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 4 月 22 日疫情

数据来源：WHO

发布时间：2021 年 4 月 22 日北京时间下午 4 点

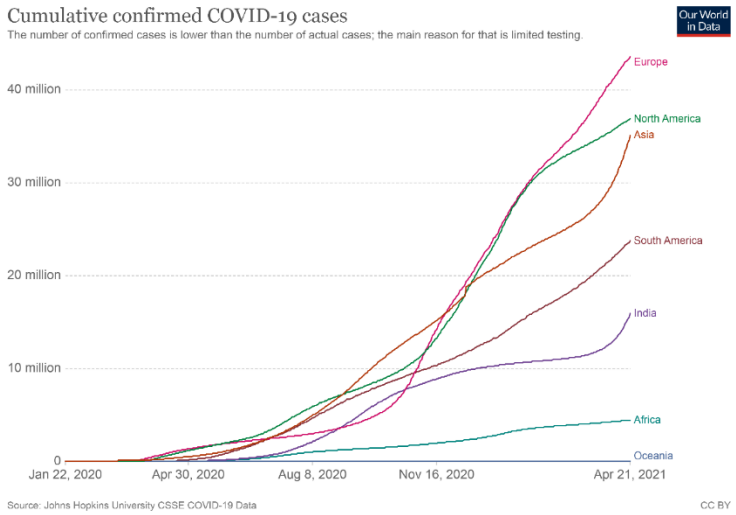
链接：https://covid19.who.int/

根据 WHO 提供的数据，2021 年 4 月 22 日全球累计确诊新型冠状病毒病人 **143,445,675** 例，当日新增确诊 **874,381** 例，累计死亡 **3,051,736** 例，当日新增死亡 **14,033**。全球至少接种一剂疫苗的人数为 **496,485,287**。

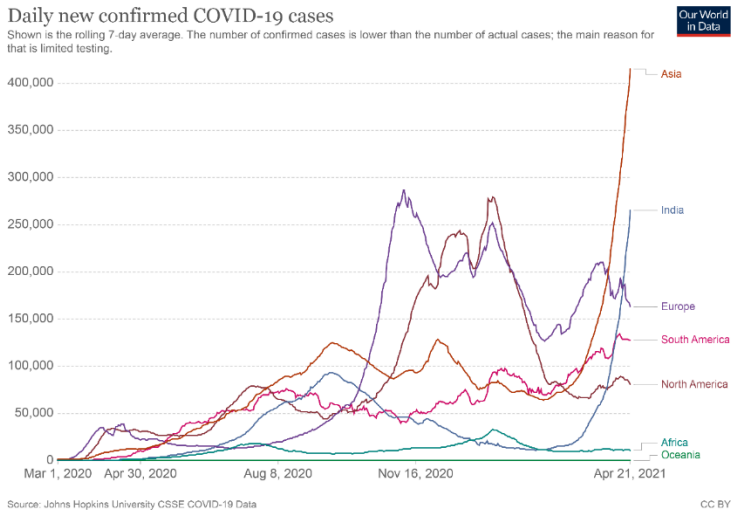
中国累计确诊 **103,382** 例，累计死亡 **4,856** 例，当日新增确诊 **11** 例，新增死亡 **0** 例。

截至 2021 年 4 月 21 日，31 个省（自治区、直辖市）和新疆生产建设兵团累计报告接种新冠病毒疫苗 **20419.1 万**剂次。

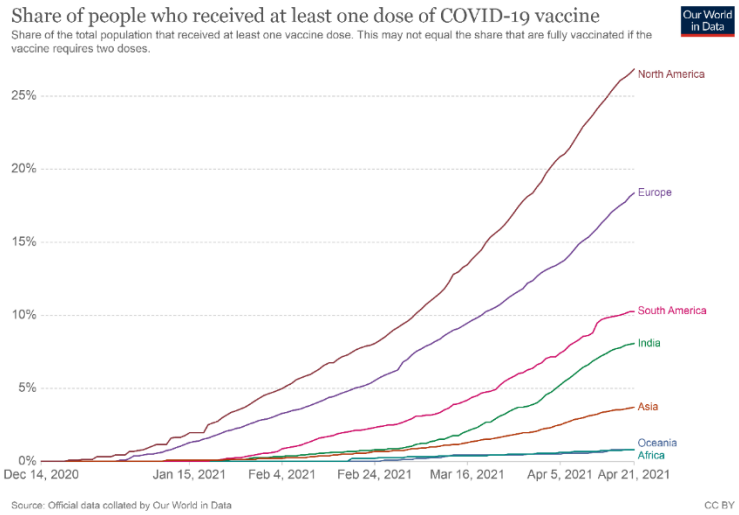
（http://www.nhc.gov.cn/xcs/yqfkdt/202104/7596959f303944f0965a75f7f9ef5539.shtml）



世界各洲及重点国家确诊人数曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



世界各洲每日新增确诊人数曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



世界各洲接受至少一剂 COVID-19 疫苗的人群比例（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（2021 年 4 月 22 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 焚尸炉烧熔，单日新增 31 万破世界纪录：印度疫情为何失控

来源：丁香园公众号

发布时间：2021-04-24

链接：https://mp.weixin.qq.com/s/hzqglnoa4FfWMQGi57F8rw

导读：

最近几天，印度新冠疫情受到了全世界的关注。

4 月 22 日，印度单日新增确诊 314835 例，创下新冠疫情爆发以来全世界单日新增确诊的最高纪录。同日，印度新增死亡 2104 例，也创下了该国单日新增死亡的最高值。

这篇文章从防疫政策改变、病毒变种、疫苗短缺等多方面分析了印度疫情加重的原因。

3. 支持新型冠状病毒空中传播的十大科学理由

Ten scientific reasons in support of airborne transmission of SARS-CoV-2

来源：The lancet
发布时间：2021-04-15
链接：https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00869-2/fulltext
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DOI 或 PUBMED ID：https://doi.org/10.1016/S0140-6736(21)00869-2
编译者：孔娟
中文摘要：
研究人员认为在某些空气样本中缺乏新型冠状病毒的直接证据来怀疑空气传播，而忽视总体证据基础的质量和强度，是一个科学错误。研究者从 10 个方面分析了新型冠状病毒通过空气传播传播的证据。首先，超传播事件解释了大量的新型冠状病毒传播；事实上，这类事件可能是大流行的主要驱动因素。第二，在隔离酒店中相互没有交叉在场的情况下相邻房间中的人之间的远距离传播。第三，无症状的传播（不咳嗽或不打喷嚏）占比高达 59%，说话会产生数以千计的气溶胶粒子和少量的大液滴这支持了空气传播。第四，新型冠状病毒的传播在室内高于室外。第五：采取了严格的接触和飞沫预防措施（这些措施不包括气溶胶暴露）的医疗机构中的院内感染。第六，在空气中检测到了存活的新型冠状病毒。第七，已在新冠肺炎患者医院的空气过滤器和建筑管道中检测出新型冠状病毒；只有通过气溶胶才能到达这些地点。第八，通过空气管道连接的未感染动物和感染动物饲养笼，未感染动物被感染。第九，据我们所知，没有研究提供强有力或一致的证据来反驳空中新型冠状病毒传播的假设。第十，支持其他主要传播途径比如呼吸道飞沫和污染物传播的证据有限。

Abstract:
we propose that it is a scientific error to use lack of direct evidence of SARS-CoV-2 in some air samples to cast doubt on airborne transmission while overlooking the quality and strength of the overall evidence base. Ten streams of evidence collectively support the hypothesis that SARS-CoV-2 is transmitted primarily by the airborne route. First, superspreading events account for substantial SARS-CoV-2 transmission; indeed, such events may be the pandemic’s primary drivers. Second, long-range transmission of SARS-CoV-2 between people in adjacent rooms but never in each other’s presence has been documented in quarantine hotels.7 Historically, it was possible to prove long-range transmission only in the complete absence of community transmission. Third, asymptomatic or presymptomatic transmission of SARS-CoV-2 from people who are not coughing or sneezing is likely to account for at least a third, and perhaps up to 59%.Fourth, transmission of SARS-CoV-2 is higher indoors than outdoors10 and is substantially reduced by indoor ventilation.5 Both observations support a predominantly airborne route of transmission. Fifth, nosocomial infections have been documented in health-care organisations. Sixth, viable SARS-CoV-2 has been detected in the air. Seventh, SARS-CoV-2 has been identified in air filters and building ducts in hospitals with COVID-19 patients; such locations could be reached only by aerosols. Eighth, studies involving infected caged animals that were connected to separately caged uninfected animals via an air duct have shown transmission of SARS-CoV-2 that

can be adequately explained only by aerosols. Ninth, no study to our knowledge has provided strong or consistent evidence to refute the hypothesis of airborne SARS-CoV-2 transmission.Tenth, there is limited evidence to support other dominant routes of transmission—ie, respiratory droplet or fomite.

4. SARS-CoV-2 变种突破疫苗感染

Vaccine Breakthrough Infections with SARS-CoV-2 Variants

来源：nejm

发布时间：2021-04-21

文章链接：https://www.nejm.org/doi/full/10.1056/NEJMoa2105000?query=TOC

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DOI: 10.1056/NEJMoa2105000

编译者：张怡

中文摘要：

SARS-CoV-2 的新变种值得临床关注。在一组 417 名至少 2 周前接受过 BNT162b2(Pfizer－BioNTech)或 mRNA-1273 (Moderna)第二剂疫苗的患者中，研究人员发现 2 名女性出现了疫苗突破感染。尽管有证据表明疫苗对这两名女性有效，但 SARS-CoV-2 感染的症状出现了，而且 SARS-CoV-2 核酸 PCR 检测呈阳性。病毒测序显示了可能具有临床重要性的变异，包括 1 名女性的 E484K 和两名女性的三个突变(T95I, del142-144 和 D614G)。这些观察结果表明，在成功接种疫苗和随后感染变异病毒后存在潜在的患病风险，并为继续努力预防和诊断感染和确定接种疫苗者的变异特征提供了支持。

Abstract

Emerging variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are of clinical concern. In a cohort of 417 persons who had received the second dose of BNT162b2 (Pfizer－BioNTech) or mRNA-1273 (Moderna) vaccine at least 2 weeks previously, we identified 2 women with vaccine breakthrough infection. Despite evidence of vaccine efficacy in both women, symptoms of coronavirus disease 2019 developed, and they tested positive for SARS-CoV-2 by polymerase-chain-reaction testing. Viral sequencing revealed variants of likely clinical importance, including E484K in 1 woman and three mutations (T95I, del142－144, and D614G) in both. These observations indicate a potential risk of illness after successful vaccination and subsequent infection with variant virus, and they provide support for continued efforts to prevent and diagnose infection and to characterize variants in vaccinated persons. (Funded by the National Institutes of Health and others.)

5. 截止 2021 年 4 月 20 日，美国 CDC 报道有 7157 位完成疫苗接种者主动报告发生突破性感染（8700 多万人完成了完整的疫苗接种）

Total number of vaccine breakthrough infections reported to CDC	7,157
Females	4,580 (64%)
People aged ≥60 years	3,265 (46%)
Asymptomatic infections	2,078 (31%)
Hospitalizations*	498 (7%)
Deaths†	88 (1%)

*167 (34%) of the 498 hospitalizations were reported as asymptomatic or not related to COVID-19.
†11 (13%) of the 88 fatal cases were reported as asymptomatic or not related to COVID-19.

发布时间：2021-04-20
来源：CDC
链接：https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html

6. TCR 谱畸变定义了儿童多系统炎症综合征

Distorted TCR repertoires define multisystem inflammatory syndrome in children
来源：medRxiv
发布时间：2021-04-15
链接：https://www.medrxiv.org/content/10.1101/2021.04.12.21255098v1
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DOI 或 PUBMED ID：
编译者：王玮
中文摘要：

虽然大多数感染 SARS-CoV-2 的儿童表现出轻微症状或无症状，但也在很少人中出现以多系统炎症综合征（MIS-C）为表现的严重疾病。临床表现多样的原因尚不清楚。该研究对 TCR 进行了测序，并对重度（n=12）或轻度（n=8）COVID-19 患儿的 TCR 序列进行了比较分析。我们将这些 TCR 组与未暴露的个体（收集的样本为前 COVID-19 大流行：n=8）以及 Adaptive Biotechnologies MIRA dataset（MIRA 数据集，其中包括超过 135000 个高置信度 SARS-CoV-2 特异性 tcr）进行了比较。该研究发现，重病儿童的基因库以 TRBV11-2 链的扩增为特征，具有高度的 junction 区域和 CDR3 多样性。此外，TRBV11-2 克隆的 CDR3 序列偏离 SARS-CoV-2 特异性 T 细胞克隆，导致 TCR 序列畸变。总之，该研究报告了 TRBV11-2+细胞的 CDR3 非依赖性扩增，缺乏 SARS-CoV-2 特异性，决定了儿童疾病的严重程度。

Abstract:

While the majority of children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) display mild or no symptoms, rare individuals develop severe disease presenting with multisystem inflammatory syndrome (MIS-C). The reason for variable clinical manifestations is not understood. Here, we carried out TCR sequencing and conducted comparative analyses of TCR repertoires between children with severe (n=12) or mild (n=8) COVID-19. We compared these repertoires with unexposed individuals (samples collected pre-COVID-19 pandemic: n=8) and with the Adaptive Biotechnologies MIRA dataset, which includes over 135,000 high-

confidence SARS-CoV-2-specific TCRs. We show that the repertoires of severely ill children are characterised by the expansion of TRBV11-2 chains with high junctional and CDR3 diversity. Moreover, the CDR3 sequences of TRBV11-2 clones shift away from SARS-CoV-2 specific T cell clones, resulting in distorted TCR repertoires. In conclusion, our study reports that CDR3-independent expansion of TRBV11-2+ cells, lacking SARS-CoV-2 specificity, defines severity of disease in children.

7. 医护人员 COVID-19 轻症 8 个月后的症状和功能障碍评估

Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers

来源：JAMA network

发布时间：2021-04-07

链接：https://jamanetwork.com/journals/jama/fullarticle/2778528

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DOI 或 PUBMED ID：10.1001/jama.2021.5612

编译者：宋张悦

中文摘要：

大约 80%的 COVID-19 住院患者在感染开始几个月后报告有持续症状。然而，对 COVID-19 轻症患者的长期预后知之甚少，发病率数据受到选择偏差和次优对照组的阻碍。本队列研究调查了医护人员中与 COVID-19 相关的长期症状。

该研究从 2020 年 4 月至 2021 年 1 月，在瑞典斯德哥尔摩 Danderyd 医院的医护人员（2149/4375 人，49%）中进行，其中有 393 人呈血清阳性。最终有 323 名（94%）血清阳性和 1072 名（84%）血清阴性参与者完成了 8 个月的随访，参与者通过智能手机应用程序报告症状等进行评估。

这项研究的结果表明，相当一部分患有轻度 COVID-19 的低风险个体报告了多种长期症状，并且这些症状扰乱了工作，社交和家庭生活。该研究的局限性包括回忆偏倚的可能性和症状的主观评价。需要进一步的研究来了解与 COVID-19 相关的长期性后遗症的潜在机制。

Abstract:

Approximately 80% of hospitalized patients with COVID-19 report persistent symptoms several months after infection onset. However, knowledge of long-term outcomes among individuals with mild COVID-19 is scarce, and prevalence data are hampered by selection bias and suboptimal control groups. This cohort study investigated COVID-19–related long-term symptoms in health care professionals.

8. 免疫细胞图谱显示地塞米松可以改变 COVID-19 特异性中性粒细胞动态变化轨迹

An Immune Cell Atlas Reveals Dynamic COVID-19 Specific Neutrophil Programming Amendable to Dexamethasone Therapy

来源：biorxiv

发布时间：2021-04-19

文章链接：https://www.biorxiv.org/content/10.1101/2021.04.18.440366v1

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doi: https://doi.org/10.1101/2021.04.18.440366
编译者：张怡
中文摘要：
SARS-CoV-2 是一种新型冠状病毒，可导致急性呼吸窘迫综合征(ARDS)、死亡和长期后遗症。先天免疫细胞对宿主防御至关重要，但也是 ARDS 的主要驱动因素。与细菌脓毒症等其他 ARDS 病因相比，COVID-19 导致的 ARDS 先天免疫细胞反应之间的关系尚不清楚。此外，地塞米松治疗在 COVID-19 重症期间的有益效果仍是推测性的，但了解其机制效应可改善循证治疗干预。为了探究这些关系，研究者们开发了一个免费访问的 scRNAseq 数据集(https://www.biernaskielab.ca/COVID_neutrophil)。与细菌性 ARDS 相比，COVID-19 伴有明显的中性粒细胞极化，其特征是干扰素(IFN)或前列腺素(PG)活性状态。来自细菌性 ARDS 的中性粒细胞有较高的抗菌分子表达，如 PLAC8 和 CD83。地塞米松治疗 COVID - 19 患者可迅速改变 IFN 激活状态，下调干扰素应答基因，激活 IL1R2+ve 中性粒细胞。地塞米松还诱导了表达免疫抑制分子 ARG1 和 ANXA1 的未成熟中性粒细胞的出现，这在健康对照中不存在。此外，地塞米松通过将中性粒细胞从信息接受者转变为信息提供者，重塑了整体的细胞相互作用。重要的是，男性患者有更高比例的 IFN 激活的中性粒细胞和更大程度的激素诱导的未成熟中性粒细胞扩增。事实上，具有 IFN 激活的中性粒细胞的最高比例与死亡率有关。这些结果定义了 COVID-19 在与其他危及生命的感染结合时所特有的中性粒细胞状态，从而增强了研究者们发现的相关性。此外，还定义了地塞米松治疗的分子效益。已确定的分子途径现在可以用于开发改进的治疗方案--支持先天免疫反应但是不偶联 IFN 放大的中心粒细胞反应的免疫治疗，这样可以限制由于中性粒细胞可能带来的病理症状，从而为重症 COVID-19 提供巨大的临床疗效。
Abstrac
SARS-CoV-2 is a novel coronavirus that causes acute respiratory distress syndrome (ARDS), death and long-term sequelae. Innate immune cells are critical for host defense but are also the primary drivers of ARDS. The relationships between innate cellular responses in ARDS resulting from COVID-19 compared to other causes of ARDS, such as bacterial sepsis is unclear. Moreover, the beneficial effects of dexamethasone therapy during severe COVID-19 remain speculative but understanding the mechanistic effects could improve evidence-based therapeutic interventions. To interrogate these relationships, we developed an scRNAseq atlas that is freely accessible (https://www.biernaskielab.ca/COVID_neutrophil). We discovered that compared to bacterial ARDS, COVID-19 was associated with distinct neutrophil polarization characterized by either interferon (IFN) or prostaglandin (PG) active states. Neutrophils from bacterial ARDS had higher expression of antibacterial molecules such as PLAC8 and CD83. Dexamethasone therapy in COVID patients rapidly altered the IFNactive state, downregulated interferon responsive genes, and activated the IL1R2+ve neutrophils. Dexamethasone also induced the emergence of immature neutrophils expressing immunosuppressive molecules ARG1 and ANXA1, which were not present in healthy controls. Moreover, dexamethasone remodeled global cellular interactions by changing neutrophils from information receivers into information providers. Importantly, male patients had higher

proportions of IFNactive neutrophils and a greater degree of steroid-induced immature neutrophil expansion. Indeed, the highest proportion of IFNactive neutrophils was associated with mortality. These results define neutrophil states unique to COVID-19 when contextualized to other life-threatening infections, thereby enhancing the relevance of our findings at the bedside. Furthermore, the molecular benefits of dexamethasone therapy are also defined. The identified molecular pathways can now be targeted to develop improved therapeutics.

9. mRNA-1273 免疫预防非人灵长类 SARS-CoV-2 感染的免疫相关性研究

Immune Correlates of Protection by mRNA-1273 Immunization against SARS-CoV-2 Infection in Nonhuman Primates

来源：bioRxiv

发布时间：2021-04-21

链接：https://www.biorxiv.org/content/10.1101/2021.04.20.440647v1

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中文摘要：

免疫保护相关动物可作为疫苗有效性的替代终点。SARS-CoV-2 感染的非人类灵长类动物（NHP）模型复制了人类感染的关键特征，可用于定义接种后保护的免疫相关关系。该研究中，NHP 没有接种疫苗或剂量范围为 0.3-100 微克的 mRNA-1273，mRNA-1273 是一种编码预扩散稳定 SARS-CoV-2 刺突（S-2P）蛋白的 mRNA 疫苗，封装在脂质纳米颗粒中。mRNA-1273 疫苗以剂量依赖的方式诱导了稳健的循环抗体和粘膜抗体反应。接种动物在暴露 SARS-CoV-2 后的支气管肺泡灌洗和鼻拭子病毒复制明显减少，减少的程度与抗 S 抗体结合以及中和活性水平密切相关。疫苗诱导的 IgG 被动转移到为接触过病毒的仓鼠，足以介导保护，这与抗体作为一种免疫防护因子一致。综合以上数据，mRNA-1273 疫苗诱导的体液免疫反应是疫苗对作为非人灵长类中抗 SARS-CoV-2 感染的免疫防护因子的机制之一。

Abstract:

Immune correlates of protection can be used as surrogate endpoints for vaccine efficacy. The nonhuman primate (NHP) model of SARS-CoV-2 infection replicates key features of human infection and may be used to define immune correlates of protection following vaccination. Here, NHP received either no vaccine or doses ranging from 0.3-100 micrograms of mRNA-1273, a mRNA vaccine encoding the prefusion-stabilized SARS-CoV-2 spike (S-2P) protein encapsulated in a lipid nanoparticle. mRNA-1273 vaccination elicited robust circulating and mucosal antibody responses in a dose-dependent manner. Viral replication was significantly reduced in bronchoalveolar lavages and nasal swabs following SARS-CoV-2 challenge in vaccinated animals and was most strongly correlated with levels of anti-S antibody binding and neutralizing activity. Consistent with antibodies being a correlate of protection, passive transfer of vaccine-induced

IgG to naive hamsters was sufficient to mediate protection. Taken together, these data show that mRNA-1273 vaccine-induced humoral immune responses are a mechanistic correlate of protection against SARS-CoV-2 infection in NHP.

10. 终于来了！国产新冠疫苗最大规模真实世界研究结果发布

来源：丁香园

发布时间：2021-04-18

链接：https://mp.weixin.qq.com/s/hvl8XaGZo5aIAvvpwMJovQ

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中文摘要：

北京时间 4 月 16 日晚，智利卫生部公布了科兴新冠疫苗的真实世界研究结果：（1）整体有效率：67%；（2）预防住院有效率：85%；（3）预防 ICU 有效率：89%；（4）预防死亡有效率：80%。以整体有效率为例，只接种第一针疫苗 14 天后，整体有效率为 16%；而接种第二针疫苗 14 天后，整体有效率提升至 67%（疫苗要发挥完全功效，需要等到第二针打完 7～14 天后）；以预防死亡有效率为例，只接种第一针疫苗 14 天后，预防死亡有效率为 40%；而接种第二针疫苗 14 天后，预防死亡有效率提升至 80%。只打一针，疫苗无法发挥出最大功效，接种者还是有较大概率感染病毒以及出现症状，只有完整接种才能有效压低曲线。所以智利卫生部的研究结论是：（1）在大流行的情况下，易感人群（老年人和慢性病患者）接种疫苗可以有效降低出现感染症状以及重症的概率；（2）因为没有 100% 有效的疫苗，全面接种疫苗很重要；（3）除了接种疫苗以外，还需要重视公共卫生措施（比如勤洗手戴口罩保持社交距离），限制人员流动也很重要。所以，经过实战考验，科兴疫苗的有效性得到了充分论证。总体而言，智利的真实世界研究是国产疫苗首个真刀真枪的考验，结果是鼓舞人心的，这个结果也给我们国内接下来的防控工作提供了指导：（1）想实现群体免疫，疫苗接种率需要达到一个非常高的数值；（2）不要一打完疫苗就出去浪，疫苗完全起效需要一定时间；（3）即便打完疫苗，做好个人的防护工作仍然非常重要。

11. 泛冠状病毒疫苗也许可以预防另一次大流行

Vaccines that can protect against many coronaviruses could prevent another pandemic

来源：Science

发表时间：2021-4-15

链 接 ： https://www.sciencemag.org/news/2021/04/vaccines-can-protect-against-many-coronaviruses-could-prevent-another-pandemic

作者：Jon Cohen（Staff writer for Science）

编译者：雷颖

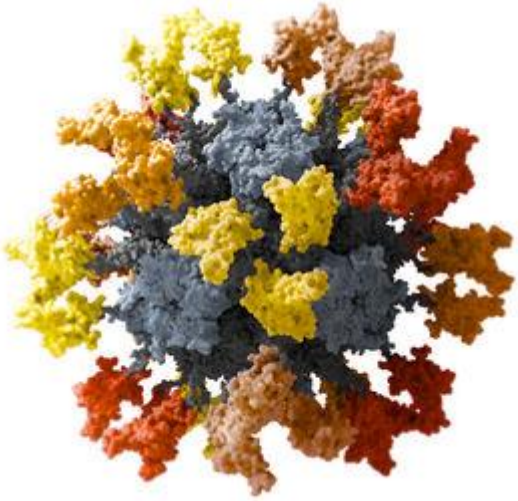
中文摘要：

尽管仍有许多未知情况，抗 SARS-CoV-2 疫苗的快速成功激发了人们的乐观情绪。不过，在未来的 10 至 50 年中，我们可能还会爆发另一起类似 SARS-CoV-2 的暴发。一种具有广泛保护作用的疫苗可能有助于结束当前的大流行并阻止下一场大流行。因此，许多科学家致力于研发这种泛冠状病毒疫苗。有些团队研究能产生广泛抗体的抗原，包括多种病毒的受体结合结构域（RBD）、刺突三聚体、S2 亚基以及 mRNA 嵌合体、小蛋白质多聚体等不同策略；有些团队则寻找可以触发 T 细胞反应且在不同冠状病毒之间差异很小的病毒蛋白区域。还有一种古老的方法可以预防泛冠状病毒，这种疫苗应同时参与 B 细胞和 T 细胞的战斗，例如结合

来自β属的四个已知谱系的代表性冠状病毒的灭活疫苗。某些抗原会提供抗体，某些抗原可能会带来更多的T细胞反应，某些抗原可能会同时起到两种作用。一些抗原可能比全身免疫更能诱导粘膜免疫。但是现在尚无泛冠状病毒疫苗进入人体试验，如何评估候选疫苗对尚未出现的疾病的防护也仍然是一个挑战。

一个反冠状病毒疫苗示意图

A pancoronavirus vaccine might contain a nanoparticle carrier (gray) that holds several different versions of the viral spike protein (other colors).



Abstract

In 2017, three leading vaccine researchers submitted a grant application with an ambitious goal. At the time, no one had proved a vaccine could stop even a single beta coronavirus—the notorious viral group then known to include the lethal agents of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), as well as several causes of the common cold and many bat viruses. But these researchers wanted to develop a vaccine against them all.

12. Ad26.COV2.S疫苗接种后的血栓性血小板减少症-制造商的回应

Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination — Response from the Manufacturer

来源：The NEW ENGLAND JOURNAL of MEDICINE

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DOI或PUBMED ID：10.1056/NEJMc2106075

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中文摘要：

Muir 等人的一例病例描述了针对严重急性呼吸系统综合症冠状病毒 2（SARS-CoV-2）的 Ad26.COV2.S 疫苗（Johnson＆Johnson / Janssen）接受者的血栓形成，包括脑静脉窦血栓形成（CVST），与严重的血小板减少症和弥散性血管内凝血有关。在我们的 Janssen

Ad26.COV2.S 疫苗临床试验计划的 75,000 多名参与者中（其中大约 50,000 名接受了活性疫苗），在疫苗接受者中发生了 1 例伴有血小板减少症的 CVST。我们暂停了我们的程序，以便从我们的第 3 阶段研究中审查此案例；与外部临床专家协商后，没有明确的因果关系，数据和安全监控委员会同意我们可以重新开始研究。随后发现该事件发生时，疫苗接种者具有针对血小板因子 4（PF4）的抗体，这一发现与 Muir 及其同事描述的情况相似。作为我们授权后药物警戒计划的一部分，Janssen 正在进行的安全性监视收到了六例 CVST 伴有血小板减少症的报告，这些病例在疫苗接种后 7 到 14 天发生，包括 Muir 等人描述的病例。 2021 年 4 月 13 日，出于谨慎考虑，美国食品药品管理局（FDA）和疾病控制与预防中心（CDC）建议暂停在美国接种 Ad26.COV2.S 疫苗，以便进行进一步研究的情况，并为医生提供有关低血小板型 CVST 的诊断，治疗和报告的指导。截至 2021.3 年 4 月 14 日，全球已有 720 万人接种了 Ad26.COV2.S 疫苗，从这些人中报告了这些病例。因此，报告率低于每 1,000,000 疫苗接种一个病例的报告率，尽管该病例可能会被漏报。

目前，证据不足以确定这些事件与 Ad26.COV2.S 疫苗之间的因果关系。CVST 是一种非常罕见的健康状况，4 到目前为止，Ad26.COV2.S 疫苗接种者的发病率在公布的背景发病率范围内（每 10 万人-年 0.2 至 1.57）。值得注意的是，与血小板减少相关的 CVST 发病率尚不清楚，FDA 和 CDC 认为这是一种危险因素非常低的风险。

Muir 等人建议使用腺病毒（Ad）载体平台的冠状病毒 2019（Covid-19）疫苗可能与血栓性血小板减少症的发生有关。需要更多的证据来阐明在接受针对 Covid-19 的疫苗的人群中血栓性血小板减少症的观察结果。

我们继续与专家和监管机构密切合作，评估数据，并支持向卫生保健专业人员和公众公开这些信息。

Abstract:

A case report by Muir et al.describes thrombosis, including cerebral venous sinus thrombosis (CVST), associated with severe thrombocytopenia and disseminated intravascular coagulation in a recipient of the Ad26.COV2.S vaccine (Johnson & Johnson/Janssen) against severe acute respiratory syndrome coronavirus (SARS-CoV-2). Among the more than 75,000 participants in the clinical trial program for our Janssen Ad26.COV2.S vaccine (of which approxi-mately 50,000 received active vaccine), a single case of CVST with thrombocytopenia occurred in a vaccine recipient. We paused our program to review this case from our first phase 3 study; after consultation with external clinical experts, no clear causality was established, and the data and safety monitoring board agreed that we could restart the study. The vaccine recipient was subsequently found to have had antibodies against platelet factor 4 (PF4) at the time of the event, a finding similar to that in the case de-scribed by Muir and colleagues. As part of our postauthorization pharmacovigilance program, Janssen ongoing safety surveillance received re-ports of six cases of CVST with thrombocytopenia occurring 7 to 14 days after vaccination, including the case described by Muir et al. On April 13, 2021, in an abundance of caution, the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) recommended a pause in vaccination with Ad26.COV2.S in the United States to allow further study of the situation and to provide physicians guidance on the diagnosis, treatment, and reporting of CVST in combination with low platelets. These cases were reported among more than 7.2 million persons who had been vaccinated with

Ad26.COV2.S globally as of April 14, 2021. Thus, the reporting rate is less than 1 in 1,000,000 vaccinations, though it is possible that the cases are underreported.

At this time, evidence is insufficient to establish a causal relationship between these events and the Ad26.COV2.S vaccine. CVST is a very rare health condition, and thus far, events reported in recipients of the Ad26.COV2.S vaccine are occurring within the range of published background incidence (0.2 to 1.57 per 100,000 person-years).It is important to note that the incidence of CVST associated with low platelets is unknown and is considered by the FDA and the CDC to be extremely low.

Muir et al. suggested that coronavirus 2019 (Covid-19) vaccines using an adenoviral (Ad) vector platform may be related to the occurrence of thrombotic thrombocytopenia. Recent reports by Greinacher et al. and Schultz et al. (both published on April 9, 2021,at NEJM.org) concluded that vaccination with the ChAdOx1 nCoV-19 vaccine (Oxford–AstraZeneca) may lead to rare thrombotic thrombocytopenia (see references S1 and S2 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). The vectors and spike (S) protein inserts used in the ChAdOx1 nCoV-19 vaccine and the Ad26.COV2.S vaccine are substantially different. The Ad26.COV2.S vaccine uses a human Ad26–based vector, whereas the ChAdOx1 nCoV-19 vaccine uses a chimpanzee adenovirus–based vector (references S3 and S4). Ad26 is from Ad species D and can engage CD46 as its cellular receptor, whereas ChAdOx1 nCoV-19 is from Ad species E and uses the Coxsackie and adenovirus receptor (CAR) and possibly other molecules as its cellular receptors; these two vectors thus use different host cell receptors and are likely to have different phylogenetic and biologic characteristics.In addition,the Ad26.COV2.S vaccine transgene codes for a membrane-bound SARS-CoV-2 S protein (prefu-sion conformation–stabilized by two proline sub-stitutions) that does not shed S1, most likely as a consequence of knocking out the furin cleavage site (reference S5), which is different from the unmodified S protein encoded by the ChAdOx1 nCoV-19 vaccine. Therefore, these two adenoviral vector Covid-19 vaccines may have quite different biologic effects. More evidence is needed to clarify the observation of thrombotic thrombocytopenia in persons receiving a vaccine against Covid-19.

We continue to work closely with experts and regulators to assess the data, and we support the open communication of this information to health care professionals and the public.

13. 抗 Covid-19 单剂量 Ad26.COV2.S 疫苗的安全性和有效性

Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

来源：The NEW ENGLAND JOURNAL of MEDICINE

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编译者：张鹏伟
中文摘要：
背景：
Ad26.COV2.S 疫苗是一种重组、复制不全的人腺病毒 26 型载体，以融合前稳定的构象编码全长严重急性呼吸综合征冠状病毒 2（SARS-CoV-2）spike 蛋白。
方法：
在一项国际性，随机，双盲，安慰剂对照的 3 期试验中，我们以 1：1 的比例随机分配了成年参与者，以接受单剂量的 Ad26.COV2.S（5×1010 病毒颗粒）或安慰剂。主要目的是针对 SARS-CoV-2 检测阴性的符合方案人群参与者中的中重度严重冠状病毒病 2019（Covid-19）的疫苗效力，至少在给药后 14 天和 28 天发病。安全性也进行了评估。
结果：
每个方案的人群包括 19630 名 SARS-CoV-2 阴性参与者，他们接受 Ad26.COV2.S 和 19691 名接受安慰剂治疗。Ad26.COV2.S 可防止中重度临界 Covid-19，在给药后至少 14 天内发病（疫苗组 116 例，安慰剂组 348 例；疗效 66.9%；调整 95%置信区间[CI]，59.0 至 73.4），并至少在给药后 28 天（66 例与 193 例；疗效 66.1%；调整 95%CI，55.0 至 74.8）。对于严重-临界 Covid-19（76.7%[调整 95%CI，54.6 至 89.1]的疫苗在≥14 天时的起效率较高，85.4%[调整 95%CI、54.2 至 96.9]的疫苗有效性在≥28 天时出现。尽管南非 91 例（94.5%）中 86 例（94.5%）具有 20H/501Y.V2 变异的序列病毒，但疫苗对中重度临界 Covid-19 的疫苗疗效分别为 52.0%和 64.0%，起效至少为 14 天和用药后 28 天，对严重临界 Covid-19 的疗效分别为 73.1%和 81.7%。Ad26.COV2.S 组的反应原性高于安慰剂组，但一般为暂时性的轻度至中度。两组之间严重不良事件的发生率是平衡的。疫苗组有 3 例死亡（无 Covid-19 相关），安慰剂组有 16 例死亡（5 例 Covid-19 相关）。
结论：
单剂量的 Ad26.COV2.S 对有症状的 Covid-19 和无症状的 SARS-CoV-2 感染有保护作用，对严重的危重疾病（包括住院和死亡）有效。安全性似乎与 Covid-19 疫苗的其他 3 期试验相似。
Abstract:
BACKGROUND
The Ad26.COV2.S vaccine is a recombinant, replication-incompetent human adenovirus type 26 vector encoding full-length severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein in a prefusion-stabilized conformation.
METHODS
In an international, randomized, double-blind, placebo-controlled, phase 3 trial, we randomly assigned adult participants in a 1:1 ratio to receive a single dose of Ad26.COV2.S (5×1010 viral particles) or placebo. The primary end points were vaccine efficacy against moderate to severe-critical coronavirus disease 2019 (Covid-19) with an onset at least 14 days and at least 28 days after administration among participants in the per-protocol population who had tested negative for SARS-CoV-2. Safety was also assessed.
RESULTS
The per-protocol population included 19,630 SARS-CoV-2-negative participants

who received Ad26.COV2.S and 19,691 who received placebo. Ad26.COV2.S protected against moderate to severe-critical Covid-19 with onset at least 14 days after administration (116 cases in the vaccine group vs. 348 in the placebo group; efficacy, 66.9%; adjusted 95% confidence interval [CI], 59.0 to 73.4) and at least 28 days after administration (66 vs. 193 cases; efficacy, 66.1%; adjusted 95% CI, 55.0 to 74.8). Vaccine efficacy was higher against severe-critical Covid-19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥14 days and 85.4% [adjusted 95% CI, 54.2 to 96.9] for onset at ≥28 days). Despite 86 of 91 cases (94.5%) in South Africa with sequenced virus having the 20H/501Y.V2 variant, vaccine efficacy was 52.0% and 64.0% against moderate to severe-critical Covid-19 with onset at least 14 days and at least 28 days after administration, respectively, and efficacy against severe-critical Covid-19 was 73.1% and 81.7%, respectively. Reactogenicity was higher with Ad26.COV2.S than with placebo but was generally mild to moderate and transient. The incidence of serious adverse events was balanced between the two groups. Three deaths occurred in the vaccine group (none were Covid-19-related), and 16 in the placebo group (5 were Covid-19-related).

CONCLUSIONS

A single dose of Ad26.COV2.S protected against symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection and was effective against severe-critical disease, including hospitalization and death. Safety appeared to be similar to that in other phase 3 trials of Covid-19 vaccines.

14. ChAdOx1 nCoV-19 疫苗接种后的血小板因子 4 的病理学抗体产生

Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination

来源：NEJM

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链接：https://www.nejm.org/doi/full/10.1056/NEJMoa2105385?query=TOC

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DOI 或 PUBMED ID：10.1056/NEJMoa2105385

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中文摘要：

控制新冠病毒大流行的主要方法是针对 SARS-CoV-2 的疫苗接种。一年之内，已经开发了几种疫苗，并交付了数百万剂。近期，阿斯利康 ChAdOx1 nCoV-19 疫苗血栓不良事件引发关注。文中报告了 23 例在接受第一剂 ChAdOx1 nCoV-19 疫苗（阿斯利康）后 6 至 24 天出现血栓形成和血小板减少症的患者中的发现。基于它们的临床和实验室特征，作者确定了一种新颖的潜在机制并提供了治疗方案。在没有先前的血栓形成性疾病的情况下，有 22 例患者表现为急性血小板减少和血栓形成，主要是脑静脉血栓形成，还有 1 例表现为孤立的血小板减少症和出血性表型。所有患者在就诊时纤维蛋白原水平较低或正常，而 d-二聚体水平升高。没有发现血栓形成或致病性沉淀的证据。抗血小板因子 4（PF4）抗体的检测在 22 例患者中呈阳性（1 个模棱两可的结果），在 1 例患者中呈阴性。根据在这些患者中观察到的病理生理特征，我们建议避免使用血小板输注治疗，因为这会增加血栓形成症状的风险，并建议首

次使用非肝素抗凝剂和静脉内免疫球蛋白进行治疗。
结论:针对 SARS-CoV-2 的疫苗接种对于控制 Covid-19 大流行仍然至关重要。在使用 ChAdOx1 nCoV-19 疫苗后，可能会发生与肝素治疗无关的致病性 PF4 依赖综合征。由于对治疗具有意义，快速鉴定这种罕见综合征很重要。

Abstract:
BACKGROUND
The mainstay of control of the coronavirus disease 2019 (Covid-19) pandemic is vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Within a year, several vaccines have been developed and millions of doses delivered. Reporting of adverse events is a critical postmarketing activity.
METHODS
We report findings in 23 patients who presented with thrombosis and thrombocytopenia 6 to 24 days after receiving the first dose of the ChAdOx1 nCoV-19 vaccine (AstraZeneca). On the basis of their clinical and laboratory features, we identify a novel underlying mechanism and address the therapeutic implications.
RESULTS
In the absence of previous prothrombotic medical conditions, 22 patients presented with acute thrombocytopenia and thrombosis, primarily cerebral venous thrombosis, and 1 patient presented with isolated thrombocytopenia and a hemorrhagic phenotype. All the patients had low or normal fibrinogen levels and elevated d-dimer levels at presentation. No evidence of thrombophilia or causative precipitants was identified. Testing for antibodies to platelet factor 4 (PF4) was positive in 22 patients (with 1 equivocal result) and negative in 1 patient. On the basis of the pathophysiological features observed in these patients, we recommend that treatment with platelet transfusions be avoided because of the risk of progression in thrombotic symptoms and that the administration of a nonheparin anticoagulant agent and intravenous immune globulin be considered for the first occurrence of these symptoms.
CONCLUSIONS
Vaccination against SARS-CoV-2 remains critical for control of the Covid-19 pandemic. A pathogenic PF4-dependent syndrome, unrelated to the use of heparin therapy, can occur after the administration of the ChAdOx1 nCoV-19 vaccine. Rapid identification of this rare syndrome is important because of the therapeutic implications.

15. 孕妇中 mRNA 新冠肺炎疫苗安全性的初步研究

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons
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第一作者：Tom T. Shimabukuro
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Promotion
DOI 或 PUBMED ID：10.1056/NEJMoa2104983
编译者：孔娟
中文摘要：
背景 美国有许多孕妇正在接受 Covid-19 mRNA 疫苗，但关于其妊娠安全性的数据有限。
方法 从 2020 年 12 月 14 日至 2021 年 2 月 28 日，研究者使用了来自“v-safe 疫苗接种后健康检查人员”监测系统、v-safe 妊娠登记处和疫苗不良事件报告系统(VAERS)的数据来表征 mRNA 新冠肺炎疫苗在孕妇中的初始安全性。
结果 总计 35691 名 16 至 54 岁的 v-safe 登记怀孕参与者。注射部位疼痛在孕妇中的报告频率高于非孕妇，而头痛、肌痛、寒战和发热的报告频率较低。在 v-safe 妊娠登记处登记的 3958 名受试者中，827 人完成妊娠，其中 115 人(13.9%)流产，712 人(86.1%)活产(大多数在妊娠晚期接种疫苗的受试者中)。不良新生儿结局包括早产(9.4%)和小于胎龄儿(3.2%)；未报告新生儿死亡。尽管不具有直接可比性，但接种新冠肺炎疫苗且已完成妊娠的受试者中不良妊娠和新生儿结局的计算比例与涉及新冠肺炎大流行前孕妇的研究中报告的发病率相似。在 VAERS 报告的 221 例妊娠相关不良事件中，最常报告的事件是自然流产(46 例)。
结论 在接受 mRNA 新冠肺炎疫苗的孕妇中，初步结果未显示明显的安全问题。然而，有必要进行更多的纵向随访，包括对大量妊娠早期接种疫苗的妇女进行随访，以提前告知孕产妇、妊娠和婴儿可能产生的情况。
Abstract
BACKGROUND
Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy.
METHODS
From December 14, 2020, to February 28, 2021, we used data from the “v-safe after vaccination health checker” surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons.
RESULTS
A total of 35,691 v-safe participants 16 to 54 years of age identified as pregnant. Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. Among 3958 participants enrolled in the v-safe pregnancy registry, 827 had a completed pregnancy, of which 115 (13.9%) resulted in a pregnancy loss and 712 (86.1%) resulted in a live birth (mostly among participants with vaccination in the third trimester). Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%); no neonatal deaths were reported. Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases).

CONCLUSIONS
Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes.

16. 佐剂 COVID-19 亚单位疫苗诱导保护性免疫

Adjuvanting a subunit COVID-19 vaccine to induce protective immunity
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通讯作者：Bali Pulendran
通讯作者单位：美国斯坦福大学
DOI 或 PUBMED ID：https://doi.org/10.1038/s41586-021-03530-2
编译者：刘焕珍
中文摘要：
为全球人们提供 COVID-19 疫苗仍然是一项紧迫的公共卫生任务。在这里，我们研究了一种亚单位疫苗，该疫苗由在蛋白纳米颗粒（RBD-NP）上展示的 SARS-CoV-2 刺突受体结合域组成，能够刺激非人类灵长类动物的强大而持久的中和抗体（nAb）反应和对 SARS-CoV-2 的保护。我们评估了五种佐剂，包括（1）Essai O/W 1849101（一种角鲨烯水乳剂）；（2）AS03（一种含 α-生育酚的水包油乳液）；（3）AS37（一种吸附到明矾上的 TLR-7 激动剂）；（4）CpG1018-Alum（明矾中配制的 TLR-9 激动剂）；（5）明矾。用 AS03、CpG1018-Alum、AS37 或明矾免疫 RBD-NP 可诱导大量的 nAb 和 CD4 T 细胞反应，并对咽部、鼻腔和支气管肺泡灌洗液中具有抗 SARS-CoV-2 感染的作用。接种 RBD/AS03 疫苗后，活病毒 nAb 应答可维持到 180 天，并与保护作用相关。RBD-NP 免疫可有效地交叉中和 B.1.1.7 变种，但对 B.1.351 变种的应答降低。RBD-NP/AS03 显示对 B.1.351 的中和作用减少了 4.5 倍，而 RBD-NP/AS37 组的中和作用有 16 倍的减少，这表明这些佐剂诱导的 nAb 反应的广度不同。此外，RBD-NP/AS03 的免疫原性与 AS03 作为佐剂的融合前稳定免疫原（Hexapro）相同。这些数据突出了 RBD-NP 佐剂疫苗在促进 SARS-CoV-2 保护性免疫方面的功效，并为该疫苗在 I/II 期临床试验（NCT04742738 和 NCT04750343）中对该疫苗的临床评价铺平了道路。
Abstract:
The development of a portfolio of COVID-19 vaccines to vaccinate the global population remains an urgent public health imperative1. Here we demonstrate the capacity of a subunit vaccine, comprising the SARS-CoV-2 spike receptor binding domain displayed on a protein nanoparticle (RBD-NP), to stimulate robust and durable neutralizing antibody (nAb) responses and protection against SARS-CoV-2 in non-human primates.We evaluated five adjuvants including Essai O/W 1849101, a squalene-in-water emulsion; AS03, an alpha-tocopherol-containing oil-in-water emulsion; AS37, a TLR-7 agonist adsorbed to Alum; CpG1018-Alum, a TLR-9 agonist formulated in Alum; and Alum. RBD-NP immunization with AS03, CpG1018-Alum, AS37 or Alum induced substantial nAb and CD4 T cell responses, and conferred protection against SARS-CoV-2 infection in the pharynges, nares and bronchoalveolar lavage. Live-virus nAb response was maintained up to 180 days post-vaccination with

RBD/AS03, and correlated with protection. RBD-NP immunization cross-neutralized the B.1.1.7 variant efficiently but showed a reduced response against the B.1.351 variant. While RBD-NP/AS03 demonstrated a 4.5-fold reduction in neutralization of B.1.351, the RBD-NP/AS37 group showed a 16-fold reduction, suggesting differences in the breadth of the nAb response induced by these adjuvants. Furthermore, RBD-NP/AS03 was as immunogenic as a prefusion stabilized Spike immunogen (Hexapro) adjuvanted with AS03. These data highlight the efficacy of the adjuvanted RBD-NP vaccine in promoting protective immunity against SARS-CoV-2, and have paved the way for the clinical evaluation of this vaccine in Phase I/II clinical trials (NCT04742738 and NCT04750343).

17. COVID 疫苗和儿童：试验开始时的五个问题

COVID vaccines and kids: five questions as trials begin

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中文摘要：

《自然》杂志研究了与成年人相比，该试验如何解释儿童免疫系统和对 COVID-19 的敏感性，以及围绕儿童医学研究增加的安全预防措施。

（1）我们需要给孩子们接种疫苗吗？儿童很少出现严重的 COVID-19，死于这种疾病的情况更为罕见。但在罕见的情况下，比如估计 1000 人中一人，或者能更低的概率的情况下，有轻微感染的儿童，后来也会患上一种有时甚至致命的疾病，称为儿童多系统炎症综合征（MIS-C）。有证据表明，疫苗可能会阻止 SARS-CoV-2 的传播，因此给儿童接种疫苗可能会在更广泛的社区产生有益的连锁反应。

（2）在儿童身上的试验将如何运作？首批受试者将是年龄较大的受试者，尽管试验最终将包括 6 个月大的儿童，但他们将接受一系列剂量的治疗，以找到一种能引发强烈免疫反应而无太多副作用的药物。当参与者是儿童时，他们的法定监护人必须同意他们的参与。

（3）儿童和成人对 COVID-19 疫苗的反应是否不同？早期试验结果显示，12-15 岁接受两个标准剂量的辉瑞-生物泰克疫苗治疗的青少年比早期试验中 16-25 岁的青少年产生了更高水平的病毒阻断抗体。

（4）科学家如何知道疫苗是否对儿童有效？我们知道疫苗可以预防成人的 COVID-19，因为临床试验就是为了证明这一点。研究人员将数万人随机分为两组，一组接受疫苗治疗，另一组接受安慰剂治疗，结果显示两组的患病率存在显著差异。塔拉特说，在这项仅涉及几千名儿童的儿科试验中，症状性感染可能太少，无法以同样的方式衡量疗效。她说，接种疫苗后观察免疫标记物更有意义。

（5）研究人员如何知道疫苗对幼儿是否安全？在涉及儿童的临床试验中，安全性是最重要的，研究人员意识到在儿童身上进行的 COVID-19 疫苗试验将得到额外的审查。

Abstract:

Nature looks at how the trials will account for differences in children’s immune systems and susceptibility to COVID-19, compared with those of adults, as well as the added safety precautions that surround medical research in kids.

（1）Do we even need to vaccinate children? Children rarely develop severe forms of COVID-19, and deaths from the disease are rarer still. But on rare occasions — one estimate1 puts it at around one case in 1,000, although it could be even lower — kids who’ve experienced even mild infections can later develop a sometimes deadly condition called multi-system inflammatory syndrome in children (MIS-C). Evidence is building that vaccines might block transmission of SARS-CoV-2, so vaccinating children could have beneficial knock-on effects in the wider community.

（2）How will the trials in kids work? The first recipients — who will be on the older end of the spectrum, although trials will eventually include children as young as six months — will receive a range of doses to find one that triggers a strong immune response without too many side effects. When participants are children, however, their legal guardian must agree to their involvement.

（3）Will children and adults respond differently to COVID-19 vaccines? Early trial results have shown that 12–15-year-olds who received two standard doses of the Pfizer–BioNTech vaccine developed substantially higher levels of virus-blocking antibodies than did 16–25-year-olds in earlier trials.

（4）How will scientists know if vaccines work in children? We know that vaccines prevent COVID-19 in adults because the clinical trials were designed to show this. They involved tens of thousands of people randomly assigned to receive either the vaccine or a placebo, and showed compelling differences in the rates of disease between the two groups. In the paediatric trials, which will involve only a few thousand children, there might be too few symptomatic infections to measure efficacy in the same way, says Talaat. It makes more sense, she says, to look at immune markers after vaccination.

（5）How will researchers know if the vaccines are safe in young children? Safety is paramount in clinical trials involving children, and researchers are aware that COVID-19 vaccine trials in kids will get extra scrutiny.

18. 接种 BNT162b2 疫苗能够在以色列高危人群中有效预防 SARS-CoV-2 变异株 B.1.1.7 的快速传播

BNT162b2 Vaccination Effectively Prevents the Rapid Rise of SARS-CoV-2 Variant B.1.1.7 in high risk populations in Israel

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编译者：宋珂

亮点：

- 在以色列，SARS-CoV-2 病毒变异株 B.1.1.7 的传播率比野生株高 45%。
- 主动监控能够显着降低疗养院中 B.1.1.7 的传播率。
- 为老年人优先接种疫苗能够预防与 B.1.1.7 有关的感染。
- 主动监控并优先接种疫苗是能够实现的。

中文摘要：

自从 SARS-CoV-2 导致的疫情出现以来，病毒已经出现了多种遗传变异。2020 年 12 月在英国出现的变异株 B.1.1.7 的传染能力提高。因此，了解其传播方式非常重要。

以色列政府制定了三项全国计划：大规模 RT-PCR 测试，对疗养院进行重点监控，以及严格优先接种 BNT162b2 疫苗接种。为了评估上述计划的影响，作者分析了从 2020 年 12 月 6 日到 2021 年 2 月 10 日间收集的大约 300,000 个 RT-PCR 样本的数据。

作者发现，B.1.1.7 的传播率比野生型病毒株高 45%（95%CI：20-60%），并在 3.5 周内即成为以色列境内的主要病毒种。尽管病毒的传播快速增加，但有针对性的 RT-PCR 测试以及疫苗优先接种计划能够阻止 B.1.1.7 变异株在老年人群体中传的播。因此，主动监控并优先接种疫苗是能够实现的，并可以降低重症患者的数量和相应死亡人数。

Highlights:

- The B.1.1.7 variant is 45% more transmissible than the wild-type strain in Israel.
- Active surveillance markedly reduces the transmission of B.1.1.7 in nursing homes.
- Prioritized vaccination prevents B.1.1.7-associated infections in the elderly.
- Proactive surveillance combined with prioritized vaccination are achievable.

Abstract:

Since the emergence of the SARS-CoV-2 pandemic, various genetic variants have been described. The B.1.1.7 variant, which emerged in England during December 2020, is associated with increased infectivity. Therefore its pattern of spread is of great importance.

The Israeli government established three national programs: massive RT-PCR testing, focused surveillance in nursing homes and robust prioritized vaccination with BNT162b2. To define the impact of the aforementioned programs, we analyze data from ~300,000 RT-PCR samples collected from December 6th 2020 to February 10th 2021.

We reveal that the B.1.1.7 is 45% (95% CI:20-60%) more transmissible than the wild-type strain, and become the dominant in Israel within 3.5 weeks. Despite the rapid increase in viral spread, focused RT-PCR testing and prioritized vaccination programs are capable of preventing the spread of the B.1.1.7 variant in the elderly. Therefore, proactive surveillance combined with prioritized vaccination are achievable, and reduce severe illness and subsequent death.

19. 单次接种 BNT162b2 疫苗后对 SARS-CoV-2 变种和人冠状病毒的体液和细胞免疫应答

Humoral and cellular immune responses against SARS-CoV-2 variants and human coronaviruses after single BNT162b2 vaccination

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DOI 或 PUBMED ID：

编译者：宋张悦

中文摘要：

疫苗诱导的中和抗体是对抗 COVID-19 大流行的关键。然而，由于疫苗供应有限而推迟加强免疫接种可能使个人长期容易受到感染和疾病。SARS-CoV-2 变种 (variants of concern, VOC)，B.1.1.7(英国)、B.1.351(南非)和 P.1(巴西)的出现可能会加剧这一问题，因为后两者能够通过抗体逃避控制。我们评估了单次和双次接种 BNT162b2 后针对 SARS-CoV-2 野生型、VOC 突变株以及地方性冠状病毒（普通感冒病毒 hCoV-OC43, hCoV229E）产生的体液免疫和 T 细胞免疫反应。单次接种后第 14 天，虽然可以检测到抗 SARS-CoV-2 S 蛋白受体结合域(RBD)的 IgG，但对 SARS-CoV-2 S 驱动的宿主细胞进入的抑制作用很弱，尤其对 B.1.351 变异的抑制作用较低。单剂接种后，许多疫苗接种者 SARS-CoV-2 特异性 T 细胞的频率较低，并受到对地方性冠状病毒免疫的影响。第二次接种显著提高了对 WT、B.1.1.7 和 B.1.351 变异株反应的 T 细胞频率。这些结果让人质疑单次接种疫苗产出的中和抗体是否对预防 COVID-19 起到显著作用，并表明细胞免疫对 COVID-19 的早期防御至关重要。

Abstract:

Vaccine-induced neutralizing antibodies are key in combating the COVID-19 pandemic. However, delays of boost immunization due to limited availability of vaccines may leave individuals vulnerable to infection and disease for prolonged periods. The emergence of SARS-CoV-2 variants of concern (VOC), B.1.1.7 (United Kingdom), B.1.351 (South Africa) and P.1 (Brazil), may reinforce this issue with the latter two being able to evade control by antibodies. We assessed humoral and T cell responses against SARS-CoV-2 WT and VOC and endemic human coronaviruses (hCoV) that were induced after single and double vaccination with BNT162b2. Despite readily detectable IgG against the receptor-binding domain (RBD) of the SARS-CoV-2 S protein at day 14 after a single vaccination, inhibition of SARS-CoV-2 S-driven host cell entry was weak and particularly low for the B.1.351 variant. Frequencies of SARS-CoV-2 specific T cells were low in many vaccinees after application of a single dose and influenced by immunity against endemic hCoV. The second vaccination significantly boosted T cell frequencies reactive for WT, B.1.1.7 and B.1.351 variants. These results call into question whether neutralizing antibodies significantly contribute to protection against COVID-19 upon single vaccination and suggest that cellular immunity is central for the early defenses against COVID-19.

20. 对冠状病毒与宿主因子蛋白相互作用基序的大规模搜索，揭示了 SARS-CoV-2 的特定机制和脆弱点

Large scale discovery of coronavirus-host factor protein interaction motifs reveals SARS-CoV-2 specific mechanisms and vulnerabilities

来源：bioRxiv

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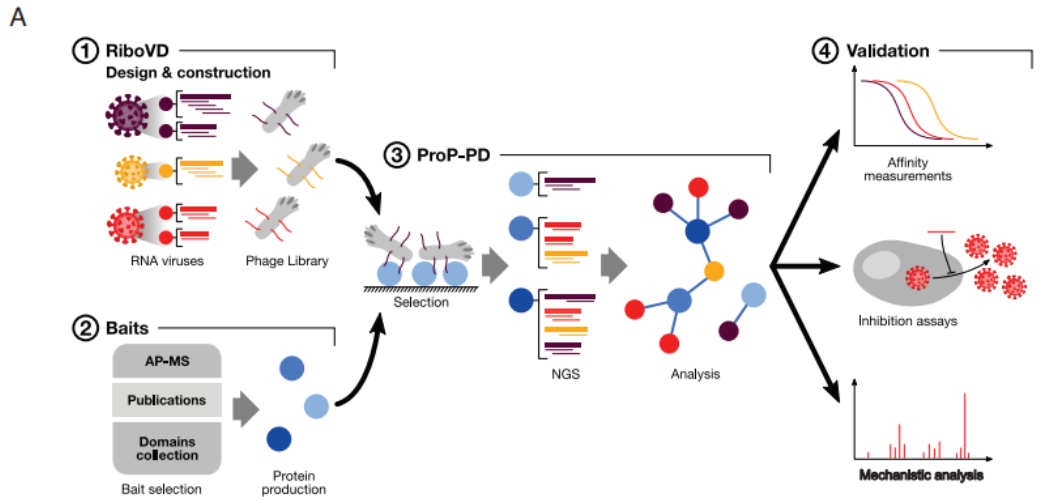
DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

病毒蛋白会大量利用短肽相互作用基序来劫持细胞宿主因子。然而，当前大多大规模的方法都无法用来鉴定此类重要的蛋白-蛋白相互作用。了解肽段介导的相互作用不仅可以提供病毒与其宿主间相互作用的分子机理，同时也为开发新型抗病毒药物奠定了基础。本文中，作者介绍了一种可扩展的病毒肽段发现方法，覆盖 229 种 RNA 病毒，可提供相关病毒与宿主直接相互作用的高分辨率信息。针对 18 种冠状病毒，作者鉴定出了 269 种基于肽段的相互作用，其中包括人源 G3BP1/2 蛋白与 SARS-CoV-2 病毒核衣壳蛋白（N）中的[FILV]xFG 肽段基序之间一种特异性的相互作用。这种相互作用促进病毒的复制过程，通过[FILV]xFG 基序，N 蛋白能够对 G3BP1/2 相互作用体进行干扰以破坏应激颗粒。利用一种干扰 G3BP1/2 与 N 相互作用的基于肽段的抑制剂，可以阻断 SARS-CoV-2 感染。这表明作者的成果能够直接转化为新型特异性抗病毒药物。

Figure 1. A pipeline for viral SLiM discovery



Abstract:
Viral proteins make extensive use of short peptide interaction motifs to hijack cellular host factors. However, most current large-scale methods do not identify this important class of protein-protein interactions. Uncovering peptide mediated interactions provides both a molecular understanding of viral interactions with their host and the foundation for developing novel antiviral reagents. Here we describe a scalable viral peptide discovery approach covering 229 RNA viruses that provides high resolution information on direct virus-host interactions. We identify 269 peptide-based interactions for 18 coronaviruses including a specific interaction between the human G3BP1/2 proteins and an [FILV]xFG peptide motif in the SARS-CoV-2 nucleocapsid (N) protein. This interaction supports viral replication and through its [FILV]xFG motif N rewires the G3BP1/2 interactome to disrupt stress granules. A peptide-based inhibitor disrupting the G3BP1/2-N interaction blocks SARS-CoV-2 infection showing that our results can be directly translated into novel specific antiviral reagents

21. 低剂量的 SARS-CoV-2 B1.1.7 突变株在仓鼠中引起的上呼吸道感染强于 D614G

Low dose inocula of SARS-CoV-2 B.1.1.7 variant initiate more robust infections in the upper respiratory tract of hamsters than earlier D614G variants

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中文摘要：

目前缺乏实验证据解释相比以前的病毒株 B1.1.1.7 突变株是怎样在人中传播更快的。我们发现 B1.1.1.7 在体外系统中比早先的 D614G 病毒株表现中更强的竞争适应性。进一步我们发现 B1.1.1.7 相比其他突变株相比，更低的剂量暴露更短的时间，鼻腔里就可以更高效地脱落。

Abstract:
There is a lack of experimental evidence to explain how the B.1.1.7 variant spreads more quickly than pre-existing variants in humans. We found that B.1.1.7 displays increased competitive fitness over earlier D614G lineages in an *in-vitro* system. Furthermore, we demonstrated that B.1.1.7 variant is able to replicate and shed more efficiently in the nasal cavity than other variants with lower dose and shorter duration of exposure.

22. 特异针对 SARS-CoV-2 衣壳蛋白的主要免疫抗原原表位的 CD8+阳性细胞很多是高度初始化的前体细胞，并且其 T 细胞受体配对存在很高的异质性

CD8+ T cells specific for an immunodominant SARS-CoV-2 nucleocapsid epitope display high naïve precursor frequency and T cell receptor promiscuity

链接：https://www.cell.com/immunity/fulltext/S1074-7613(21)00171-0#%20

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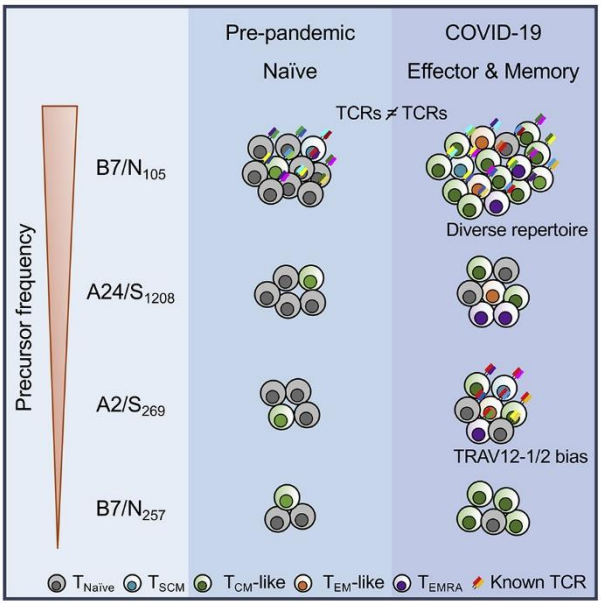
Graphic Abstract:



中文摘要：
考察未经过处理的 SARS-CoV-2 特异的 T 细胞对更好理解 COVID-19 引起的原发性以及继发性的 T 细胞反应很重要。用肽-HLA 四聚体进行离体分析，作者们考察了在 COVID-19 病人以及未暴露个体中 SARS-CoV-2 抗原表位特异的 CD8+ T 细胞。和靶向次优势表位 B7/N257, A2/S269 以及 A24/S1208 的 CD8+ T 细胞不一样，靶向免疫优势地位的 B7/N105 表位在疫情前的样品中同样以很高的频率存在，同时在急性 COVID-19 病人以及康复病人中的频率也都增加了。SARS-CoV-2 特异的 CD8+ T 细胞在疫情以前的样品（不管是儿童，成年人还是老年人）都表现出初始 T 细胞的表型，提示此前并没有对能发生交叉反应的病原物的暴露。T 细胞受体分析揭示 TCRαβ 谱具备多样性，同时 B7/N105+CD8+ T 细胞中 αβ 受体配对也具备很高的异质性。

Abstract:
To better understand primary and recall T cell responses during COVID-19, it is important to examine unmanipulated SARS-CoV-2-specific T cells. Using peptide-HLA tetramers for direct *ex vivo* analysis, we characterized CD8+ T cells specific for SARS-CoV-2 epitopes in COVID-19 patients and unexposed individuals. Unlike CD8+ T cells directed towards subdominant epitopes - B7/N257, A2/S269 and A24/S1208 - CD8+ T cells specific for the immunodominant B7/N105 epitope were detected at high frequency in pre-pandemic samples, and at increased frequency during acute COVID-19 and convalescence. SARS-CoV-2-specific CD8+ T cells in pre-pandemic samples from children, adults and elderly individuals predominantly displayed a naïve phenotype, indicating a lack of previous cross-reactive exposures. T cell receptor (TCR) analyses revealed

diverse TCRαβ repertoires and promiscuous αβ-TCR pairing within B7/N105+CD8+ T cells. Our study demonstrates high naive precursor frequency and TCRαβ diversity within immunodominant B7/N105-specific CD8+ T cells, and provides insight into SARS-CoV-2-specific T cell origins and subsequent responses.