新型冠状病毒信息简报

第 85 期（2020 年 12 月 19 日-12 月 25 日周报）

上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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内容介绍

分类	标题名称
疫情播报	1. 2020 年 12 月 24 日疫情 2. 2020 年 12 月 26 日我国新增确诊病例 22 例，其中本土病例 12 例
流行病学	3. 无症状与有症状 COVID-19 的感染性 4. 一种具有多个 S 蛋白突变的 SARS-CoV-2 病毒株系在南非出现和快速传播 5. 真实世界的数据表明，SARS-CoV-2 抗体阳性与未来感染风险的降低有关
疾病监测	6. 不存在适用所有人的 COVID-19 测试方法
疾病病理	7. 中和抗体驱动 Spike 介导的 SARS-CoV-2 逃逸 8. 去岩藻糖基化的 IgG 是包膜病毒反应的特征，和 COVID-19 的症状严重程度相关
疫苗研	9. 关于 COVID-19 疫苗的全球储备和全球分配的横断面分析 10. NIH 和 Moderna 公司可能会开展新冠疫苗低剂量临床试验以提高疫苗供应能力 11. 辉瑞与 BioNTech 共同研发的新冠疫苗获得人用医药产品委员会（CHMP）的肯定 12. 中国康希诺的 COVID-19 疫苗试验招募了 20,000 多人 13. 土耳其宣布中国科兴公司新冠疫苗具备有效性 14. 巴西公布中国疫苗关键数据，媒体：预计多国将使用 15. 国药中生新冠病毒灭活疫苗（Vero）上市申请获得 NMPA 受理
临床试验	16. 一种治疗 Covid-19 住院患者的中和单克隆抗体
基础研究	17. 造成 COVID-19 疫情的 SARS-CoV-2 病毒中的 ORF3a 蛋白能够阻断形成自溶酶体所需的由 HOPS 复合物介导的 SNARE 复合物的组装 18. 叙利亚仓鼠的纵向组学与人类数据相结合揭示了 SARS-CoV-2 中度免疫应答的复杂性 19. COVID-19 患者产生的抗体能够靶向 SARS-CoV-2 spike 蛋白的特定位点，导致病毒感染能力增强 20. 未能复制罕见的 I 型 IFN 免疫基因功能缺失变异与严重 COVID-19 的关联 21. 人类冠状病毒通过抗原进化来逃避抗体免疫
资源介绍	22. 新冠快讯——Mesoblast 干细胞疗法 III 期临床失败，诺华、辉瑞和强生疫苗供应链和产能情况

1. 2020 年 12 月 24 日疫情

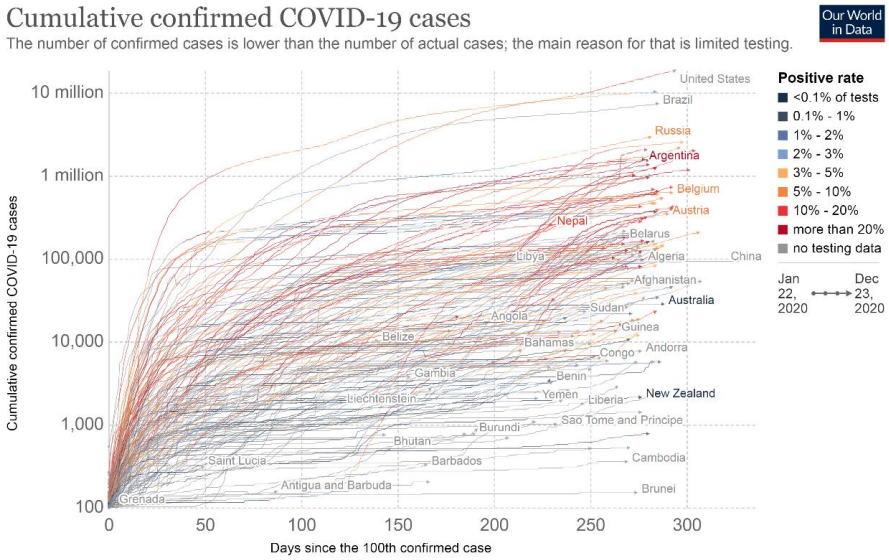
数据来源：WHO

发布时间：2020 年 12 月 24 日北京时间下午 4 点

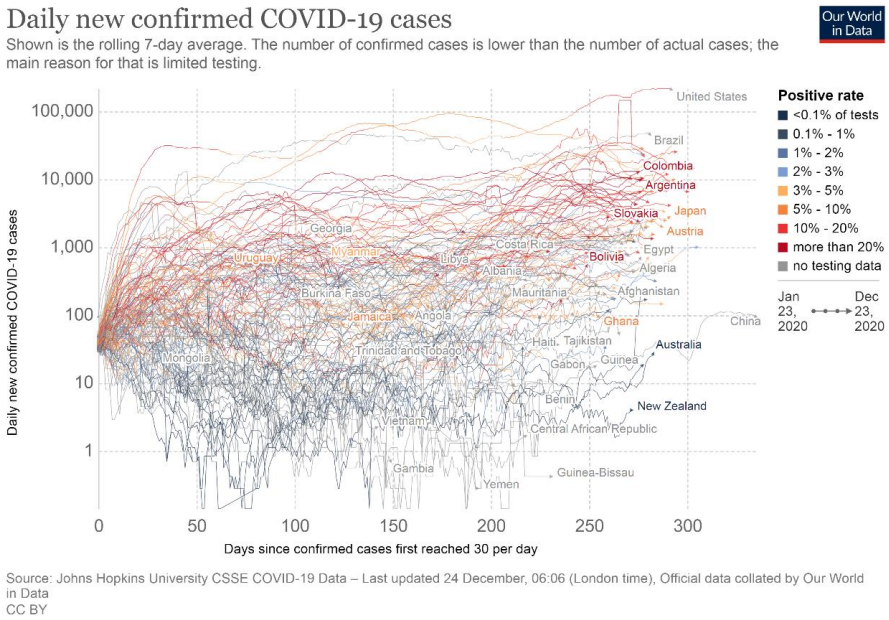
链接：https://covid19.who.int/

根据 WHO 提供的数据，2020 年 12 月 24 日全球累计确诊新型冠状病毒病人 **77,530,799** 例，当日新增确诊 **13,061** 例，累计死亡 **1,724,904** 例，当日新增死亡 **13,061**。

中国累计确诊 96,074 例，累计死亡 4,774 例，当日新增确诊 76 例，新增死亡 1 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（12 月 24 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 2020 年 12 月 26 日我国新增确诊病例 22 例，其中本土病例 12 例

来源：新华社微信公众号

发布时间：2020-12-27

链接：https://mp.weixin.qq.com/s/m90kfcCKh_wLaujJ3a506g

摘要（转）

12 月 26 日 0—24 时，31 个省（自治区、直辖市）和新疆生产建设兵团报告新增确诊病例 22 例，其中境外输入病例 10 例（上海 4 例，北京 3 例，浙江 2 例，安徽 1 例），本土病例 12 例（**辽宁 7 例，北京 5 例**）；无新增死亡病例；无新增疑似病例。

3. 无症状与有症状 COVID-19 的感染性

Infectivity of asymptomatic versus symptomatic COVID-19

来源：The Lancet

发布时间：2020-12-18

链接：https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32651-9/fulltext

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doi：https://doi.org/10.1016/S0140-6736(20)32651-9

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中文摘要：

方法及结果：

为了根据新冠肺炎患者的症状和血清学状态确定他们的相对传染性，作者研究了所有在 2020 年 8 月 1 日至 10 月 11 日期间完成隔离的人。这些人是感染者的密切社区接触者，作为新冠肺炎状况评估的一部分，也接受了血清学测试。居住在外来务工人员宿舍的密切接触

者被排除在这一分析之外，因为他们的生活环境与社区密切接触者的背景不同，而且在确定病例及其在宿舍内的密切接触者方面存在更多的挑战。应用 Python3.7.1 版(Python Software Foundation，Wilmington，DE，USA)进行负二项回归，调整指标病例的症状和血清学状态，计算社区新冠肺炎阳性人群中隔离人群的发病率比，双尾统计显著性设为 0.05。628 名新冠肺炎患者纳入本次分析。3790 人是一例报告的病例的密切接触者，已被隔离。平均每个报告的病例隔离社区 6.0 人。总体而言，在 3,790 名密切社区接触者中，89 人(2%)在隔离期间患上了新冠肺炎。在这些病例中，89 名接触者中有 50 名(56%)因无症状指征病例而被隔离，而 39 名接触者(44%)因有症状病例而被隔离。43 名接触者(48%)因血清指数阴性病例而被隔离，而 46 名接触者(52%)因血清阳性指数病例而被隔离。负二项回归分析显示，调整报告的病例的年龄、性别和血清学因素后，有症状报告的病例密切接触者新冠肺炎的发病率是无症状报告的病例密切接触者的 3.85 倍(95%CI 为 2.06~7.19；P<0.0001)。

结论

无症状新冠肺炎患者是有传染性的，但传染性可能低于有症状的病例。作者还发现，密切接触者感染的比例并不取决于报告的病例的血清学状态。这种观察的一个原因可能是，密切接触者往往与报告的病例一起生活或工作，并因为他们经常接触血清呈阳性之前具有传染性的人而暴露在这种情况下。

Abstract

To identify the relative infectivity of people with COVID-19 on the basis of their symptom and serology status, we studied all people who completed their quarantine between Aug 1 and Oct 11, 2020, as a result of being close community contacts of people who were infected and who had also undergone serology tests as part of their COVID-19 status assessment. Close contacts who lived in migrant worker dormitories were excluded from this analysis because their living environments were contextually different from community close contacts and because there were separate challenges in identifying cases and their close contacts within the dormitories. Negative binomial regression was done using Python version 3.7.1 (Python Software Foundation, Wilmington, DE, USA) to calculate the incidence rate ratios of a quarantined person from the community testing positive for COVID-19, adjusting for the symptom and serology status of the index case; two-tailed statistical significance was set at 0·05.

628 people with COVID-19 were included in this analysis (appendix). 3790 people were close contacts of an index case and were quarantined. On average, 6·0 people from the community were quarantined per index case. Overall, 89 (2%) of 3790 close community contacts developed COVID-19 while in quarantine. Of these, 50 (56%) of 89 contacts were quarantined because of an asymptomatic index case, whereas 39 (44%) contacts were quarantined because of a symptomatic case. 43 (48%) contacts were quarantined because of a seronegative index case, whereas 46 (52%) were quarantined because of a seropositive index case. Negative binomial regression revealed that when adjusted for age, gender, and serology of index case, the incidence of COVID-19 among close contacts of a symptomatic index case was 3·85 times higher than for close contacts of an asymptomatic index case (95% CI 2·06–7·19; p<0·0001; appendix).

Our findings suggest that people with asymptomatic COVID-19 are infectious but might be less infectious than symptomatic cases. We also identified that the

proportion of close contacts who became infected did not depend on the serology status of the index case. One reason for this observation could be that close contacts tend to live or work with the index case and are exposed because of their regular contact with a person who was infectious before turning seropositive

4. 一种具有多个 S 蛋白突变的 SARS-CoV-2 病毒株系在南非出现和快速传播

Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa

来源：medrxiv

发布时间：2020-12-22

链接：https://www.medrxiv.org/content/10.1101/2020.12.21.20248640v1

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中文摘要：

SARS-CoV-2 在世界许多地区的持续无控制的传播，为病毒的重大进化创造了条件。该研究描述了一个新的变异 SARS-CoV-2 病毒株系（501Y.V2），其特征是在 S 蛋白中出现了 8 个突变，包括受体结合域（K417N、E484K 和 N501Y）中的三个重要残基，它们可能具有功能意义。该病毒株在南非东开普省海岸的纳尔逊曼德拉湾（Nelson Mandela Bay）中的第一次疫情爆发中出现。这种变异 SARS-CoV-2 病毒株系迅速传播，几周内成为东开普省和西开普省的主要病毒株。尽管突变的全部意义尚待确定，但基因组数据表明其他株系快速替换，可能与该病毒株更高的传染性有关。

Abstract:

Continued uncontrolled transmission of the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) in many parts of the world is creating the conditions for significant virus evolution. Here, we describe a new SARS-CoV-2 lineage (501Y.V2) characterised by eight lineage-defining mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y) that may have functional significance. This lineage emerged in South Africa after the first epidemic wave in a severely affected metropolitan area, Nelson Mandela Bay, located on the coast of the Eastern Cape Province. This lineage spread rapidly, becoming within weeks the dominant lineage in the Eastern Cape and Western Cape Provinces. Whilst the full significance of the mutations is yet to be determined, the genomic data, showing the rapid displacement of other lineages, suggest that this lineage may be associated with increased transmissibility.

5. 真实世界的数据表明，SARS-CoV-2 抗体阳性与未来感染风险的降低有关

Real-world data suggest antibody positivity to SARS-CoV-2 is associated with a

decreased risk of future infection

来源：medrxiv
发布时间：2020.12.20
链接：https://www.medrxiv.org/content/10.1101/2020.12.18.20248336v1

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doi: https://doi.org/10.1101/2020.12.18.20248336

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设计：
该研究利用一个国家样本，从一个由商业实验室测试结果、公开和内部的医疗和药房索赔、电子健康记录、医院账单(chargemaster)数据和来自美国的付款人登记文件组成的去除个人信息后构建了一个队列。根据数据库中记录的首次 SARS-CoV-2 抗体检测结果，将患者分为抗体阳性或抗体阴性。排除掉在指标日期超过 1 个抗体检测结果不一致的患者。
主要结果/测量主要终点:
抗体检测结果和核酸诊断(NAAT)结果，感染定义为阳性诊断试验后指数，按 30 天间隔(0-30，31-60，61-90，>90 天)测量。其他措施包括指数抗体测试时的人口统计、地理和临床特征，如记录的体征和症状或新冠肺炎(诊断或 NAT+)的先前证据和记录的合并症。
结果:
研究纳入了 3,257,478 名独特的患者，进行了指数抗体测试。其中 287673 例(88.3%)为阴性，378,606 例(11.6%)为阳性，2099 例(0.1%)为阴性。抗体测试阴性的患者在指数上比结果阳性的患者(平均年龄为 48 岁 Vs.44 岁)稍大一些。一小部分(18.4%)最初血清阳性的个体在随访期间转为血清阴性。在随访期内，0~30 天、31~60 天、0.24~0.35 天、>90 天的核酸诊断（NAAT）阳性与阴性的比值分别为 2.85(2.73~2.97)、0.67(0.6~0.74)、0.29(0.24~0.35)、0.10(0.05~0.19)，差异有统计学意义(P<0.05)。
结论：
抗体检测呈阳性的患者最初核酸诊断（NAAT）呈阳性的可能性更大，这与 RNA 长时间脱落一致，但随着时间的推移，核酸诊断（NAAT）呈阳性的可能性明显降低。这一结果表明，使用商业上可用的检测方法的血清阳性与预防感染有关。保护的持续时间是未知的，可能会随着时间的推移而减弱；这一参数需要在延长随访持续时间的研究中加以解决。

Abstract
Participants
The study utilized a national sample to create cohorts from a de-identified dataset composed of commercial laboratory test results, open and closed medical and pharmacy claims, electronic health records, hospital billing (chargemaster) data, and payer enrollment files from the United States. Patients were indexed as antibody-positive or antibody-negative according to their first SARS-CoV-2 antibody test recorded in the database. Patients with more than 1 antibody test on the index date where results were discordant were excluded.
Main Outcomes/Measures
Primary endpoints were index antibody test results and post-index diagnostic NAAT (nucleic acid amplification test) results, with infection defined as a positive diagnostic test post-index, as measured in 30-day intervals (0-30, 31-60, 61-90, >90 days). Additional measures included demographic, geographic, and

clinical characteristics at the time of the index antibody test, such as recorded signs and symptoms or prior evidence of COVID-19 (diagnoses or NAAT+) and recorded comorbidities.

Results

We included 3,257,478 unique patients with an index antibody test. Of these, 2,876,773 (88.3%) had a negative index antibody result, 378,606 (11.6%) had a positive index antibody result, and 2,099 (0.1%) had an inconclusive index antibody result. Patients with a negative antibody test were somewhat older at index than those with a positive result (mean of 48 versus 44 years). A fraction (18.4%) of individuals who were initially seropositive converted to seronegative over the follow up period. During the follow-up periods, the ratio (CI) of positive NAAT results among individuals who had a positive antibody test at index versus those with a negative antibody test at index was 2.85 (2.73 - 2.97) at 0-30 days, 0.67 (0.6 - 0.74) at 31-60 days, 0.29 (0.24 - 0.35) at 61-90 days), and 0.10 (0.05 - 0.19) at >90 days.

Conclusions

Patients who display positive antibody tests are initially more likely to have a positive NAAT, consistent with prolonged RNA shedding, but over time become markedly less likely to have a positive NAAT. This result suggests seropositivity using commercially available assays is associated with protection from infection. The duration of protection is unknown and may wane over time; this parameter will need to be addressed in a study with extended duration of follow up.

6. 不存在适用所有人的 COVID-19 测试方法

COVID-19 testing: One size does not fit all

来源：Science

发布时间：2020-12-21

链接：https://science.sciencemag.org/content/early/2020/12/18/science.abe9187

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DOI 或 PUBMED ID：10.1126/science.abe9187

编译者：刘焕珍

中文摘要：

为了控制大流行，检测应该被视为一种公共卫生工具。COVID-19 测试是抗击 SARS-CoV-2/COVID-19 的核心。虽然大多数努力都集中在作为临床医疗诊断工具的测试方法上，但是根据 Michael Mina 博士的说法，帮助控制 COVID-19 疫情的最有力的检测形式却很少得到使用或认可。Mina 和他的合著者 Kristian G. Andersen 博士描述了聚焦于减少病毒在人群层面传播的公共卫生筛查的力量，以及它如何可能是一种关键但被忽视的工具。Mina 说，“这种筛查的方式是让足够多的人频繁地进行自我测试---比如说，每周两次---最好是使用快速测试。通过让人们了解自己的传播状况，我们可以在整个社区层面有效地减缓传播。”这两名作者还讨论了“入口筛查（entrance screening）”的作用，即个人在进入办公室、工作场所、餐厅等场所时进行筛查。Mina 说，“当与公共卫生筛查相结合时，入口筛查可以增加另一层保护，这样就可以让经济更容易开放。”

Abstract:
To control the pandemic, testing should be considered a public health tool. During a 2-week period, ~80% of the population was screened using rapid antigen tests. With 50,000 cases identified, combined with other pub-lic health measures, it reduced incidence by 82% within 2 weeks. Key to use of tests for entrance screening is that a negative test alone should not be considered sufficient to enter—that should be based on satis-fying other requirements, including masks and physical dis-tancing. It is necessary to be innovative and produce, distribute, and con-tinuously improve the tests that exist to save lives and gain control of the COVID-19 pandemic.

7. 中和抗体驱动 Spike 介导的 SARS-CoV-2 逃逸

Neutralising antibodies drive Spike mediated SARS-CoV-2 evasion
来源：medRxiv
发布时间：2020-12-19
链接：https://www.medrxiv.org/content/10.1101/2020.12.05.20241927v2.supplementary-material
第一作者：Kemp SA
通讯作者：Gupta RK
通讯作者单位：Division of Infection and Immunity, University College London, London, UK.
DOI 或 PUBMED ID：
编译者：张鹏伟
中文摘要：
在这里，我们报告了一个用恢复期血浆治疗的免疫抑制个体的致命性 SARS-CoV-2 从中和抗体中逃逸，通过短读和长读技术在 101 天的 23 个时间点上产生了全基因组超深序列。尽管服用了两个疗程的伦德西韦，在最初的 65 天内，病毒种群几乎没有发生进化变化。然而，在使用恢复血浆治疗后，我们观察到动态病毒种群转移，出现了一种主要的病毒株，其在 S2 的 S2 NTD 中带有 D796H，在 S1 的 NTD 中具有 ΔH69/ΔV70。随着血清中和作用的减弱，带有逃逸基因型的病毒频率降低，最后在一个不成功的恢复期血浆治疗疗程的最后回升。在体外实验中，Spike 逃逸变体降低了对不同康复患者的恢复期血浆/血清的敏感性，同时保持了与野生型相似的传染性。这些数据揭示了在恢复血浆疗法期间对 SARS-CoV-2 的强阳性选择，并将 Spike 突变 D796H 和 ΔH69/ΔV70 的组合确定为针对常见的 SARS-CoV-2 抗体应答的广泛抗体耐药机制。
Abstract:
SARS-CoV-2 Spike protein is critical for virus infection via engagement of ACE2, and amino acid variation in Spike is increasingly appreciated. Given both vaccines and therapeutics are designed around Wuhan-1 Spike, this raises the theoretical possibility of virus escape, particularly in immunocompromised individuals where prolonged viral replication occurs. Here we report fatal SARS-CoV-2 escape from neutralising antibodies in an immune suppressed individual treated with convalescent plasma, generating whole genome ultradeep sequences by both short and long read technologies over 23 time points spanning 101 days. Little evolutionary change was observed in the viral population over the first

65 days despite two courses of remdesivir. However, following convalescent plasma we observed dynamic virus population shifts, with the emergence of a dominant viral strain bearing D796H in S2 and ΔH69/ΔV70 in the S1 NTD of the Spike protein. As serum neutralisation waned, viruses with the escape genotype diminished in frequency, before returning during a final, unsuccessful course of convalescent plasma. In vitro, the Spike escape variant conferred decreased sensitivity to multiple units of convalescent plasma/sera from different recovered patients, whilst maintaining infectivity similar to wild type. These data reveal strong positive selection on SARS-CoV-2 during convalescent plasma therapy and identify the combination of Spike mutations D796H and ΔH69/ΔV70 as a broad antibody resistance mechanism against commonly occurring antibody responses to SARS-CoV-2.

8. 去岩藻糖基化的 IgG 是包膜病毒反应的特征，和 COVID-19 的症状严重程度相关

Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity

来源：science

发布时间：2020-12-23

链接：https://science.sciencemag.org/content/early/2020/12/22/science.abc8378

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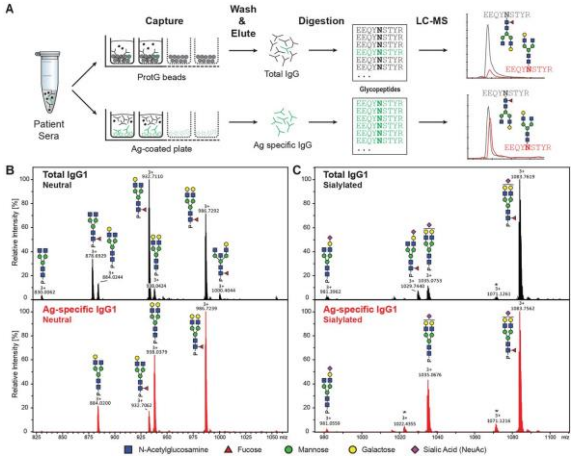
DOI 或 PUBMED ID：DOI: 10.1126/science.abc8378

编译者：蒋立春

中文摘要：

IgG 抗体对于保护宿主免于入侵病原物有重要作用。在 IgG 的 Fc 片段上有一个高度保守的 N 连接糖基化位点，对于 IgG 的功能是必须的，其组成在人类中表现出多样性。去岩藻糖基化 IgG 变体已经其通过 Fc 受体(FcγRIIIa)提高活性而已经被用于抗癌症治疗抗体。作者报道了去岩藻糖基化的 IgG（占到人 IgG 总量的约 6%）特异性的针对有披膜的病毒而一般不针对其他的抗原。IgG 的去岩藻糖基化介导了更强的 FcγRIIIa 的反应，但同时也放大了酝酿中的细胞因子风暴以及免疫介导的病理过程。高水平的去岩藻糖基化的 IgG 只存在于危重的 COVID-19 病人而不存在于轻症病人中。作者推断抗体糖基化在针对包括 COVID-19 在内的包膜病毒的免疫反应中起到关键作用。



Flowchart of antibody-specific IgG1 glycosylation analysis by mass spectrometry. (A) Antibodies were captured from sera using Protein G beads and antigen-coated 96-well plates resulting in total and antigen-specific IgG fractions, respectively. Thereafter, isolated IgG were digested with trypsin and the resulting glycopeptides were analyzed by nano liquid chromatography-mass spectrometry. (B and C) Representative mass spectra of glycopeptides encompassing the Fc glycosylation site Asn297. Neutral (B) and sialylated (C) IgG1 glycopeptides are shown from a single patient's total (upper panel, in black) and antigen-specific (lower panel, in red) IgG1 fraction. Asterisks indicate non-Fc glycopeptides.

Abstract:
IgG antibodies are crucial for protection against invading pathogens. A highly conserved N-linked glycan within the IgG-Fc tail, essential for IgG function, shows variable composition in humans. Afucosylated IgG variants are already used in anti-cancer therapeutic antibodies for their elevated activity through Fc receptors (FcγRIIIa).Here, we report that afucosylated IgG (~6% of total IgG in humans) are specifically formed against enveloped viruses but generally not against other antigens. This mediates stronger FcγRIIIa responses, but also amplifies brewing cytokine storms and immune-mediated pathologies. Critically ill COVID-19 patients, but not those with mild symptoms, had high levels of afucosylated IgG antibodies against SARS-CoV-2, amplifying pro-inflammatory cytokine release and acute phase responses. Thus, antibody glycosylation plays a critical role in immune responses to enveloped viruses, including COVID-19.

9. 关于 COVID-19 疫苗的全球储备和全球分配的横断面分析

Reserving coronavirus disease 2019 vaccines for global access: cross sectional analysis

来源：medRxiv

发布时间： 2020-12-15

链接： https://www.bmj.com/content/371/bmj.m4750

第一作者：Anthony D So

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DOI 或 PUBMED ID： https://doi.org/10.1136/bmj.m4750

编译者：蒋立春

中文摘要：

作者对 2020 年 11 月 15 日之前公开宣布的 COVID-19 疫苗上市前的购买许诺进行了分析。数据来源包括世界卫生组织 COVID-19 候选疫苗进展,公司对美国证券交易委员会的披露，公司和基金的媒体披露，政府公告以及媒体报道等。

作者分析的内容包括了 COVID-19 上市前的购买许诺以及每一疗程的价格，疫苗平台以及研发阶段，以及采购机构和接受国家。截止到 2020 年 11 月 15 日，多个国家做出了 COVID-19 疫苗上市前购买的承诺。这些上市前购买一共包括了 13 家疫苗生产商的 74.8 亿剂，或者 37.6 亿疗程。刚好有超过一半（51%）会流向代表了 14%全世界人口的高收入发达国家。美

国预留了 8 亿剂，但是美国的 COVID-19 病例占到全球所有病例的 1/5（1102 万），而日本、澳大利亚和加拿大一共预留了多余 10 亿剂的疫苗，却这些国家的病例目前只占到全球 COVID-19 病例的 1%（45 万）。如果这些候选疫苗都能规模化生产，预计到 2021 年年底总产能将达到 59.6 亿疗程。这些厂家的疫苗最高会有 40%（23.4）亿的疫苗疗程可能会留给中低收入国家。如果发达国家扩大储备则这个比例会更低，而如果发达国家分享他们的采购的则这个比例会更高一些。这些疫苗的价格差异可以高达 10 倍，每一疗程的价格在 6 美金到 74 美金不等。美国和俄罗斯之外有更多国家广泛地参与到 COVAX 机构—COVAX 机构是世界卫生组织“使用 COVID-19 工具（ACT）加速器”的疫苗支柱。目前 COVAX 已获得至少 5 亿剂或 2.5 亿疗程的资金，预计在 2021 年底前达到 20 亿剂目标的一半，以支持协调全球获取 covid-19 疫苗。

这项研究概述了高收入国家如何确保将来获得 covid-19 疫苗的供应，但世界其他地区获取疫苗的情况尚不明确。政府和制造商应提高透明度和问责制，为公平分配 covid-19 疫苗提供急需的保障。

Abstract

Objective To analyze the premarket purchase commitments for coronavirus disease 2019 (covid-19) vaccines from leading manufacturers to recipient countries.

Design Cross sectional analysis.

Data sources World Health Organization’s draft landscape of covid-19 candidate vaccines, along with company disclosures to the US Securities and Exchange Commission, company and foundation press releases, government press releases, and media reports.

Eligibility criteria and data analysis Premarket purchase commitments for covid-19 vaccines, publicly announced by 15 November 2020.

Main outcome measures Premarket purchase commitments for covid-19 vaccine candidates and price per course, vaccine platform, and stage of research and development, as well as procurement agent and recipient country.

Results

As of 15 November 2020, several countries have made premarket purchase commitments totaling 7.48 billion doses, or 3.76 billion courses, of covid-19 vaccines from 13 vaccine manufacturers. Just over half (51%) of these doses will go to high income countries, which represent 14% of the world’s population. The US has reserved 800 million doses but accounts for a fifth of all covid-19 cases globally (11.02 million cases), whereas Japan, Australia, and Canada have collectively reserved more than one billion doses but do not account for even 1% of current global covid-19 cases globally (0.45 million cases). If these vaccine candidates were all successfully scaled, the total projected manufacturing capacity would be 5.96 billion courses by the end of 2021. Up to 40% (or 2.34 billion) of vaccine courses from these manufacturers might potentially remain for low and middle income countries‐less if high income countries exercise scale-up options and more if high income countries share what they have procured. Prices for these vaccines vary by more than 10-fold, from $6.00 (£4.50; €4.90) per course to as high as $74 per course. With broad country participation apart from the US and Russia, the COVAX Facility—the vaccines pillar of the World Health Organization’s Access to COVID-19 Tools (ACT) Accelerator—has secured

at least 500 million doses, or 250 million courses, and financing for half of the targeted two billion doses by the end of 2021 in efforts to support globally coordinated access to covid-19 vaccines.Conclusions This study provides an overview of how high income countries have secured future supplies of covid-19 vaccines but that access for the rest of the world is uncertain. Governments and manufacturers might provide much needed assurances for equitable allocation of covid-19 vaccines through greater transparency and accountability over these arrangements.

10. NIH 和 Moderna 公司可能会开展新冠疫苗低剂量临床试验以提高疫苗供应能力

NIH, Moderna may test smaller dose of COVID-19 vaccine to increase supplies

来源：BIOCENTURY

发布时间：2020-12-24

链接：https://www.biocentury.com/article/633029

第一作者：STEVE USDIN

编译者：姜连连

中文摘要：

美国政府计划开展一项可以提高 Moderna 新冠疫苗供应的临床试验，同时也寻找辉瑞-BioNTech 疫苗免疫后出现少量严重过敏反应的诱因。美国“空间机战行动”（ Operation Warp Speed）负责人 Slaoui 并不认同 Mederna 公司和辉瑞-BioNTech 公司单剂量疫苗免疫的提议，并表示就现阶段而言单剂量免疫完全不可行，因为 mRNA 和其他疫苗一样，所引发的免疫应答会在体内快速降低，二次免疫将会强化机体防御反应而确保提供机体高效持久的保护力。追求单剂量免疫策略将会导致疫苗免疫事倍功半，且应该用试验数据验证而不能根据两家疫苗临床试验中 7 天或 14 天观察到的保护力进行推断。但对于 Moderna 疫苗的双剂量免疫中 mRNA 剂量减半观点，Slaoui 却持乐观态度。目前，被授权的疫苗接种单针剂量为 100 ug。而 Moderna 疫苗临床数据结果显示，尤其是在年轻群体中，50 和 100 ug 剂量免疫效果基本上相同。Slaoui 表示 NIH 正积极讨论 Moderna 尝试低剂量免疫而使疫苗受益人群翻倍。但他并未提供该临床试验的具体日程表。Slaoui 提及正在研发中的强生新冠疫苗单剂量免疫后即可提供更强更持久的免疫保护力，且这种保护水平可持续大约 3 个月。该疫苗的临时或最终保护效率数据将在明年一月份获得。若疫苗有效，美国 FDA 将最迟在明年 1 月份或 2 月份即可对该疫苗进行紧急授权。

Abstract:

The U.S. government is planning to conduct trials to explore options for increasing supplies of Moderna’s COVID-19 vaccine and to address concerns about rare, serious allergic reactions to the Pfizer-BioNTech vaccine. Moncef Slaoui, co-leader of Operation Warp Speed, pushed back on suggestions that mRNA vaccines from Moderna or Pfizer-BioNTech should be administered in a single-dose regimen, saying that “a one-dose vaccine is totally inappropriate at this stage.” For mRNA and other vaccine modalities that are quickly eliminated from the body, a second vaccination to boost the response to the initial dose is essential to ensure robust, durable protection. Pursuing a one-dose strategy where the half-life is short is something should be tested experimentally, not inferred because we see protection for seven days or 14 days in the Moderna or the Pfizer trials. Slaoui was more optimistic about the potential for doubling supplies of the

Moderna vaccine by halving the amount of vaccine administered in a two-dose regimen. The vaccine has been authorized for administration as two 100 μg doses. Data from trials of Moderna's vaccine "suggested that the 50 and 100 μg doses were substantially equivalent, particularly [in trial participants who were] not very old," Slaoui said NIH is in active discussions with Moderna about testing a lower dose, which could double supplies, but he did not provide a timetable for the trials. Johnson & Johnson vaccine is developing could provide strong, lasting protection with a single dose because it persists in the body for almost three months after vaccination, Interim or final efficacy data about the JNJ-78436735 vaccine candidate could be available in January, and if it is favorable, FDA could issue an emergency use authorization in late January or February,

11. 辉瑞与 BioNTech 共同研发的新冠疫苗获得人用医药产品委员会（CHMP）的肯定

Pfizer and BioNTech Receive CHMP Positive Opinion for their COVID-19 Vaccine

来源： Pharmaceutical Investing News

发布时间：2020-12-21

链 接 ： https://investingnews.com/news/pharmaceutical-investing/pfizer-and-biontech-receive-chmp-positive-opinion-for-their-covid-19-vaccine/

第一作者：Stephanie Ebbs

编译者：姜连连

中文摘要：

欧洲委员会决定即将启动有条件的市场紧急授权。CHMP 肯定态度也是追随全世界多个国家已通过的紧急授权案例。CHMP 机构参考了所有的辉瑞新冠疫苗研究数据，包括III期临床保护效率和安全性实验数据。如果 BNT162b2 获得授权，那将会是在欧盟市场上第一个使用的新冠疫苗。CHMP 专家是参考 11 月份辉瑞-BioNTech 公司公布的III期临床数据及本月刚发表在新英格兰杂志的临床数据后给出肯定意见，欧洲委员会将在评估 CHMP 建议后最终决定近期是否会通过该疫苗紧急市场授权。如果通过的话，则该授权决议将立刻在 27 个欧盟成员国生效。目前，该疫苗已经在 15 多个国家取得了紧急使用授权，而一些国家正在进行常规评估流程，更多的授权申请也在不断提交中。目前，BNT162b2 尚未取得美国 FDA 的认可和授权，但美国 FDA 已使用紧急使用授权容许该疫苗在 16 岁以上人群使用以预防新冠肺炎，但该授权会随着疫情好转或授权取消而被终止。

Abstract:

European Commission decision on conditional marketing authorization expected imminently. Positive CHMP opinion follows several emergency use authorizations worldwide; committee reviewed totality of scientific evidence, including Phase 3 efficacy and safety data. If authorized, BNT162b2 will be the first COVID-19 vaccine available in the European Union. The CHMP advisors based their positive opinion on the scientific evidence supporting the BNT162b2, including data from a Phase 3 clinical study announced last month and published in The New England Journal of Medicine. The European Commission (EC) will review the CHMP recommendation and is expected to make a final decision on the conditional marketing authorization in the near future. If the EC grants the CMA, the decision will be immediately applicable to all 27 EU member states. To date, the vaccine has been authorized or approved for emergency use in more than 15 countries.

Regulatory reviews are underway in several countries, with more submissions anticipated. The Vaccine has not been approved or licensed by the U.S. FDA, but has been authorized for emergency use by FDA to prevent COVID-19 for use in individuals 16 years of age and older. The emergency use of this product is only authorized for the duration of the declaration unless the declaration is terminated or authorization revoked sooner.

12. 中国康希诺的 COVID-19 疫苗试验招募了 20,000 多人

China CanSinoBIO's COVID-19 vaccine trials recruit over 20,000 people

来源：News.yahoo

发布时间：2020-12-21

链接：https://news.yahoo.com/china-cansinobios-covid-19-vaccine-132349722.html

编译者：张鹏伟

中文摘要：

中国卫生部一位官员周一表示，中国康希诺生物制品有限公司（CanSino Biologics Inc.）已经招募了超过 2 万人参加其冠状病毒疫苗的海外人体试验。这种被称为 Ad5ncov 或 Convidecia 的候选疫苗是中国已进入第三阶段临床试验的五种疫苗之一，康希诺正在与中国军方支持的一个研究机构联合开发该疫苗。最新的临床试验注册数据显示，康希诺候选疫苗的临床三期试验计划总共有 4 万人参与，已经开始在巴基斯坦、俄罗斯、墨西哥和智利招募参与者。这个候选疫苗也在阿根廷进行了临床试验，并与墨西哥达成了供应协议。康希诺首席执行官俞雪峰在 11 月 28 日的一次产业活动中表示，自今年 6 月获得批准用于军事人员以来，这种一剂疫苗已经给了大约 4 万至 5 万紧急使用的人。周一郑表示，中国医学科学院研制的疫苗可能很快开始临床三期试验，但没有具体说明将在何处进行试验。

Abstract:

BEIJING (Reuters) - China's CanSino Biologics Inc. has recruited over 20,000 participants for late-stage human trials overseas for its coronavirus vaccine, a health official said on Monday.

The candidate, known as Ad5-nCoV or Convidecia, which CanSinoBIO is jointly developing with a research institute backed by the Chinese military, is among the five vaccines China has moved into Phase 3 clinical trials to test their efficacy.

"As for now, the number of recruited participants has exceeded 20,000 people, and the progress is relatively fast," said Zheng Zhongwei, an official at China's National Health Commission, told a press conference.

Phase 3 trials for CanSinoBIO's candidate, which are planned to involve 40,000 participants in total, have begun enrolling participants in Pakistan, Russia, Mexico and Chile, the latest clinical trial registration data showed. https://bit.ly/3mHzt8R

The candidate also has trials lined up in Argentina, and has secured a supply deal with Mexico.

The one-dose vaccine had been given to about 40,000-50,000 people in emergency use since it obtained approval to be used in military personnel in June, CanSinoBIO Chief Executive Yu Xuefeng said in an industrial event on Nov. 28.

A vaccine developed by Chinese Academy of Medical Sciences could start Phase 3

clinical trial soon, Zheng said on Monday, without specifying where it will be tested.

13. 土耳其宣布中国科兴公司新冠疫苗具备有效性

来源：新华网

发布时间：2020-12-26

链接：http://www.xinhuanet.com/politics/2020-12/26/c_1126909114.htm

摘要（转）：

新华社安卡拉 12 月 25 日电（记者郑思远　施洋）土耳其卫生部长科贾 24 日晚表示，土耳其确定中国北京科兴中维生物技术有限公司研发的新冠灭活疫苗适用于土耳其人民，是有效且安全的。

科贾在当晚召开的新闻发布会上说，对土耳其自愿接种科兴新冠疫苗志愿者数据的初步分析显示，科兴新冠疫苗的有效性达 91.25%，临床试验期间未发现严重副作用。中方已经批准向土方出口有关疫苗，如果一切顺利，来自中国的首批 300 万剂疫苗将于近日抵达土耳其。

14. 巴西公布中国疫苗关键数据，媒体：预计多国将使用

来源：环球网新闻

发布时间：2020-12-24

链接：http://news.jstv.com/a/20201224/1608772789699.shtml

编译者：孔娟

中文摘要：

巴西公布科兴研发的新冠疫苗在该国三期试验的结果数据。声明称，科兴疫苗在多国的试验数据表明，在不同年龄组中都展现出良好的耐受性，并可引发产生抗体。该疫苗在巴西、印尼、土耳其和智利共有超过 2 万名志愿者参与三期试验。据《华尔街日报》22 日援引参与试验的人士称，试验结果显示科兴疫苗超过国际科学家认为提供保护所需要的 50%的有效性门槛。巴西媒体称，在有效率等三期试验数据公布后，布坦坦研究所将在当天向巴西国家卫生监督局（Anvisa）正式申请注册该疫苗，后者将对此做出评估。如果能获得 Anvisa 快速批准，巴西圣保罗州政府将按计划在明年 1 月 25 日开启疫苗接种。由于对保存温度要求不高，且价格具备竞争性，科兴疫苗被认为是巴西等诸多发展中国家的希望。科兴疫苗也在印尼展开了三期试验，但因为招募的志愿者较少，且缺少易感染人群如医务工作者等，目前为止还没有获得批准注册所需的数据。与此同时，阿联酋正在使用中国国药疫苗启动面向全国成年人的接种，国药集团研发的新冠灭活疫苗 12 月 9 日在该国获得正式注册。

15. 国药中生新冠病毒灭活疫苗（Vero）上市申请获得 NMPA 受理

来源：佰傲谷 BioValley 微信公众号

发布时间：2020-12-24

链接：https://mp.weixin.qq.com/s/voV7AA0EAtmgwshTye1PKA

编译者：孔娟

12 月 24 日，国药中生北京生物制品研究所的新冠病毒灭活疫苗（Vero）上市申请获得 NMPA 受理，系国内首个上市申请获正式受理的新冠疫苗。目前，国药中生研发的新型冠状病毒疫苗已经在 10 个国家和地区开展三期临床试验，近 6 万人入组试验。二期车间本月内建成，2021 年将实现新冠疫苗产能 10 亿剂。国药集团董事长刘敬桢在谈及新冠疫苗相关话题时透露，目前已有数十万人紧急接种国药集团旗下两款新冠灭活疫苗，没有一例严重不良反应，

接种后离境人数达 5.6 万人，目前无一感染。12 月 9 日，阿联酋正式批准了中生北京的新冠灭活疫苗。阿联酋卫生和预防部与阿布扎比卫生部对该疫苗三期临床试验数据进行了复核。在一项由 125 个不同国籍的约 3.1 万名志愿者进行的临床实验显示，中生北京的新冠灭活疫苗对抗病毒感染的有效性为 86%，中和抗体转阳率为 99%，能 100%预防中度和重度的新冠肺炎病例。除国药疫苗外，还有康希诺，科兴，智飞龙科马等公司研发的新冠疫苗已经进入 III 期。

16. 一种治疗 Covid-19 住院患者的中和单克隆抗体（临床无效）

A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19

来源：NEJM

发布时间：2020-12-22

链接：https://www.nejm.org/doi/full/10.1056/NEJMoa2033130?query=featured_home

第一作者：ACTIV-3/TICO LY-CoV555 Study Group

通讯作者：ACTIV-3/TICO LY-CoV555 Study Group

通讯作者单位：美国

DOI 或 PUBMED ID：10.1056/NEJMoa2033130

编译者：刘焕珍

中文摘要：

中和性单克隆抗体 LY-CoV555 与 remdesivir 并用时，在未发生终末器官衰竭的 Covid-19 住院患者中未显示出疗效。在这个治疗药物的试验中，作者以 1:1 的比例随机分配患有 Covid-19 且无终末器官衰竭的住院患者，接受 LY-CoV555 或匹配的安慰剂。LY-CoV555（剂量为 7000 mg）或安慰剂在 1 小时内以单次静脉内输注的形式给药。根据事件发生时间分析，主要结果是 90 天内持续恢复。在第 5 天根据肺功能的 7 类序数进行临时无效评估。2020 年 10 月 26 日，数据和安全监控委员会建议在对 314 例患者（LY-CoV555 组中的 163 名患者和安慰剂组中的 151 名患者）进行随机和输注。自症状发作以来的中位间隔为 7 天。在第 5 天，LY-CoV555 组的 81 例患者（50%）和安慰剂组的 81 例（54%）属于肺结局的两个最有利类别之一。在这七个类别中，LY-CoV555 组比安慰剂组处于更有利类别的几率是 0.85。LY-CoV555 组和安慰剂组中具有主要安全性结果的患者百分比在 LY-CoV555 组和安慰剂组中相似。

Abstract:

BACKGROUND

LY-CoV555, a neutralizing monoclonal antibody, has been associated with a decrease in viral load and the frequency of hospitalizations or emergency department visits among outpatients with coronavirus disease 2019 (Covid-19). Data are needed on the effect of this antibody in patients who are hospitalized with Covid-19.

METHODS

In this platform trial of therapeutic agents, we randomly assigned hospitalized patients who had Covid-19 without end-organ failure in a 1:1 ratio to receive either LY-CoV555 or matching placebo. In addition, all the patients received high-quality supportive care as background therapy, including the antiviral drug remdesivir and, when indicated, supplemental oxygen and glucocorticoids. LY-CoV555 (at a dose of 7000 mg) or placebo was administered as a single intravenous infusion over a 1-hour period. The primary outcome was a sustained recovery

during a 90-day period, as assessed in a time-to-event analysis. An interim futility assessment was performed on the basis of a seven-category ordinal scale for pulmonary function on day 5.

RESULTS

On October 26, 2020, the data and safety monitoring board recommended stopping enrollment for futility after 314 patients (163 in the LY-CoV555 group and 151 in the placebo group) had undergone randomization and infusion. The median interval since the onset of symptoms was 7 days (interquartile range, 5 to 9). At day 5, a total of 81 patients (50%) in the LY-CoV555 group and 81 (54%) in the placebo group were in one of the two most favorable categories of the pulmonary outcome. Across the seven categories, the odds ratio of being in a more favorable category in the LY-CoV555 group than in the placebo group was 0.85 (95% confidence interval [CI], 0.56 to 1.29; P=0.45). The percentage of patients with the primary safety outcome (a composite of death, serious adverse events, or clinical grade 3 or 4 adverse events through day 5) was similar in the LY-CoV555 group and the placebo group (19% and 14%, respectively; odds ratio, 1.56; 95% CI, 0.78 to 3.10; P=0.20). The rate ratio for a sustained recovery was 1.06 (95% CI, 0.77 to 1.47).

CONCLUSIONS

Monoclonal antibody LY-CoV555, when coadministered with remdesivir, did not demonstrate efficacy among hospitalized patients who had Covid-19 without end-organ failure.

17. 造成 COVID-19 疫情的 SARS-CoV-2 病毒中的 ORF3a 蛋白能够阻断形成自溶酶体所需的由 HOPS 复合物介导的 SNARE 复合物的组装

ORF3a of the COVID-19 virus SARS-CoV-2 blocks HOPS complex-mediated assembly of the SNARE complex required for autolysosome formation

来源：Developmental Cell

发布时间：2020-12-11

链接：https://www.cell.com/developmental-cell/fulltext/S1534-5807(20)31016-9

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DOI 或 PUBMED ID：10.1016/j.devcel.2020.12.010

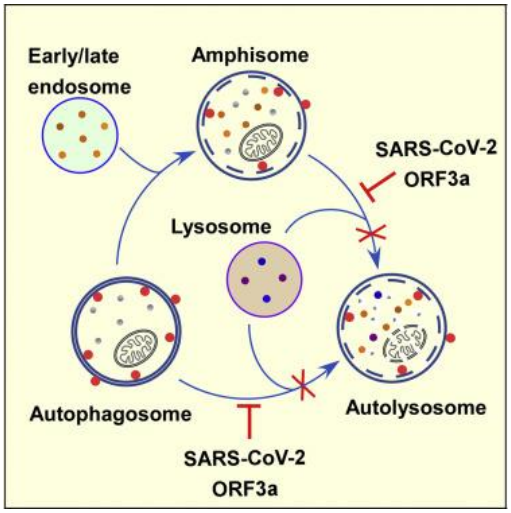
编译者：宋珂

亮点：

- SARS-CoV-2 病毒感染或 ORF3a 蛋白的表达能够阻断自溶酶体的形成
- SARS-CoV-2 ORF3a 蛋白能够俘获晚期内体中 HOPS 的 VPS39 单元
- SARS-CoV-2 ORF3a 蛋白能够阻碍 STX17-SNAP29-VAMP8 SNARE 复合物的组装
- SARS 病毒的 ORF3a 蛋白无法与 VPS39 相互作用或对自噬活动造成影响

中文摘要：

自噬是细胞抵抗入侵病原体的一种监察机制。病毒已经进化出各种策略来阻止自噬，甚至通过破坏自噬来达到自我复制和释放的目的。本文中，作者发现引起 COVID-19 的 SARS-CoV-2 病毒中的 ORF3a 蛋白能够通过阻断自噬体/自噬内涵体与溶酶体的融合来抑制自噬活动。晚期内体附近的 ORF3a 蛋白能够直接与 HOPS 的 VPS39 单元相互作用，并将其俘获，从而阻止 HOPS 复合物与自噬性 SNARE 蛋白 STX17 相互作用。从而阻断了 STX17-SNAP29-VAMP8 SNARE 复合物的组装，而该复合物能够介导自噬体/自噬内涵体与溶酶体融合。ORF3a 蛋白的表达也会破坏溶酶体并损害其功能。SARS-CoV-2 病毒的感染会阻断自噬，导致自噬体/自噬内涵体积累，引起晚期内体中 VPS39 的隔离。令人惊讶的是，引起 SARS 的 SARS-CoV 病毒中的 ORF3a 蛋白却无法与 HOPS 相互作用或阻断自噬。作者的研究揭示了 SARS-CoV-2 逃避溶酶体破坏的机制，并为开发治疗 COVID-19 的新策略提供了思路。



Highlights:

- SARS-CoV-2 virus infection or expression of ORF3a blocks formation of autolysosomes
- SARS-CoV-2 ORF3a sequestrates the HOPS component VPS39 on late endosomes
- SARS-CoV-2 ORF3a impairs the assembly of the STX17-SNAP29-VAMP8 SNARE complex
- SARS virus ORF3a fails to interact with VPS39 or affect autophagy activity

Summary:

Autophagy acts as a cellular surveillance mechanism to combat invading pathogens. Viruses have evolved various strategies to block autophagy and even subvert it for their replication and release. Here we demonstrated that ORF3a of the COVID-19 virus SARS-CoV-2 inhibits autophagy activity by blocking fusion of autophagosomes/amphisomes with lysosomes. The late endosome-localized ORF3a directly interacts with and sequestrates the HOPS component VPS39, thereby preventing HOPS complex from interacting with the autophagosomal SNARE protein STX17. This blocks assembly of the STX17-SNAP29-VAMP8 SNARE complex, which mediates autophagosome/amphisome fusion with lysosomes. Expression of ORF3a also damages lysosomes and impairs their function. SARS-CoV-2 virus infection blocks autophagy, resulting in accumulation of autophagosomes/amphisomes, and causes

late endosomal sequestration of VPS39. Surprisingly, ORF3a from the SARS virus SARS-CoV fails to interact with HOPS or block autophagy. Our study reveals a mechanism by which SARS-CoV-2 evades lysosomal destruction and provides insights for developing new strategies to treat COVID-19.

18. **叙利亚仓鼠的纵向组学与人类数据相结合揭示了 SARS-CoV-2 中度免疫应答的复杂**

Longitudinal omics in Syrian hamsters integrated with human data unravel complexity of moderate immune responses to SARS-CoV-2

来源：biorxiv

发布时间：2020-12-19

链接：https://www.biorxiv.org/content/10.1101/2020.12.18.423524v1

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编译者：王玮

中文摘要：

在 COVID-19 中，免疫反应在很大程度上决定了疾病的严重程度，是治疗策略的关键。SARS-CoV-2 感染导致炎症性肺损伤和组织修复的细胞机制，尤其是内皮细胞的参与，仍不清楚。我们对感染 SARS-CoV-2 的叙利亚仓鼠的细胞和分子过程进行了详细的时空分析。仓鼠单细胞测序和蛋白质组学与 COVID-19 患者的数据集的比较表明宿主-病原体相互作用在细胞和分子水平上物种间的一致性。深入的血管和肺室分析（i）支持单核细胞源性巨噬细胞主导炎症的假设，（ii）显示内皮炎症状态和 T 细胞相互吸引，以及（iii）显示 CD4+和 CD8+细胞毒性 T 细胞反应导致病毒清除。利用自限性的中度 COVID-19 的叙利亚仓鼠模型，定义了内皮细胞和上皮细胞，以及其他髓系和非髓系肺细胞亚型在决定疾病进程中的具体作用。

Abstract:

In COVID-19, the immune response largely determines disease severity and is key to therapeutic strategies. Cellular mechanisms contributing to inflammatory lung injury and tissue repair in SARS-CoV-2 infection, particularly endothelial cell involvement, remain ill-defined. We performed detailed spatiotemporal analyses of cellular and molecular processes in SARS-CoV-2 infected Syrian hamsters. Comparison of hamster single-cell sequencing and proteomics with data sets from COVID-19 patients demonstrated inter-species concordance of cellular and molecular host-pathogen interactions. In depth vascular and pulmonary compartment analyses (i) supported the hypothesis that monocyte-derived macrophages dominate

inflammation, (ii) revealed endothelial inflammation status and T-cell attraction, and (iii) showed that CD4+ and CD8+ cytotoxic T-cell responses precede viral elimination. Using the Syrian hamster model of self-limited moderate COVID-19, we defined the specific roles of endothelial and epithelial cells, among other myeloid and non-myeloid lung cell subtypes, for determining the disease course.

19. COVID-19 患者产生的抗体能够靶向 SARS-CoV-2 spike 蛋白的特定位点，导致病毒感染能力增强

An infectivity-enhancing site on the SARS-CoV-2 spike protein is targeted by COVID-19 patient antibodies

来源：bioRxiv

发布时间：2020-12-18

链接：https://www.biorxiv.org/content/10.1101/2020.12.18.423358v1

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中文摘要：

SARS-CoV-2 病毒的感染会在部分患者中引发严重的症状，说明存在某些尚不明确的危险因素。尽管针对 SARS-CoV-2 spike 蛋白上受体结合结构域（RBD）的抗体已经显示出能够预防 SARS-CoV-2 感染的能力，但针对 spike 蛋白上其他结构域的抗体的效果在很大程度上尚不明确。本文中，作者从 COVID-19 患者中筛选出了一系列抗 spike 蛋白的单克隆抗体。并发现其中一部分抗体的表位在 spike 蛋白的 N 端结构域（NTD），这些抗体能够显著增强 spike 蛋白与 ACE2 的结合能力，从而导致 SARS-CoV-2 病毒的感染能力提高。出人意料的是，突变分析表明，所有导致病毒感染能力增强的抗体都识别 NTD 表面的特定位点。本研究中，在所有住院的 COVID-19 患者样本中都检测到了这种针对感染能力增强位点的抗体。然而，患者中感染能力增强抗体与中和抗体的比例不同。此外，在 48 个未感染的供体样本中，有 3 例检测到了针对感染能力增强位点的抗体，尽管其水平很低。这些发现表明，针对 SARS-CoV-2 病毒感染能力增强位点的抗体的出现，可以被认为是 COVID-19 可能在恶化的因素。而且，在安全疫苗的研发过程中，可能需要考虑在 spike 蛋白中排除这些表位，尤其是对于预先存在增强抗体的个体来说。

Abstract:

SARS-CoV-2 infection causes severe symptoms in a subset of patients, suggesting the presence of certain unknown risk factors. Although antibodies against the receptor-binding domain (RBD) of the SARS-CoV-2 spike have been shown prevent SARS-CoV-2 infection, the effects of antibodies against other spike protein domains are largely unknown. Here, we screened a series of anti-spike monoclonal antibodies from COVID-19 patients, and found that some of antibodies against the N-terminal domain (NTD) dramatically enhanced the binding capacity of the spike protein to ACE2, and thus increased SARS-CoV2 infectivity. Surprisingly, mutational analysis revealed that all the infectivity-enhancing antibodies

recognized a specific site on the surface of the NTD. The antibodies against this infectivity-enhancing site were detected in all samples of hospitalized COVID-19 patients in the study. However, the ratio of infectivity-enhancing antibodies to neutralizing antibodies differed among patients. Furthermore, the antibodies against the infectivity-enhancing site were detected in 3 out of 48 uninfected donors, albeit at low levels. These findings suggest that the production of antibodies against SARS-CoV-2 infectivity-enhancing site could be considered as a possible exacerbating factors for COVID-19 and that a spike protein lacking such antibody epitopes may be required for safe vaccine development, especially for individuals with pre-existing enhancing antibodies.

20. 未能重现罕见的 I 型 IFN 免疫基因功能缺失变异与严重 COVID-19 的关联

Failure to replicate the association of rare loss-of-function variants in type I IFN immunity genes with severe COVID-19

来源：medRxiv

发布时间：2020-10-21

链接：https://www.medrxiv.org/content/10.1101/2020.12.18.20248226v2

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DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

最近的一份报告发现，在 TLR3-和 IRF7-依赖的 I 型 IFN 通路的 13 个候选基因中，罕见的预测功能缺失(pLOF)变异可解释高达 3.5%的严重 COVID-19 病例。我们对 4 个独立的 COVID-19 生物库进行了 1,934 例 COVID-19 病例(713 例重症和 1,221 例轻症)和 15251 个祖先匹配人群进行了全外显子组或全基因组测序。然后我们检测这 13 个基因中罕见的 pLOF 变异是否与严重 COVID-19 相关。在 713 例重症 COVID-19 患者中，我们只在这些基因中发现了一种罕见的 pLOF 突变，与人口对照组或轻度 COVID-19 患者相比，重症患者的 pLOFs 没有富集。我们没有发现 13 个候选基因中罕见的功能缺失变异与严重 COVID-19 结局相关的证据。

Abstract:

A recent report found that rare predicted loss-of-function (pLOF) variants across 13 candidate genes in TLR3- and IRF7-dependent type I IFN pathways explain up to 3.5% of severe COVID-19 cases. We performed whole-exome or whole-genome sequencing of 1,934 COVID-19 cases (713 with severe and 1,221 with mild disease) and 15,251 ancestry-matched population controls across four independent COVID-19 biobanks. We then tested if rare pLOF variants in these 13 genes were associated with severe COVID-19. We identified only one rare pLOF mutation across these genes amongst 713 cases with severe COVID-19 and observed no enrichment of pLOFs in severe cases compared to population controls or mild COVID-19 cases. We find no evidence of association of rare loss-of-function variants in the proposed 13 candidate genes with severe COVID-19 outcomes.

21. 人类冠状病毒通过抗原进化来逃避抗体免疫

A human coronavirus evolves antigenically to escape antibody immunity

来源：bioRxiv

发布时间：2020-12-18

链接：https://www.biorxiv.org/content/10.1101/2020.12.17.423313v1

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DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

人们对冠状病毒抗体免疫有浓厚兴趣。然而，目前尚不清楚冠状病毒是否会进化以逃避这种免疫，如果会，其进化速度有多快。这里我们通过描述人类冠状病毒 229E 的历史进化来解决这个问题。我们发现，20 世纪 80 年代和 90 年代的人类血清对同期 229E 具有中和效价，其效价与 SARS-CoV-2 感染或接种疫苗诱导的抗 SARS-CoV-2 效价相当。我们将这些血清与采集后分离的 229E 株进行了测试，发现对这些“未来”病毒的中和滴度较低。在某些情况下，血清中和同期的滴度为 1:100 的 229E 病毒株不能检测到中和 8-17 年后分离的株。“未来”病毒中和性的降低是由于病毒刺突的抗原进化，特别是在受体结合区域。如果这些结果也适用于其他冠状病毒，那么建议定期更新 SARS-CoV-2 疫苗。

Abstract:

There is intense interest in antibody immunity to coronaviruses. However, it is unknown if coronaviruses evolve to escape such immunity, and if so, how rapidly. Here we address this question by characterizing the historical evolution of human coronavirus 229E. We identify human sera from the 1980s and 1990s that have neutralizing titers against contemporaneous 229E that are comparable to the anti-SARS-CoV-2 titers induced by SARS-CoV-2 infection or vaccination. We test these sera against 229E strains isolated after sera collection, and find that neutralizing titers are lower against these “future” viruses. In some cases, sera that neutralize contemporaneous 229E viral strains with titers >1:100 do not detectably neutralize strains isolated 8–17 years later. The decreased neutralization of “future” viruses is due to antigenic evolution of the viral spike, especially in the receptor-binding domain. If these results extrapolate to other coronaviruses, then it may be advisable to periodically update SARS-CoV-2 vaccines.

22. 新冠快讯——Mesoblast 干细胞疗法 III 期临床失败，诺华、辉瑞和强生疫苗供应链和产能情况

COVID Quick Takes: COVAX tops up as Mesoblast falls on Phase III data; plus Novavax, Pfizer-BioNTech, J&J and COVAX.

来源：biocentury

发布时间：2020-12-19

链接：https://www.biocentury.com/article/632851

作者：Sandi Wong 编辑

编译者：孔娟

中文摘要：

COVAX 表示，目前已经达成交易，为 190 个参与国提供近 20 亿剂 COVID-19 疫苗。最近公布的交易包括与阿斯利康公司的提前购买协议，购买 1.7 亿剂牛津阿斯利康大学疫苗，以及与强生公司签署价值 5 亿美元的候选剂量。旨在确保所有国家都能快速，公平地获得 COVID-19 疫苗。

Mesoblast Ltd 公司的同种异体间充质干细胞（MSC）疗法 Ryoncil（remestemcel-L）在 III 期试验中未能达到达到降低 30 天新冠肺炎死亡率的主要终点。

欧盟委员会从诺华采购 1 亿剂 NVX-CoV2373，并选择追加采购 1 亿剂。该公司宣布了与新西兰的 1070 万剂疫苗预购协议，并计划在 2021 年年中前交付初始剂量。

强生公司评估 JNJ-78436735 单次免疫的 45000 名受试者 III 期系综试验预计将在 1 月底获得这项关键研究的中期数据。强生还在 III 期 ENSEMBLE 2 试验中测试了腺病毒载体疫苗的初免-加强给药。

根据辉瑞发言人的说法，来自 BioNTech SE 和 Pfizer 的所有 BNT162b2 药瓶在最初五次给药后都有不同量的剩余疫苗。以公共卫生紧急事件为由，FDA 表示从每个药瓶中“使用所有可获得的全部剂量是可接受的”。

Abstract

COVAX said it now has deals in place to access nearly 2 billion doses of COVID-19 vaccines for 190 participating economies. Those territories will have access to doses in 1H21, contingent upon approvals and readiness for delivery. Deals unveiled Friday include an advance purchase agreement with AstraZeneca plc (LSE:AZN; NASDAQ:AZN) for 170 million doses of the AstraZeneca-University of Oxford vaccine, and a memorandum of understanding with Johnson & Johnson (NYSE:JNJ) for 500 million doses of the Janssen candidate. The global initiative, which is co-led by Gavi, the Coalition for Epidemic Preparedness Innovations and WHO, aims to ensure rapid and equitable access to COVID-19 vaccines for all countries.

A miss for Mesoblast’s stem cell therapy

Mesoblast Ltd. (ASX:MSB; NASDAQ:MESO) lost A$1.36 (36%) to A$2.41 in Australia and $4.30 (32%) to $9.27 in New York after a third interim analysis of data from 180 patients found remestemcel-L is unlikely to meet the primary endpoint of reducing 30-day COVID-19 mortality in a Phase III trial. The double-blind trial has enrolled 223 ventilator-dependent patients with moderate to severe acute respiratory distress syndrome due to COVID-19; and the interim analysis was based on 180 patients.

In November, Novartis AG (NYSE:NVS; SIX:NOVN) gained exclusive rights to develop, manufacture and commercialize the bone marrow-derived mesenchymal stromal cell therapy for indications outside graft-versus-host disease.

Novavax procurement deals with EC, New Zealand

The European Commission concluded on Thursday exploratory talks to procure 100 million doses of NVX-CoV2373 from Novavax Inc. (NASDAQ:NVAX), with an option for 100 million more doses. Late Wednesday, the company announced an advanced purchase agreement with New Zealand for 10.7 million vaccine doses, with a plan to deliver initial doses by mid-2021.

J&J expects data end of January

Johnson & Johnson (NYSE:JNJ) said Thursday the 45,000-subject Phase III ENSEMBLE trial evaluating a single immunization with JNJ-78436735 is fully enrolled. It expects to have interim data from the pivotal study by the end of January. J&J is also testing prime-boost administration of the adenoviral vector vaccine in the Phase III ENSEMBLE 2 trial.

Potential to stretch BioNTech vaccine supply

All vials of BNT162b2 from BioNTech SE (NASDAQ:BNTX) and Pfizer Inc. (NYSE:PFE) have a variable amount of vaccine left over after the initial five doses, according to a Pfizer spokesperson. Citing the public health emergency, FDA has said "it is acceptable to use every full dose obtainable" from each vial. The agency and Pfizer stressed that vaccine product from multiple vials should not be pooled.