population underscores the need for broadly active countermeasures. We employed a directed evolution approach to engineer three SARS-CoV-2 antibodies for enhanced neutralization breadth and potency. One of the affinity-matured variants, ADG-2, displays strong binding activity to a large panel of sarbecovirus receptor binding domains (RBDs) and neutralizes representative epidemic sarbecoviruses with high potency. Structural and biochemical studies demonstrate that ADG-2 employs a distinct angle of approach to recognize a highly conserved epitope overlapping the receptor binding site. In immunocompetent mouse models of SARS and COVID-19, prophylactic administration of ADG-2 provided complete protection against respiratory burden, viral replication in the lungs, and lung pathology. Altogether, ADG-2 represents a promising broad-spectrum therapeutic candidate against clade 1 sarbecoviruses.

17. 重症 COVID-19 病人中保护性免疫状态的全身性缺失以及靶向全身性免疫作为治疗手段
Global absence and targeting of protective immune states in severe COVID-19
来源：nature
发布时间：2021-01-25
文章链接：https://www.nature.com/articles/s41586-021-03234-7
第一作者：Alexis J. Combes
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中文摘要：
虽然 SARS-CoV-2 感染对一些患者有多效性和全身性影响，但许多其他患者的症状较轻。研究者寻求对 COVID-19 病理学中严重/轻微区别及其起源的全面理解。采用了全血液单细胞分析方案，整合所有主要细胞类型的贡献，包括中性粒细胞、单核细胞、血小板、淋巴细胞和血清含量。轻度 COVID-19 疾病患者在每个细胞群中都显示出协调的干扰素刺激基因(ISG)表达的模式，而这些细胞在重度疾病患者中不存在。非常矛盾的是：与轻症患者相比，重症 COVID-19 患者的抗 SARS-CoV-2 抗体滴度也非常高，病毒载量也更低。对重症患者血清的检测表明，他们特异地产生一些抗体，这些抗体通过参与保守的信号传导途径来减弱干扰素对细胞的反应，功能上阻止与轻度疾病相关的 ISG 表达细胞的产生。在许多 COVID-19 患者中，抗体反应过度会导致免疫系统自我对抗，可能在其他病毒感染中也是如此。这项研究确定了重症患者免疫治疗的靶点，以重新启动病毒防御。

Abstract
While SARS-CoV-2 infection has pleiotropic and systemic effects in some patients, many others experience milder symptoms. We sought a holistic understanding of the severe/mild distinction in COVID-19 pathology, and its origins. We performed a whole-blood preserving single-cell analysis protocol to integrate contributions from all major cell types including neutrophils, monocytes, platelets, lymphocytes and the contents of serum. Patients with mild COVID-19 disease display a coordinated pattern of interferon-stimulated gene (ISG) expression3 across every cell population and these cells are systemically absent in patients with severe disease. Severe COVID-19 patients also paradoxically produce very high anti-SARS-CoV-2 antibody titers and have lower viral load as compared to mild disease. Examination of the serum from severe patients demonstrates that they uniquely produce antibodies that functionally block the production of the mild disease-associated ISG-expressing cells, by engaging conserved signaling circuits that dampen cellular responses to interferons. Overzealous antibody responses pit the immune system against itself in many COVID-19 patients and perhaps in other viral infections and this study defines targets for immunotherapies in severe patients to re-engage viral defense.

18. SARS-CoV-2 S 蛋白中的 N501Y 突变导致肥胖和老年小鼠发病，并被恢复期和接种后的人类血清中和

The N501Y mutation in SARS-CoV-2 spike leads to morbidity in obese and aged mice and is neutralized by convalescent and post-vaccination human sera

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中文摘要：
目前由 SARS-CoV-2 引起的 COVID-19 的大流行，老年人，患有肥胖症和相关 2 型糖尿病等共病的人易感。小动物模型对于成功开发和验证抗病毒疫苗、治疗以及研究共病对病毒感染结局的作用至关重要。原始的 SARS-CoV-2 分离株需要适应，才能能够结合小鼠受体蛋白血管紧张素转换酶 2（mACE-2）并有效地感染小鼠呼吸道细胞。该研究通过连续传代小鼠肺中的临床分离病毒获得了“小鼠适应”的 SARS-CoV-2。之后在老年、糖尿病和肥胖的小鼠模型中使用低剂量的这种病毒株。与人类的 SARS-CoV-2 感染相似，感染“小鼠适应”的 SARS-CoV-2 导致老年和糖尿病肥胖小鼠发病率增加。与小鼠适应相关的突变发生在 S、M、N 和 ORF8 基因中。有趣的是，S 蛋白受体结合域的一个突变导致天冬酰胺在 501 位变为酪氨酸残基（N501Y）。这种突变也出现在英国报道的新出现的 SARS-COV-2 变异病毒（20B/501Y.V1，B1.1.7 谱系）中，该流行病与人与人之间的高传播性相关。该研究也发现，人类恢复期和接种（接种的是辉瑞疫苗）后血清可以中和新出现的 N501Y 病毒变体，其效力与参考 USA-WA1/2020 病毒相似，这表明当前的 SARS-CoV-2 疫苗将对 20B/501Y.V1 株具有保护作用。
Abstract:
The current COVID-19 (coronavirus disease 19) pandemic, caused by SARS-CoV-2, disproportionally affects the elderly and people with comorbidities like obesity and associated type 2 diabetes mellitus. Small animal models are crucial for the successful development and validation of antiviral vaccines, therapies and to study the role that comorbidities have on the outcome of viral infections. The initially available SARS-CoV-2 isolates require adaptation in order to use the mouse angiotensin converting enzyme 2 (mACE-2) entry receptor and to productively infect the cells of the murine respiratory tract. We have “mouse-adapted” SARS-CoV-2 by serial passaging a clinical virus isolate in the lungs of mice. We then used low doses of this virus in mouse models for advanced age, diabetes and obesity. Similar to SARS-CoV-2 infection in humans, the outcome of infection with mouse-adapted SARS-CoV-2 resulted in enhanced morbidity in aged and diabetic obese mice. Mutations associated with mouse adaptation occurred in the S, M, N and ORF8 genes. Interestingly, one mutation in the receptor binding domain of the S protein results in the change of an asparagine to tyrosine residue at position 501 (N501Y). This mutation is also present in the newly emerging SARS-CoV-2 variant viruses reported in the U.K. (20B/501Y.V1, B1.1.7 lineage) that is epidemiologically associated with high human to human transmission. We show that human convalescent and post vaccination sera can neutralize the newly emerging N501Y virus variant with similar efficiency as that of the reference USA-WA1/2020 virus, suggesting that current SARS-CoV-2 vaccines will protect against the 20B/501Y.V1 strain.