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

联系人：蒋立春 jianglch@shanghaitech.edu.cn

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1. 2021 年 2 月 4 日疫情

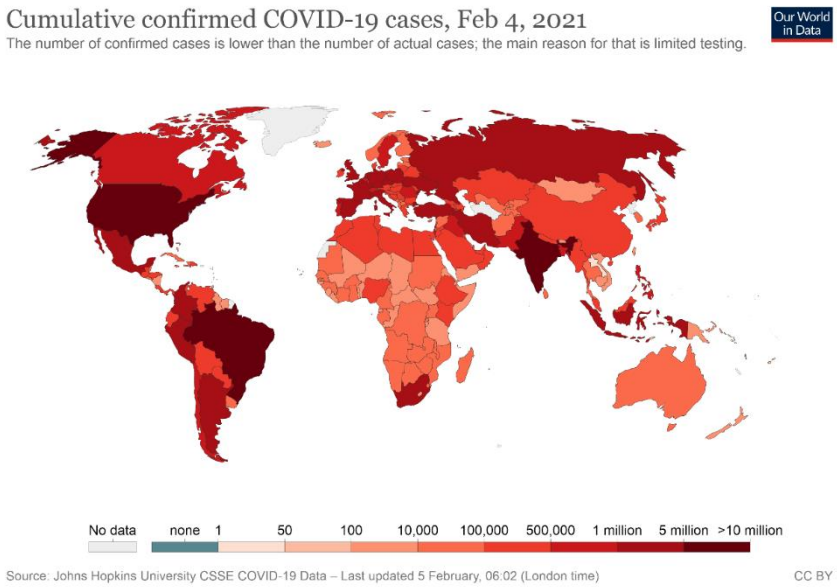
数据来源：WHO

发布时间：2021 年 2 月 4 日北京时间下午 4 点

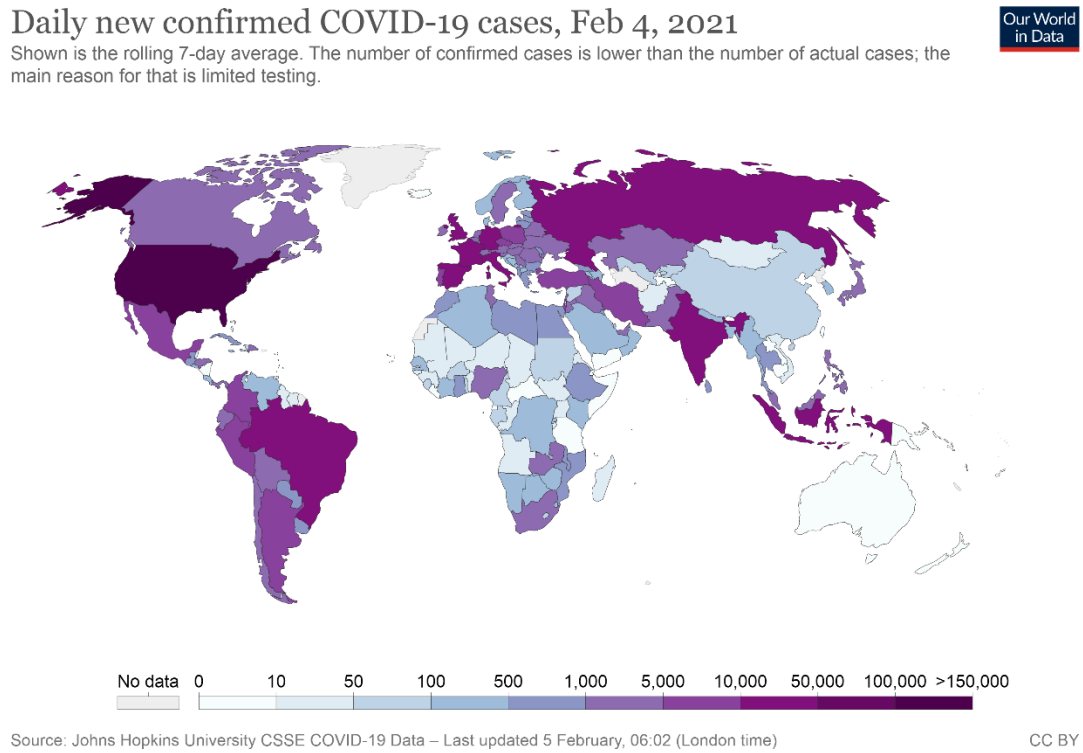
链接：https://covid19.who.int/

根据 WHO 提供的数据，2021 年 2 月 4 日全球累计确诊新型冠状病毒病人 **103,989,900** 例，当日新增确诊 **464,613** 例，累计死亡 **2,260,259** 例，当日新增死亡 **13,004**。

中国累计确诊 101,143 例，累计死亡 4,829 例，当日新增确诊 51 例，新增死亡 1 例。



世界各国确诊人数分布图（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



世界各国每日新增确诊人数分布图（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（2 月 4 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. SARS-CoV-2 变异株 B.1.1.7 对症状、再感染和传播的影响

The effect of SARS-CoV-2 variant B.1.1.7 on symptomatology, re-infection and transmissibility

来源：medrxiv

发布时间：2021-01-29

链接：https://www.medrxiv.org/content/10.1101/2021.01.28.21250680v1

第一作者：Mark S. Graham, Carole H. Sudre

通讯作者：Sebastien Ourselin

通讯作者单位：School of Biomedical Engineering & Imaging Sciences, King’s College London, London,UK

DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

新的 SARS-CoV-2 变异株 B.1.1.7 于 2020 年 12 月在英格兰东南部发现，并在频率和地理分布上迅速增加。虽然有一些证据表明这种变异的可传播性增加，但不知道新变异是否表现出症状或病程的变异，以前感染的个体是否可能再次感染新变异。利用 2020 年 9 月 28 日至 12 月 27 日期间对 36920 名 Covid 症状研究应用程序测试 Covid-19 阳性用户的纵向症状和测试报告，检验了 B.1.1.7 的比例与报告症状、病程、再感染率和传播率之间的关联。**没有发现与 B.1.1.7 与症状、疾病严重程度和疾病持续时间发生变化相关的证据。发现可能的再感染率约为 0.7%（95% CI 0.6-0.8），但没有证据表明这比老菌株更高。还发现 R（t）增加了 1.35 倍（95% CI 1.02-1.69）。**尽管如此，该研究还发现在 B.1.1.7 比例非常高的地区，区域和国家进行封锁已经将 R（t）降低到 1 以下。

Abstract:

The new SARS-CoV-2 variant B.1.1.7 was identified in December 2020 in the

South-East of England, and rapidly increased in frequency and geographic spread. While there is some evidence for increased transmissibility of this variant, it is not known if the new variant presents with variation in symptoms or disease course, or if previously infected individuals may become reinfected with the new variant. Using longitudinal symptom and test reports of 36,920 users of the Covid Symptom Study app testing positive for COVID-19 between 28 September and 27 December 2020, we examined the association between the regional proportion of B.1.1.7 and reported symptoms, disease course, rates of reinfection, and transmissibility. We found no evidence for changes in reported symptoms, disease severity and disease duration associated with B.1.1.7. We found a likely reinfection rate of around 0.7% (95% CI 0.6-0.8), but no evidence that this was higher compared to older strains. We found an increase in R(t) by a factor of 1.35 (95% CI 1.02-1.69). Despite this, we found that regional and national lockdowns have reduced R(t) below 1 in regions with very high proportions of B.1.1.7.

3. Nature/Science/NEJM 等发文认为新冠病毒可以在某些免疫缺陷病人快速演化

来源： CNS 导读公众号

发布时间：2021-02-06

链接：https://mp.weixin.qq.com/s/Mk_83MYM86HCP3kSZvBCGg

供稿（赵素文）

摘要：

Nature 刚刚发表来自剑桥大学 Ravindra Gupta 等对一位接受抗病毒药物（remdesivir）以及康复者血浆（convalescent plasma）治疗的**免疫缺陷新冠患者**持续测序追踪新冠病毒演化的工作（101 天，23 个时间点超高深度测序）。

该工作发现，病人早期，**只接受抗病毒药物治疗的时候很难检测到突变；然而当患者接受康复者血浆治疗后，新冠病毒在病人体内快速突变，特别是在中和抗体发挥作用的靶点（也就是新冠病毒的刺突蛋白（SARS-CoV-2 Spike protein））。**体外实验显示这些突变一方面帮助病毒免疫逃逸，另一方面增加传染性。研究人员据此结果以及之前康复者血浆临床试验相关数据（其临床效果，特别是对于重症患者，尚不确切）表示：**对于免疫缺陷的新冠患者，康复者血浆应该非常谨慎使用。**

Science 以及 NEJM 近日也报道类似的病例，**一致发现新冠病毒可以在免疫缺陷病人快速演化。**

原论文链接：https://www.nejm.org/doi/full/10.1056/NEJMc2031364

原论文链接：https://www.nature.com/articles/s41586-021-03291-y

原论文链接：https://science.sciencemag.org/content/early/2021/02/02/science.abf6950

4. 消息：病毒突变致核酸检测失效？揭国内多地无症状爆发谜底

来源：CC 情报局微信公众号

通讯作者：张洪涛

通讯作者单位：宾夕法尼亚大学医学院

发布时间：2021-02-03

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

核心提示：

1. 新冠病毒突变导致部分核酸检测试剂盒失效，国内外多地出现“多次检测阴性后转阳”现象。为提高病毒检出率，中国推出肛拭子检测项目，部分欧美国家近日开始效仿。2.
2. 肛拭子检测并不一定比鼻咽拭子更为灵敏，尤其可能不适用于筛查早期感染者。其原因可能是，病毒聚集的部位随着病毒感染进程的变化而发生改变。
3. 尽管粪便检测是优先选项，但相比粪便标本，肛拭子采集具有不易造假的优点。
4. 针对病毒突变可能给核酸检测带来的影响，有关部门应加强对检测试剂盒生产者的监督，增加三靶标的试剂盒，以及对已经隔离 14 天的人员进行 IgM 检测而非肛拭子检测。

5. PCR 检测可增强对 SARS-CoV-2 变异体的全球监测

PCR assay to enhance global surveillance for SARS-CoV-2 variants of concern

来源：medrxiv

发布时间：2021-02-01

链接：https://www.medrxiv.org/content/10.1101/2021.01.28.21250486v1

第一作者：Chantal B.F. Vogels

通讯作者：Chantal B.F. Vogels, Joseph R. Fauver, Nathan D. Grubaugh

通讯作者单位：美国耶鲁公共卫生学院，美国耶鲁大学

编译者：刘焕珍

中文摘要：

随着 SARS-CoV-2 变体的出现，可能会增加可传播性和/或导致逃避免疫反应，因此迫切需要对循环谱系进行有针对性的监测。已发现，ThermoFisher TaqPath COVID-19 PCR 检测法可偶然检测到在英国首次发现的 B.1.1.7（501Y.V1）变体，因为这些病毒中的关键缺失（spike Δ69-70）会导致结果是“spike 基因靶标失败”（SGTF）。但是，该测定法无法检测到其他缺乏 spike Δ69-70 的相关变体，例如在南非检测到的 B.1.351（501Y.V2）和最近在巴西检测到的 P.1（501Y.V3）。我们在所有三个变体中鉴定出 ORF1a 基因（ORF1a Δ3675-3677）的缺失，尚未在其他 SARS-CoV-2 谱系中广泛检测到。我们使用 ORF1a Δ3675-3677 作为主要靶标，并使用 spike Δ69-70 进行区分，我们设计并验证了开源 PCR 分析法，以检测相关的 SARS-CoV-2 变体。我们的测定法可以快速部署到世界各地的实验室中，以增强对 B.1.1.7，B.1.351 和 P.1 本地出现扩散的监视。

Abstract:

With the emergence of SARS-CoV-2 variants that may increase transmissibility and/or cause escape from immune responses, there is an urgent need for the targeted surveillance of circulating lineages. It was found that the B.1.1.7 (also 501Y.V1) variant first detected in the UK could be serendipitously detected by the ThermoFisher TaqPath COVID-19 PCR assay because a key deletion in these viruses, spike Δ69-70, would cause a “spike gene target failure” (SGTF) result. However, a SGTF result is not definitive for B.1.1.7, and this assay cannot detect other variants of concern that lack spike Δ69-70, such as B.1.351 (also 501Y.V2) detected in South Africa and P.1 (also 501Y.V3) recently detected in Brazil. We identified a deletion in the ORF1a gene (ORF1a Δ3675-3677) in all three variants, which has not yet been widely detected in other SARS-CoV-2 lineages. Using ORF1a Δ3675-3677 as the primary target and spike Δ69-70 to differentiate, we designed and validated an open source PCR assay to detect SARS-CoV-2 variants of concern. Our assay can be rapidly deployed in laboratories around the world to enhance surveillance for the local emergence spread of

B.1.1.7, B.1.351, and P.1.

6. 中国大规模单细胞转录组学揭示新冠肺炎免疫学特征

COVID-19 immune features revealed by a large-scale single cell transcriptome atlas

来源：CELL

发布时间：2021-02-03（接受但未校正）

链接: https://www.cell.com/cell/fulltext/S0092-8674(21)00148-3

第一作者：Xianwen Ren

通讯作者：Zeming Zhang 等

通讯作者单位：北京大学等

编译：蒋立春

Highlights

Detailed COVID-19 immune landscape depicted by integrated 1.46 million single cells

Peripheral immune subtypes differentially associated with distinct clinical features

SARS-CoV-2 RNAs are present in diverse epithelial and immune cells

Megakaryocytes and monocyte subsets may contribute to cytokine storms

Summary

Dysfunctional immune response in the COVID-19 patients is a recurrent theme impacting symptoms and mortality, yet the detailed understanding of pertinent immune cells is not complete. We applied single-cell RNA sequencing to 284 samples from 196 COVID-19 patients and controls and created a comprehensive immune landscape with 1.46 million cells.

The large dataset enabled us to identify that different peripheral immune subtype changes were associated with distinct clinical features including age, sex, severity, and disease stages of COVID-19.

SARS-CoV-2 RNAs were found in diverse epithelial and immune cell types, accompanied by dramatic transcriptomic changes within viral positive cells. Systemic up-regulation of S100A8/A9, mainly by megakaryocytes and monocytes in the peripheral blood, may contribute to the cytokine storms frequently observed in severe patients. Our data provide a rich resource for understanding the pathogenesis and developing effective therapeutic strategies for COVID-19.

要点:

整合 146 万单细胞分析了新冠的免疫特征

不同的外周免疫分型和迥异的临床特征相关联

SARS-CoV-2 RNA 存在于不同的上皮细胞和免疫细胞中

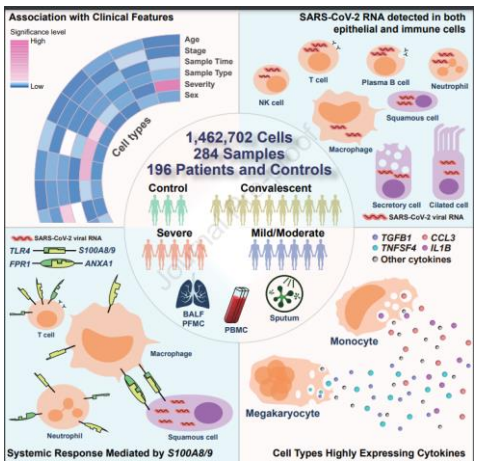
巨核细胞和单核细胞可能对细胞因子风暴有作用

总结：

COVID-19 病人中失效的免疫反应是对新冠症状和致死率有重要影响的不断重复被提出来的议题，但是我们仍然缺乏对相关免疫细胞的详细了解。该项目总共对 196 个 COVID-19 病人以及对照组的 284 个样品进行了单细胞 RNA 测序。该研究用 146 万个细胞的数据构建了一个关于 COVID-19 的综合免疫特征图谱。这个大的数据集使得研究者们鉴定出和包括年龄、

性别、症状严重层度以及 COVID-19 疾病阶段的不同的临床特征相关的外周免疫亚型变化。在不同类型的上皮细胞和免疫细胞中，都发现了 SARS-CoV-2 RNA，伴随病毒阳性细胞中显著的转录变化。外周血中由巨核细胞核单核细胞主导的系统性的上调 S100A8/A9 基因表达，可能在重症病人中频繁观察到的细胞因子风暴的原因。该数据为研究 COVID-19 的疾病发生以及开发有效的治疗手段提供了丰富的资源。

文章的图文摘要示意



该文的涉及到的测序数据分析后数据在 NCBI GEO 代码为 GSE158055.

数据可视化网站：http://covid19.cancer-pku.cn

单细胞测序公众号的解读

Cell ｜ “新冠肺炎单细胞研究中国联盟”揭示新冠肺炎免疫学特征

链接：https://mp.weixin.qq.com/s/ek9_B9FBmlsbHvbKdvGZig

为在快速解决这一难题，我国十多个省市四十多家医院大学和研究机构在 2020 年 5 月自发组建了**“新冠肺炎单细胞研究中国联盟**(Single Cell Consortium for COVID-19 in China (SC4))”，旨在协同建立新冠肺炎单细胞转录组大队列大数据，为揭示新冠肺炎发病机制和免疫学特征发出中国的声音。经过四个半月的日夜奋战，联盟共获得 196 个新冠病人（包括正常对照）的 284 个样本（包括痰液、肺泡灌洗液、胸水、外周血等）超过 25T 近 150 万个细胞的单细胞转录组测序数据，并迅速完成了数据整合与分析，揭示了新冠病毒感染机制和在不同疾病发病阶段机体免疫反应特点。该研究成果于 2020 年 9 月以 *“COVID-19 immune features revealed by a large-scale single cell transcriptome atlas”* 为题投稿至 *Cell* 杂志，2021 年 2 月 3 日在线发表。

本项研究发现，除了传统认为的呼吸系统上皮细胞以外，多种免疫细胞中被检测到新冠病毒核酸序列，包括中性粒细胞、巨噬细胞、浆细胞、T 细胞和自然杀伤细胞之中，其表达特征也呈现出了亚基因组转录特点，提示新冠病毒在这些免疫细胞中曾经发生过活跃的转录与复制，亦即不能排除新冠病毒宿主细胞范围不仅包括上皮细胞还包括免疫细胞的可能。这可能是新冠病毒区别于 SARS 的重要特点，也可能是新冠病毒具有较强传染力的原因。这一发现与新冠病毒核酸阳性细胞具有较强的干扰素反应一致，并且通过对新冠病毒 S 蛋白进行组织切片染色得到了证实。有趣的是，新冠受体蛋白 ACE2 在免疫细胞中几乎不表达，提示新冠病毒可能存在潜在的新受体来感染宿主细胞。

进一步生物信息学分析发现，不同的上皮细胞在新冠病毒感染后会引发不同的反应。病毒核酸阳性和阴性的纤毛上皮细胞、分泌型上皮细胞以及鳞状上皮细胞分别具有不同的差异基因表达。新冠病毒阳性的纤毛上皮细胞更倾向于从组织上脱落下来不引起免疫反应；而新冠病毒阳性的鳞状上皮细胞会倾向于增强其与中性粒细胞、巨噬细胞的相互作用，推测是利用 ANXA1-FPR1、S100A8/9-TLR4 配体-受体分子，触发与启动机体的免疫反应。新冠病毒阳性的

鳞状上皮细胞会上调 ANXA1、S100A8、S100A9，和在中性粒细胞、巨噬细胞上高表达的 FPR1、TLR4 发生相互作用，从而触发机体的天然免疫反应。值得注意的是,ANXA1、S100A8/9 会在发病期重症病人的外周血中的免疫细胞中普遍上调表达，提示重症病人可能发生了由 ANXA1-FPR1、S100A8/9-TLR4 介导的全身的系统免疫反应风暴。

本研究也为解析新冠肺炎严重程度、病程阶段、年龄、性别以及其他技术因素对机体外周血中免疫细胞组成的影响奠定了基础。方差分析显示，新冠肺炎的重症病人外周血中会有更高比例的增殖中的浆细胞与 T 细胞，而总体 T 细胞水平显著低于轻症病人或健康对照以及康复期病人。这些升高的增殖的浆细胞与 T 细胞与疾病严重程度存在显著的统计相关性；而 B 细胞整体更倾向于与发病阶段相关，即在康复期有较高的 B 细胞水平。流行病学研究揭示了年龄和性别和新冠患者病症有关。本研究发现，年龄主要和中性粒细胞、幼稚 CD8+ T 细胞相关，性别差异主要体现在效应 T 细胞。年龄与性别不仅会影响外周血不同免疫细胞亚群的水平高低，而且会影响 B 细胞或者 T 细胞受体谱的多样性。年龄大的患者的 B 细胞或 T 细胞谱的多样性较低，男性的较低，可能与机体的整体免疫力相关。

虽然细胞因子风暴在新冠肺炎的致病机制中存在一定的争议，但本研究为揭示细胞因子的潜在细胞源头提供了详实的证据。其中，巨核细胞以及单核细胞的部分亚群会高表达各类细胞因子，并在重症病人中具有更高的表达水平，是潜在的细胞因子风暴的来源。基于血浆的细胞因子检测实验证实了这些细胞在细胞因子风暴中的潜在作用。由于部分细胞因子是分泌型的，这些细胞因子也构成了外周血与肺部感染病灶相互作用的桥梁，形成了复杂的机体细胞因子相互作用网络。

7. 第二支国产新冠疫苗（科兴）即将上市！有效率数据曾“一波三折”，如何解读？

来源： 生物制品圈微信公众号

发表时间：2021-02-06

链接：https://mp.weixin.qq.com/s/MKcMKBO2ztNMZ5lKLkbYMg

摘要：

国内有望迎来第二支获准上市的新冠疫苗！继国药疫苗之后，科兴新冠疫苗有条件上市申请获国家药监局受理。

2 月 3 日，科兴中维宣布，其研制的新型冠状病毒灭活疫苗克尔来福当天正式向国家药监局提交附条件上市申请，并获得受理。业界预计，如果依照国药中生北京新冠疫苗的审批速度，克尔来福疫苗最快将在春节前获批。

8. 欧盟拟开审，6 国总统近百政要接种，中国疫苗全球 10 亿订单曝光

来源：CC 情报局微信公众号

发布时间：2021-02-04

链接：https://mp.weixin.qq.com/s/w6gV7d0l0-d5ZQ2AZkajIA

1、由于欧盟内部疫苗供给短缺、俄罗斯疫苗产能不足，塞尔维亚与匈牙利率先批准使用中国疫苗。法德与欧盟方面表示条件成熟后可能会使用中俄疫苗。

2、与依靠西方疫苗的欧美不同，阿联酋、巴林、约旦等海湾国家的接种效率较高，是因为其很早就订购中国疫苗，政要与王室积极参与疫苗临床试验。这些国家之所以选择中国疫苗，除了其安全性高之外，还因为其拿不到西方疫苗。

3、中国疫苗目前已在 10 多个国家地区批准上市，全球订单已达 10 亿剂，覆盖全球 40 多个国家。印尼、土耳其、塞舌尔等国总统接种了中国疫苗，塞尔维亚、秘鲁、智利总统明确即将接种中国疫苗。

4、中国疫苗因更高的安全性以及无需超低温储存，为发展中国家偏远地区人民带来希望。巴西、印尼已订购上亿剂中国疫苗，智利、土耳其、马来西亚等国订单量超千万剂。据目前可靠信息预测，未来将有更多国家与地区使用中国疫苗。

9. 保质期 5 年的 DNA 疫苗成为国产新冠疫苗的又一秘密武器

来源：澎湃新闻　生物制品圈

发布时间：2021-2-2

链接：https://mp.weixin.qq.com/s/YPSw-is7FQvqVQbd_jfmgA

编译者：张鹏伟

中文摘要：

我国在研新冠疫苗队伍中，有一款 DNA 疫苗在标准冷藏温度（2-8℃）下保质期可达 5 年，室温下可保持稳定 1 年以上。这款 DNA 疫苗由艾棣维欣与美国生物制药公司 INOVIO 联合研发，目前正在中美同步开展 2 期临床试验。由于技术门槛较高，目前全球还没有 DNA 疫苗成功上市。这也是我国第一款获批进入临床的预防性 DAN 疫苗。2020 年 7 月，艾棣维欣新冠 DNA 疫苗获批在中国进入临床试验。1 期临床试验已在上海华山医院顺利开展，同年 9 月实现首例受试者接种，现已完成全部 45 名健康受试者两针接种，进入随访阶段。2020 年 12 月，这款 DNA 疫苗在国内正式进入 2 期临床试验，该试验与江苏省疾控中心合作在江苏省开展。目前，艾棣维欣正在建设中国最大的 DNA 疫苗与质粒生产基地，新冠 DNA 疫苗的产业化工程正在分阶段建设，第一阶段设计产能 2000 万剂/年，第二阶段设计产能在 1 亿剂/年，截至 2021 年 1 月，第一阶段建设已接近尾声。

10. 如何重新设计 COVID 疫苗来对抗变异株

How to redesign COVID vaccines so they protect against variants

来源：Nature

发布时间：2021-1-29

链接：https://www.nature.com/articles/d41586-021-00241-6

作者：Ewen Callaway & Heidi Ledford

DOI：https://doi.org/10.1038/d41586-021-00241-6

编译者：雷颖

中文摘要：

随着越来越多的证据表明 SARS-CoV-2 冠状病毒的新变种可以逃避疫苗或先前感染产生的免疫力，科学家正在探索重新设计目前正在全球范围内推广的疫苗的想法。COVID-19 疫苗更新可以遵循的一种模式是季节性流感疫苗。尚不清楚批准 COVID-19 疫苗更新需要多少临床数据。新的季节性流感疫苗通常不需要新的试验。但是，COVID-19 疫苗并不具有数十年的经验和临床数据，监管机构无法保证其使用。一些有抱负的疫苗生产商已经开始关注逃逸变种可能从一开始就构成的威胁。艾默里维尔（Emeryville）公司总裁安德鲁·艾伦（Andrew Allen）说，Gritstone 肿瘤学团队决定通过设计针对几种病毒蛋白多个位点的疫苗来关注这一潜在问题，这与仅针对刺突蛋白的第一代疫苗相反。加利福尼亚希望该疫苗将很快开始临床试验，将使该病毒难以逃避免疫，因为为此需要进行许多基因改变。一些研究人员预计，像流感一样，定期更新冠状病毒疫苗将成为一种生活方式。

Abstract

As evidence grows that new variants of the SARS-CoV-2 coronavirus can evade immunity produced by vaccines or previous infections, scientists are exploring the idea of redesigning the vaccines currently being rolled out worldwide.

11. 血清阳性个体注射单剂 SARS-CoV-2 mRNA 疫苗后增强了 spike 抗体反应并增加了反应原性

Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine

来源：medrxiv

发布时间：2021-02-01

链接：https://www.medrxiv.org/content/10.1101/2021.01.29.21250653v1

第一作者：Florian Krammer

通讯作者：Florian Krammer, Viviana Simon

通讯作者单位：美国纽约西奈山伊坎医学院

DOI 或 PUBMED ID：https://doi.org/10.1101/2021.01.29.21250653

编译者：刘焕珍

中文摘要：

随着 COVID-19 疫苗的推出，出现了一个重要的问题：**那些已经感染了 SARS-CoV-2 病毒的人是否应该注射一到两针目前批准的 mRNA 疫苗**。这篇简短的报告表明，在已有免疫力的个体中，对第一剂疫苗的抗体反应等于甚至超过未感染个体在注射第二剂疫苗后的滴度。我们还发现，在过去感染过 SARS-CoV-2 的个体中，这种反应性明显更高。只给这些人注射一剂疫苗不会对他们的抗体滴度产生影响，使他们免于不必要的痛苦，并释放出许多急需的疫苗剂量。

Abstract:

An important question is arising as COVID-19 vaccines are getting rolled out: Should individuals who already had a SARS-CoV-2 infection receive one or two shots of the currently authorized mRNA vaccines. In this short report, we show that the antibody response to the first vaccine dose in individuals with pre-existing immunity is equal to or even exceeds the titers found in naïve individuals after the second dose. We also show that the reactogenicity is significantly higher in individuals who have been infected with SARS-CoV-2 in the past. Changing the policy to give these individuals only one dose of vaccine would not negatively impact on their antibody titers, spare them from unnecessary pain and free up many urgently needed vaccine doses.

12. “这是一个关于选择的问题” 辉瑞疫苗负责人关于面临新的新冠病毒突变株的看法

‘A question of choices.’ Pfizer vaccine leader on confronting new coronavirus variants

来源：science

发表日期：2021-02-03

链接：https://www.sciencemag.org/news/2021/02/question-choices-pfizer-vaccine-leader-confronting-new-coronavirus-variants

编译：蒋立春

Abstract:

辉瑞公司和德国公司 BioNTech 合作开发的 mRNA 疫苗最近获得了美国 FDA 的紧急使用授权。近日一些实验室研究和最新公布的临床实验结果显示 SARS-CoV-2 出现了新的突变，可能对辉瑞的疫苗有抗性。辉瑞的疫苗是一种需要注射间隔 3 周接种 2 次的疫苗。目前该疫苗在包

括美国的 50 多个国家使用。辉瑞表示到 5 月底会为美国提供 2 亿剂，并且预期在 2021 年在全球范围内发货 20 亿。

Science 发表了关于辉瑞疫苗部门该怎么应对新突变对 Domitzer 博士做了采访。

采访中文翻译：

问题：上周，研究者了发表了预印本的文章，讲述辉瑞疫苗接种者血液中的抗体对首次发生在南非的突变株以及首次在英国新发现的高传染性的病毒突变株的中和能力的。他们发现针对南非株，抗体的中和能力下降了6.5倍，对英国病毒株的中和能力或者的滴度下降了2倍。辉瑞接种者需要对这些结果表示担忧吗？

回答：

我不知道自己是否该使用担忧这个词语。这些实验室的发现本身并没有告诉我们需要在疫苗生产中改变所使用的病毒株。但是我们需要为疫苗的降低有效性降低的可能性做好准备。目前我们还没有看到证据。从我们自己临床试验的结果来看，第一针接种后的 12 到 14 天之后就开始有部分的保护作用。而第一针接种后的 12 到 14 天的时候，在接种者血内几乎还检测到中和性抗体。除了高滴度的中和抗体之外，一定还有其他什么东西在起到保护作用。是细胞介导的免疫，还是底滴度的中和抗体在发挥作用，我们还不了解。

问题：你们是否要要就你们得疫苗到底对这些突变会有什么反应要进行全面的实验分析呢？

回答：我们已经做了。可以讲总体而言我们的结论和其他人得到的结果非常相似—针对南非突变株的中和能力相比英国突变株下降要更厉害。我们也在针对在巴西首先发现的一个突变进行类似的分析。很快可以看到到南非株和巴西株的数据了。病毒在不断发生突变，很长一段时间内我们都会继续这样的工作。

问题：您预计你们的疫苗对暴露给新病毒突变株的人的保护有效性会是怎样的？

回答：鉴于我们看到了除了高水平的中和性抗体之外的因素起到了保护作用，让我们乐观地认为疫苗会对突变株保持保护效力。但是数据胜过一切！我们预期主要将会有两类临床数据来说明这个问题。首先，我们在南非和巴西也有三期临床试验。开始这些临床试验的时候，这些新的突变还没有成为主要流行突变株。但是对临床试验者的持续跟踪会告诉我们是否会有接种过我们疫苗的人因感染新的突变株而患病。

第二，流行病学数据会告诉我们一些信息：比如患病的人数是否因为接种疫苗而单纯地下降或者先下降然后又开始增加。

问题：关于特定地改造疫苗以使其能有效应对新突变，辉瑞有采取哪些行动吗？

回答：在这些突变出现之前我们就开始了相关工作—通过基础研究来理解可能的突变。当前构建突变体的 DNA 模板是我们的常规操作。我们也一直在内部以及和监管单位进行相关进展的沟通。

问题：目前你们需要改变疫苗来对抗新的突变吗？

回答：不。在实验室的抗体中和试验测试中观察到的中和能力下降并不能告诉你你需要去对疫苗做改动。只需要为之做准备。不管最后是否真的需要对疫苗做出改动，都必须为对疫苗进行改动做准备工作。

对流感疫苗研究中我们的一个观察是：经过几次初次免疫后，几个月之后的加强免疫不仅仅能产生很强的免疫，而且能产生很广的免疫。所以，一个可能性是需要对疫苗做出改动。另一个可能性是你只需要加强免疫。

水涨船高。这就是为什么需要做临床研究。我们需要理解 SARS-CoV-2 的加强免疫是怎样的，它到底给了我们什么样子的免疫反应。

问题：对于监管者而言，一个改动过的疫苗面临哪些困难呢？还需要做动物试验或者大的临床试验吗？

回答：这些问题很关键。对于流感而言，由于我们已经做了几十年的疫苗，规则非常明确：

如果血红细胞凝集的抑制滴度（这个是测试血中针对流感病毒的抗体水平的一个指标）降低了 4 倍，那么就需要对疫苗做出变动。

但是我们知道 COVID-19 和流感有些地方非常不一样。对于流感而言，在一个好的年份有一个好的毒株匹配，我们可以看到疫苗的有效性只有 60%。但是我们在 COVID-19 里面观察到高达 95%的有效性。我们—公司、和监管者、每一个人需要共同去弄清楚 COVID-19 疫苗的游戏规则。这个是我们现在正在努力的事情。

问题：你们需要额外的工厂来制造改动过的疫苗吗？

回答：我们有非常大的生产能力。我们对当前疫苗的生产能力是 2021 年 20 亿剂。

所以我不认为资源是一个问题，选择才是问题。如果你要换成针对一个新的病毒株的疫苗，你就需要降低当前疫苗的产量。这些是真的关键的决定。

问题：其他疫苗产商讲只需要 6 周甚至更短的时间来换一个 mRNA 载体来针对新的突变体。这种说法对辉瑞来讲也是对的吗？

回答：应对大流行，我有非常多年的工作经验。我学习到的经验是大多数人们讲他们多快能做什么的时候，你必须仔细地审视那些说法。在实验室里换一个 mRNA,是很快的。但是最大的问题是你需要做哪些实验室测试、哪些动物试验或者临床试验。当然，一个有效性的研究现在变得几乎不可能了，因为你需要延迟安慰剂组的疫苗接种了。

问题：你对于做人体挑战试验有兴趣吗？

回答：个人而言，我不会这么做。我觉得这是在承担不必要的风险，因为我们有别的办法获得相关信息。整体而言我并不反对人体挑战试验—我们目前就在做一个呼吸道融合病毒的人体挑战试验。但是我们仍然对 COVID-19 的所有后果不够了解，还在不断学习中。

英文全文：

Philip Dormitzer led Pfizer's successful coronavirus vaccine research effort, which yielded a vaccine with a stunning 95% efficacy in interim results from a clinical trial last year. That vaccine, developed with the German firm BioNTech, relies on a new technology employing messenger RNA (mRNA). It was the first to win emergency use authorization from the Food and Drug Administration for use against COVID-19 in the United States.

However, recent lab studies and new clinical trial results have suggested recently emerged variants of SARS-CoV-2, the pandemic coronavirus, have evolved resistance to vaccines, including Pfizer's.

The company's vaccine, which requires two doses 3 weeks apart, is now being administered in more than 50 countries, including the United States. Pfizer says it is on track to supply 200 million doses to the United States by the end of May and aims to ship 2 billion doses globally this year.

Dormitzer, who has an M.D. and Ph.D. from Stanford University, has a history with pandemics. He was U.S. research chief at Novartis Vaccines, where he steered that company's work creating—in what is still record time—a successful vaccine against the 2009 H1N1 pandemic flu. He has been at Pfizer since 2015.

Dormitzer spoke with *Science*Insider about how the company is responding to the new variants and what challenges it foresees as SARS-CoV-2 continues to evolve in unpredictable ways. This interview has been edited for brevity and clarity.

Q: The pandemic is moving into a new phase as vaccination campaigns gear up while viral variants, or strains, proliferate. What keeps you up at night?

A: Things were supposed to get much, much calmer after we had the vaccine

authorized. But things just don't hold still. The virus throws out new variants and we need to evaluate those and be prepared to respond. And there are many other things: … How will the vaccine work in special populations? What reactions are people having? How do we improve things like temperature stability? The vaccine's authorized. It's wonderful to see it being used. But it's not the end of the process.

Q: Last week, researchers published a preprint looking, in the lab, at how well antibodies from the blood of Pfizer vaccinees attacked two of the new coronavirus strains—one first identified in South Africa and a highly contagious strain first identified in the United Kingdom. They found a 6.5-fold reduction in antibodies that neutralize the variant identified in South Africa, and a twofold reduction in the levels, or titers, of these neutralizing antibodies against the other variant. Should Pfizer vaccinees be concerned about these results?

A: I don't know if I would use the word concerned exactly. These laboratory findings don't of themselves tell us that a strain change [in the vaccine] is necessary. But we need to be prepared for the possibility that there could be some reduction in effectiveness. We see no evidence of that yet. We know [from our trial results] that we see protection—not full protection, but protection—starting at 12 to 14 days after that first dose. At that time [12 to 14 days out from the first dose] there are almost no neutralizing antibodies [that our tests detect in the blood of vaccinees].

There must be something other than high neutralizing antibody titers that can protect. Whether it's cell-mediated immunity, whether it's low neutralizing antibody titers, we don't know.

Q: Do you intend to run a comprehensive lab analysis of how your vaccine works against the suite of mutations seen in the new variants?

A: We already have. I can say broadly that our findings are very similar to others', in that you do see more reduction in neutralization with the South African variant than with the U.K. variant. We are also running similar tests against [a concerning variant first identified in Brazil]. We are hoping to get both the South African and the Brazilian data out very soon. At the rate that this virus is spinning out variants, we will be continuing to do this for quite some time.

Q: What do you expect will be the effectiveness of your vaccine in human beings exposed to the new viral strains?

A: The fact that we see protection by means other than high neutralizing antibody [levels] makes me optimistic that we are going to see preserved protection. But nothing trumps the data. There are two main kinds of clinical data we might expect. First, we ran our phase 3 trial at sites including in Brazil and South Africa. At the time … these new variants … had not become dominant. But continuing to monitor what goes on in those clinical trial participants will give us some idea [if anyone who has been vaccinated gets sick with a new variant]. Second, the pattern of epidemiological findings could give us information, [for example whether] the instance of disease simply falls with immunization, or falls

[but then] starts to increase.

Q: What is Pfizer doing to tailor its vaccine to be effective against these variants?

A: The work started well before the variants had emerged … through basic scientific research [on potential mutations]. … We are now at the point where we are routinely making the DNA templates for variants. And we are having discussions, internally and with regulators, about how far we progress each of these.

Q: Do you need to change your vaccine now to beat the new variants?

A: No. Simply seeing a reduction in a lab neutralization test does not tell you that you need to change [the vaccine]. You just have to be prepared. You have to do the work to prepare for a [vaccine] change regardless of whether you actually need to execute one or not.

The other possibility is you simply boost.

So, one possibility is you do a [vaccine] change.

The other observation we have from pandemic flu is that after a couple of priming doses, a boosting dose months later gives not only very strong immunity but very broad immunity.

And a rising tide lifts all boats. This is why you need to do the clinical studies. We need to understand what a SARS-CoV-2 booster looks like and what kind of immune response it gives you.

Q: What hurdles would an adapted vaccine face with regulators? Would you need to do animal studies or big clinical trials?

A: Those are key questions. For flu, since we have been doing it for decades, the rules are very clear: A fourfold reduction in hemagglutination inhibition titers [a measure of the level of antibodies against the virus in the blood of vaccinees] suggests you need to change the [vaccine]. But we know that something is very different between the flu and COVID-19. For flu, in a good year with a good strain match, you see about 60% [vaccine] efficacy. Here we see about 95% efficacy. We—the companies, the regulators, everybody—now need to figure out the rules of the game for COVID-19 vaccines. That's what we're working through right now.

Q: Do you need additional manufacturing plants to make an adapted vaccine?

A: We have tremendous manufacturing capacity. Our goal for the current vaccine is 2 billion doses in 2021.

So, I don't think it's a question of having the resources. It's more a question of choices. If you are going to switch [the vaccine] to a new strain, it means you are going to have to reduce production of the current [vaccine]. There are real decisions to make.

Q: Other vaccinemakers have said changing the mRNA construct **to target a new variant can be done in 6 weeks or less. Is that right, in Pfizer's case?**

A: I have been working in pandemic response for a very, very long time. I have learned that what most people say about how fast they can do something—you have to examine those statements very carefully.

The part that’s done in the lab, switching one mRNA to another, is very quick. … But the biggest question is what laboratory, animal, or clinical testing you need to do. And of course, an efficacy study would be almost impossible now because you would need to deny vaccine to people in the placebo group.

Q: Would you be interested in doing a human challenge study?

A: Personally, I would not. I think it’s imposing a risk that’s not necessary because we can get the information in other ways. I don’t have an objection to human challenge studies in general—we are doing one right now with respiratory syncytial virus … but we are still learning about all the consequences of COVID-19 disease.

13. 9 成老人接种，病例减少 40%！以色列超大规模疫苗接种结果出炉

来源：药明康德公众号

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摘要：

近来，世界上多个国家和地区已经开展大规模的新冠疫苗接种活动来控制新冠疫情的发展。虽然目前广泛使用的有些疫苗在 3 期临床试验中显示的保护能力达到 95%，但是在真实世界的情况下，它们的效果到底如何呢？我们什么时候才能够看到大规模疫苗接种带来的保护效果？

今日，《自然》杂志对以色列疫苗接种的最新进展进行了报道。以色列在全球范围内是疫苗接种速度最快的国家之一。截至今年 2 月 2 日，该国 42.8%的人口已经接种过至少一剂疫苗或者从 COVID-19 中康复。可喜的是，早期数据显示在国家人口水平上，COVID-19 患病率出现显著下降。《自然》发表的报道表示，这是首次在真实世界环境下，观察到新冠疫苗在人口水平上对 COVID-19 的影响。

14. 腺病毒载体 rAd26 和 rAd5 构建的异源性新冠肺炎疫苗的安全性和有效性:俄罗斯 III 期临床随机对照试验的中期结果分析

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

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https://www.sciencedirect.com/science/article/pii/S0140673621002348?via%3Dihub 第一作者：Denis Y Logunov and Inna V Dolzhikova

通讯作者： Alexander L Gintsburg

通讯作者单位：Federal State Autonomous Educational Institution of Higher Education I M Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation

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编译者：姜连连

中文摘要：

背景：一种基于异源重组腺病毒(rAd)的新冠疫苗 Gam-COVID-Vac (Sputnik V)显示出良好

的安全性，并在 I 期和 II 期临床试验的受试者中诱导了高滴度的体液和细胞免疫反应。本研究报告了 Gam-COVID-Vac 疫苗的 III 期临床试验中期分析获得的该疫苗有效性和安全性的初步结果。

方法：本研究在俄罗斯的 25 家医院和诊所进行了一项随机、双盲及安慰剂对照的 III 期临床试验。受试者年龄均超过为 18 岁且新冠病毒 SARS-CoV-2 PCR 和相关抗体检测均为阴性，并在接种前 14 天内未感染其他传染病且 30 天内未接种其他疫苗。受试者按年龄被随机分配(3:1)接种疫苗或安慰剂。统计员、受试者和研究者均危告知分组情况。疫苗按初始强化方案进行肌肉注射(0.5 毫升/剂):第一剂(rAd26)和第二剂(rAd5)免疫间隔为 21 天，两种载体均携带全长 SARS-CoV-2 糖蛋白 S 基因。第一剂免疫后第 21 天利用 PCR 检测受试者新冠感染的比例。所有分析均排除了违反方案的受试者，结果均在接受两剂疫苗或安慰剂的受试者中进行评估，严重不良事件锁定接受至少一剂疫苗的受试者中评估，罕见不良事件锁定时接受两剂疫苗且经验证的受试者中评估。该临床试验已在政府注册(NCT04530396)。

结果：III 期临床试验期间，21977 名受试者被随机分配到疫苗组(n=16，501)或安慰剂组(n=5，476)。19866 名受试者免疫两剂疫苗或安慰剂而被纳入数据分析。从初次接种疫苗后 21 天，疫苗组 14964 位受试者中有 16 名(0.1%)，安慰剂组 4902 名受试者有 62 位(1.3%)被确认患有新冠肺炎；疫苗效力为 91.6% (95%，CI 85.6－95.2)。多数不良事件为 1 级。疫苗组 16427 名受试者中有 45 名(0.3%)和安慰剂组 5435 名受试者中有 23 名(0.4%)出现严重不良事件；经确认，无一例与疫苗接种有关。试验期间有 4 例死亡(疫苗组有 3 例[<0.1%]死亡，安慰剂组 1 例[<0.1%])，且死亡均与疫苗无关。

解释：Gam-COVID-Vac 三期临床试验的这一中期分析显示，对 COVID-19 的疗效为 91.6%，在一个大的队列中耐受性良好。

Abstract:

Background A heterologous recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), showed a good safety profile and induced strong humoral and cellular immune responses in participants in phase 1/2 clinical trials. Here, we report preliminary results on the efficacy and safety of Gam-COVID-Vac from the interim analysis of this phase 3 trial.

Methods We did a randomised, double-blind, placebo-controlled, phase 3 trial at 25 hospitals and polyclinics in Moscow, Russia. We included participants aged at least 18 years, with negative SARS-CoV-2 PCR and IgG and IgM tests, no infectious diseases in the 14 days before enrolment, and no other vaccinations in the 30 days before enrolment. Participants were randomly assigned (3:1) to receive vaccine or placebo, with stratification by age group. Investigators, participants, and all study staff were masked to group assignment. The vaccine was administered (0.5 mL/dose) intramuscularly in a prime-boost regimen: a 21-day interval between the first dose (rAd26) and the second dose (rAd5), both vectors carrying the gene for the full-length SARS-CoV-2 glycoprotein S. The primary outcome was the proportion of participants with PCR-confirmed COVID-19 from day 21 after receiving the first dose. All analyses excluded participants with protocol violations: the primary outcome was assessed in participants who had received two doses of vaccine or placebo, serious adverse events were assessed in all participants who had received at least one dose at the time of database lock, and rare adverse events were assessed in all participants who had received two doses and for whom all available data were verified in the case report form at

the time of database lock. The trial is registered at ClinicalTrials.gov (NCT04530396).
Findings Between Sept 7 and Nov 24, 2020, 21 977 adults were randomly assigned to the vaccine group (n=16 501) or the placebo group (n=5476). 19 866 received two doses of vaccine or placebo and were included in the primary outcome analysis. From 21 days after the first dose of vaccine (the day of dose 2), 16 (0.1%) of 14 964 participants in the vaccine group and 62 (1.3%) of 4902 in the placebo group were confirmed to have COVID-19; vaccine efficacy was 91.6% (95% CI 85.6-95.2). Most reported adverse events were grade 1. 45 (0.3%) in the vaccine group and 23 (0.4%) in the placebo group had serious adverse events; none were considered associated with vaccination, with confirmation. Four deaths were reported during the study, none of which were considered related to the vaccine.
Interpretation This interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91·6% efficacy against COVID-19 and was well tolerated in a large cohort.

15. COVID-19 蛋白亚单位候选疫苗 S-三聚体（SCB-2019）1 期临床试验分析

Safety and immunogenicity of S-Trimer (SCB-2019), a protein subunit vaccine candidate for COVID-19 in healthy adults a phase 1, randomised, double-blind, placebo-controlled trial
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第一作者：Peter Richmond
通讯作者：Ralf Clemens
通讯作者单位：巴西全球传染病研究
DOI:https://doi.org/10.1016/S0140-6736(21)00241-5
编译者：张怡
中文摘要：
作为加速研发 SARS-CoV-2 疫苗的一部分，研究者报道了 SCB-2019 疫苗的剂量发现和佐剂合理性研究。SCB-2019 是一种蛋白亚单位候选疫苗，含有稳定的三聚体形式的刺突（S）-蛋白（S-三聚体），并结合两种不同的佐剂。
研究者在澳大利亚的一个专业临床试验中心进行了一项临床 1 期、随机、双盲、安慰剂对照试验，将健康成人志愿者分为两个年龄组：年轻人（18-54 岁）和老年人（55-75 岁）。将参与者随机分组,每隔 21 天分别接种两剂 SCB-2019(3μg、9μg 或 30μg)或安慰剂(0.9%NaCl)。SCB-2019 要么不使用佐剂（仅 S-三聚体蛋白），要么使用 AS03 或 CpG/明矾佐剂。在每次接种后 7 天内评估反应性。体液反应通过 ELISA 检测 SCB-2019 结合 IgG 抗体和 ACE2 竞争性阻断 IgG 抗体，通过野生型 SARS-CoV-2 微中和试验检测中和抗体。通过流式细胞术细胞内细胞因子染色检测细胞对聚合 S 蛋白多肽的反应。
2020 年 6 月 19 日至 9 月 23 日，共有 151 名志愿者被纳入研究。148 名志愿者在第二次给药后至少进行了 4 周的随访，并纳入本次分析。接种疫苗的耐受性良好，仅有两例发生 3 级不良事件。大多数局部不良事件为轻度注射部位疼痛，含有 AS03 佐剂的 SCB-2019 制剂的局部事件发生率（44-69%）高于含有 CpG/明矾佐剂（6-44%）或无佐剂（3-13%）的 SCB-2019 制剂。

首次给药后，年轻人的全身不良事件发生率（38%）高于老年人（17%），但第二次给药后，两个年龄组的不良事件发生率相差不大（老年人 30%，年轻人 34%）。不含佐剂的 SCB-2019 引起最小的免疫反应（第 50 天发生三次血清转化），但固定剂量 SCB-2019 添加 AS03 或 CpG/明矾佐剂，在年轻人和老年人中诱导了结合和中和抗体的高滴度和血清转化率。所有 AS03 剂量组和 CpG/Alum 30μg 组的滴度均高于 COVID-19 患者恢复期血清样本的滴度。这两种添加佐剂的 SCB-2019 制剂均能诱导 T-辅助-1 偏向性 CD4+T 细胞应答。

研究结果表明，SCB-2019 疫苗由 S-三聚体蛋白与 AS03 或 CpG/明矾佐剂组成，可诱导针对 SARS-CoV-2 的强大体液和细胞免疫应答，具有高病毒中和活性，且患者耐受性良好。

Abstract

Background As part of the accelerated development of vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), we report a dose-finding and adjuvant justification study of SCB-2019, a protein subunit vaccine candidate containing a stabilised trimeric form of the spike (S)-protein (S-Trimer) combined with two different adjuvants.

Methods Our study is a phase 1, randomised, double-blind placebo-controlled trial at a specialised clinical trials centre in Australia. We enrolled healthy adult volunteers in two age groups: younger adults (aged 18–54 years) and older adults (aged 55–75 years). Participants were randomly allocated either vaccine or placebo using a list prepared by the study funder. Participants were to receive two doses of SCB-2019 (either 3 μg, 9 μg, or 30 μg) or a placebo (0·9% NaCl) 21 days apart. SCB-2019 either had no adjuvant (S-Trimer protein alone) or was adjuvanted with AS03 or CpG/Alum. The assigned treatment was administered in opaque syringes to maintain masking of assignments. Reactogenicity was assessed for 7 days after each vaccination. Humoral responses were measured as SCB-2019 binding IgG antibodies and ACE2-competitive blocking IgG antibodies by ELISA and as neutralising antibodies by wild-type SARS-CoV-2 microneutralisation assay. Cellular responses to pooled S-protein peptides were measured by flow-cytometric intracellular cytokine staining. This trial is registered with ClinicalTrials.gov, NCT04405908; this is an interim analysis and the study is continuing.

Findings Between June 19 and Sept 23, 2020, 151 volunteers were enrolled; three people withdrew, two for personal reasons and one with an unrelated serious adverse event (pituitary adenoma). 148 participants had at least 4 weeks of follow-up after dose two and were included in this analysis (database lock, Oct 23, 2020). Vaccination was well tolerated, with two grade 3 solicited adverse events (pain in 9 μg AS03-adjuvanted and 9 μg CpG/Alum-adjuvanted groups). Most local adverse events were mild injection-site pain, and local events were more frequent with SCB-2019 formulations containing AS03 adjuvant (44–69%) than with those containing CpG/Alum adjuvant (6–44%) or no adjuvant (3–13%). Systemic adverse events were more frequent in younger adults (38%) than in older adults (17%) after the first dose but increased to similar levels in both age groups after the second dose (30% in older and 34% in younger adults). SCB-2019 with no adjuvant elicited minimal immune responses (three seroconversions by day 50), but SCB-2019 with fixed doses of either AS03 or CpG/Alum adjuvants induced high titres and seroconversion rates of binding and neutralising antibodies in

both younger and older adults (anti-SCB-2019 IgG antibody geometric mean titres at day 36 were 1567－4452 with AS03 and 174－2440 with CpG/Alum). Titres in all AS03 dose groups and the CpG/Alum 30 μg group were higher than were those recorded in a panel of convalescent serum samples from patients with COVID-19. Both adjuvanted SCB-2019 formulations elicited T-helper-1-biased CD4+ T-cell responses.

Interpretation The SCB-2019 vaccine, comprising S-Trimer protein formulated with either AS03 or CpG/Alum adjuvants, elicited robust humoral and cellular immune responses against SARS-CoV-2, with high viral neutralising activity. Both adjuvanted vaccine formulations were well tolerated and are suitable for further clinical development.

16. mRNA-1273 疫苗的有效性和安全性评价

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

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第一作者：L.R. Baden, H.M. El Sahly, B

通讯作者：L.R. Baden, H.M. El Sahly, B

通讯作者单位：The Division of Infectious Diseases, Brigham and Women’s Hospital,

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编译者：孔娟

中文摘要：

背景：急需疫苗以预防 Covid-19 并保护高并发症风险的人群。mRNA-1273 疫苗是一种脂质纳米颗粒封装的基于 mRNA 的疫苗，它编码导致 Covid-19 的 SARS-CoV-2 病毒的融合前稳定全长刺突蛋白。

方法：研究组在美国 99 个中心进行了一项临床 3 期、随机、观察者盲的安慰剂对照试验。将有 SARS-CoV-2 感染或其并发症高风险的人群按 1:1 的比例随机分配，间隔 28 天接受两次 mRNA-1273 (100 μg)肌肉注射或安慰剂注射。主要终点是预防之前没有感染过 SARS-CoV-2 的参与者在第二次注射后至少 14 天的 Covid-19 发病率。

结果：试验招募了 30，420 名志愿者，按 1:1 的比例随机分配接受疫苗或安慰剂(每组 15，210 名参与者)。超过 96%的受试者接受了两次注射，2.2%的受试者在基线时有感染 SARS-CoV-2 的证据(血清学、病毒学或两者兼有)。安慰剂组中有 185 名参与者最终确诊为有症状的 Covid-19 发生率为 56.5/1000 人-年；mRNA-1273 疫苗组中有 11 名参与者患病，发生率每 1000 人-年 3.3 例,组间差异显著。疫苗效果为 94.1% (95% CI,89.3 ~ 96.8%);P<0.001)。二次分析的疗效均相差不大，包括第一次注射后 14 天的评估，基线时有 SARS-CoV-2 感染证据的参与者的分析，以及 65 岁及以上参与者的分析。安慰剂组中有 30 名参与者发生严重的 Covid-19，其中一名死亡。接种疫苗后，中度、短暂的反应原性在 mRNA-1273 组中更为常见。严重不良事件很少见，两组的发生率相似。

结论：研究结果表明，mRNA-1273 疫苗在预防 Covid-19 疾病（包括严重疾病）方面显示出 94.1%的功效。除短暂的局部和全身反应外，未发现安全隐患。

Abstract

BACKGROUND

Vaccines are needed to prevent coronavirus disease 2019 (Covid-19) and to protect

persons who are at high risk for complications. The mRNA-1273 vaccine is a lipid nanoparticle-encapsulated mRNA-based vaccine that encodes the prefusion stabilized full-length spike protein of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19.

METHODS

This phase 3 randomized, observer-blinded, placebo-controlled trial was conducted at 99 centers across the United States. Persons at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 μg) or placebo 28 days apart. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with SARS-CoV-2.

RESULTS

The trial enrolled 30,420 volunteers who were randomly assigned in a 1:1 ratio to receive either vaccine or placebo (15,210 participants in each group). More than 96% of participants received both injections, and 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline. Symptomatic Covid-19 illness was confirmed in 185 participants in the placebo group (56.5 per 1000 person-years; 95% confidence interval [CI], 48.7 to 65.3) and in 11 participants in the mRNA-1273 group (3.3 per 1000 person-years; 95% CI, 1.7 to 6.0); vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001). Efficacy was similar across key secondary analyses, including assessment 14 days after the first dose, analyses that included participants who had evidence of SARS-CoV-2 infection at baseline, and analyses in participants 65 years of age or older. Severe Covid-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group. Moderate, transient reactogenicity after vaccination occurred more frequently in the mRNA-1273 group. Serious adverse events were rare, and the incidence was similar in the two groups.

CONCLUSIONS

The mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. Aside from transient local and systemic reactions, no safety concerns were identified. (Funded by the Biomedical Advanced Research and Development Authority and the National Institute of Allergy and Infectious Diseases; COVE ClinicalTrials.gov number, NCT04470427. opens in new tab.)

17. 在第一剂 BNT162b2 疫苗免疫后 13-24 天 SARS-CoV-2 感染保护的有效性:现实生活中的数据

The effectiveness of the first dose of BNT162 b 2 vaccine in reducing SARS-CoV-2 infection 13-24 days after immunization: real-world evidence

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第一作者：Gabriel Chodick, PhD

通讯作者：Gabriel Chodick, PhD

通讯作者单位：Maccabi Institute for Research & Innovation
DOI 或 PUBMED ID：preprint
编译者：孔娟
中文摘要：
背景：在一项随机对照 III 期试验中，BNT162b2 疫苗对新冠肺炎病毒表现出较高疗效。在全球疾病激增的情况下，迫切需要在现实生活中进行疫苗有效性评估。文中研究者评估了第一剂 BNT162b2 疫苗抗 SARS-CoV-2 感染的短期有效性。鉴于 BNT162b2III 期结果，研究者假设疫苗接种者中的 SARS-CoV-2 感染累积发病率与接种后最初的几天相比将在免疫后 12 天下降。
方法：这是一项回顾性队列研究，使用的数据来自以色列 260 万个成员国授权的医疗服务提供者。研究人群包括 2020 年 12 月 19 日至 2021 年 1 月 15 日期间接种 BNT162b2 疫苗的所有 16 岁或以上成员。研究者收集了从第一次给药后至 2021 年 1 月 17 日的病史和核酸检测阳性的信息。使用卡普兰-迈耶生存分析及广义线性模型，对接种后第 1-12 天与 13-24 天的每日和累积感染率进行比较。
结果：分析了 503，875 人(平均年龄 59.7 岁，SD=14.7，47.8%为男性)的数据，其中 351，897 人接受了 13-24 天的随访。第 1-12 天的 SARS-CoV-2 感染累积发生率为 0.57% (n=2484)，第 13-24 天为 0.27%(n = 614)。以 SARS-CoV-2 感染的加权平均每日发生率计算相对风险减少 51.4%(RRR)，从免疫后第 1-12 天的 43.41/100，000(SE=12.07)降至第 13-24 天的 21.08/100，000(SE=6.16)。从第一次给药后第 18 天开始，发病率明显下降。在 60 岁或以上的个体(44.5%)、较年轻的个体(50.2%)、女性(50.0%)和男性(52.1%)中计算的相对风险降低水平相似，在各种合并症的亚人群和患者中的计算结果相似。
结论：研究显示在接种第一剂 BNT162b2 疫苗后 13-24 天其对 SARS-CoV-2 的有效性为 51%，应继续进行第二剂免疫接种，以达到预期的保护效果。
Abstract
Background：BNT162b2 vaccines showed high efficacy against COVID-19 in a randomised controlled phase-III trial. A vaccine effectiveness evaluation in real life settings is urgently needed, especially given the global disease surge. Hence, we assessed the short-term effectiveness of the first dose of BNT162b2-vaccine against SARS-CoV-2 infection. Given the BNT162b2 Phase-III results, we hypothesized that the cumulative incidence of SARS-CoV-2 infection among vaccinees will decline after 12 days following immunization compared to the incidence during the preceding days.
Methods： We conducted a retrospective cohort study using data from 2.6 million-member state-mandated health provider in Israel. Study population consisted of all members aged 16 or above years who were vaccinated with BNT162b2-vaccine between December/19/2020 and January/15/2021. We collected information regarding medical history and positive SARSCoV-2 polymerase chain reaction test from days after first dose to January/17/2021. Daily and cumulative infection rates in days 13-24 were compared to days 1-12 after first dose using Kaplan-Meier survival analysis and generalized linear models.
Findings：Data of 503,875 individuals (mean age 59.7 years SD=14.7, 47.8% males) were analysed, of whom 351,897 had 13-24 days of follow-up. The cumulative incidence of SARS-CoV-2 infection was 0.57% (n=2484) during days 1-12 and 0.27% (n=614) in days 13-24. A 51.4% relative risk reduction (RRR) was calculated in

weighted-average daily incidence of SARSCoV-2 infection from 43.41-per-100,000(SE=12.07) in days 1-12 to 21.08-per-100,000(SE=6.16) in days 13-24 following immunization. The decrement in incidence wasevident from day 18 after first dose. Similar RRRs were calculated in individuals aged 60 or above (44.5%), younger individuals (50.2%), females (50.0%) and males (52.1%).Findings were similar in sub-populations and patients with various comorbidities.
Conclusions： We demonstrated an effectiveness of 51% of BNT162b2 vaccine against SARS-CoV-2 infection 13-24 days after immunization with the first dose. Immunization with the second dose should be continued to attain the anticipated protection.

18. 靶向 SARS-CoV-2 spike N 末端结构域的治疗性抗体可保护致命感染的 K18-hACE2 小鼠

Therapeutic antibodies, targeting the SARS-CoV-2 spike N-terminal domain, protect lethally infected K18-hACE2 mice

来源：bioRxiv

发布时间：2021-2-2

链接：https://www.biorxiv.org/content/10.1101/2021.02.02.428995v1

第一作者：Tal Noy-Pora

通讯作者：Ronit Rosenfeld

通讯作者单位：Israel Institute for Biological Research, Ness-Ziona, Israel.

DOI 或 PUBMED ID：

编译者：张鹏伟

中文摘要：

自从当前的 COVID-19 大流行开始以来，中和抗体的开发就被高度重视，这是设计对策和根除该疾病的治疗策略的关键方法。以前，我们报道了具有极高保护能力的人类治疗性单克隆抗体（mAb）的开发。这些 mAb 识别 SARS-CoV-2 的加标受体结合域（RBD）上的表位，被认为代表 SARS-CoV-2 病毒参与受体的主要途径。病毒变体的最新出现强调了这样一种观念，即有效的抗体治疗需要依靠针对几种不同关键表位的 mAb 来规避治疗逃逸突变体的发生。在这里，我们报告了 12 种中和 mAb 的分离和表征，通过筛选从严重 COVID-19 患者收集的淋巴细胞构建的噬菌体展示文库来鉴定。抗体靶向 SARS-CoV-2 的尖峰 N 末端结构域（NTD）上的三个不同表位，其中一个定义了病毒易感性的主要部位。这些 mAb 的广泛表征表明中和机制依赖于病毒对氨基酸和 N-聚糖的识别以及靶细胞上 hACE2 以外的受体的参与。在体内进一步评估了在体外表现出优异的中和能力的所选单克隆抗体中的两个，证明了即使在低剂量和感染后后期给药时，它们也能完全保护 K18-hACE2 转基因小鼠的能力。这项研究证明了单克隆抗体具有治疗 SARS-CoV-2 感染的巨大潜力，并强调了 NTD 在介导通过典型 ACE2 受体以外的其他细胞门感染宿主细胞方面的可能作用。

Abstract:

Since the onset of the current COVID-19 pandemic, high priority is given to the development of neutralizing antibodies, as a key approach for the design of therapeutic strategies to countermeasure and eradicate the disease. Previously, we reported the development of human therapeutic monoclonal antibodies (mAbs) exhibiting very high protective ability. These mAbs recognize epitopes on the spike receptor binding domain (RBD) of SARS-CoV-2 that is considered to represent the main rout of receptor engagement by the SARS-CoV-2 virus. The recent emergence

of viral variants emphasizes the notion that efficient antibody treatments need to rely on mAbs against several distinct key epitopes in order to circumvent the occurrence of therapy escape-mutants. Here we report the isolation and characterization of 12 neutralizing mAbs, identified by screening a phage-display library constructed from lymphatic cells collected from severe COVID-19 patients. The antibodies target three distinct epitopes on the spike N-terminal domain (NTD) of SARS-CoV-2, one of them defining a major site of vulnerability of the virus. Extensive characterization of these mAbs suggests a neutralization mechanism which relies both on amino-acid and *N*-glycan recognition on the virus, and involvement of receptors other than the hACE2 on the target cell. Two of the selected mAbs, which demonstrated superior neutralization potency *in vitro*, were further evaluated *in vivo*, demonstrating their ability to fully protect K18-hACE2 transgenic mice even when administered at low doses and late after infection. The study demonstrates the high potential of the mAbs for therapy of SARS-CoV-2 infection and underlines the possible role of the NTD in mediating infection of host cells via alternative cellular portals other than the canonical ACE2 receptor.

19. 机体内激发的抗病毒 I 型干扰素系统是抵抗新冠病毒病理入侵的第一道防线

Leveraging the antiviral type-I interferon system as a first line defense against SARSCoV-2 pathogenicity

来源：Immunity

发布时间：2021-01-29

链接：https://www.cell.com/immunity/fulltext/S1074-7613(21)00040-6

第一作者：Daisy A. Hoagland

通讯作者：Benjamin R. tenOever

通讯作者单位： Icahn School of Medicine at Mount Sinai

DOI 或 PUBMED ID: https://doi.org/10.1016/j.immuni.2021.01.017 R

编译者：姜连连

中文摘要：

新冠疫情的大流行导致了全球范围的高发病率，死亡率和社会秩序紊乱。更好了解病毒和宿主制衡关系有利于寻求控制感染的治疗方法。本文利用病理组织和转录分析系统性研究仓鼠感染 SARS-CoV-2 后免疫系统反应的动力学。新冠病毒感染会导致仓鼠上呼吸道和下呼吸道持续携带高水平的病毒，并在一些远端组织出现零星病毒。一项纵向队列研究显示无论有无病毒存在，机体所有组织均会产生一轮明显的炎症反应，其中包括 I 型干扰素(IFNI)反应，但反应强度不足以阻止疾病进程。通过鼻内给予重组 IFN-I 来增强机体抗病毒能力，可降低新冠感染发病率，阻止病毒传播，并降低体内炎症反应。这项研究证明宿主对新冠病毒 SARS-CoV-2 感染产生全身系统性炎症反应，且使用鼻内补充 IFN-I 可作为早期治疗的有效措施。

Abstract:

The emergence and spread of SARS-CoV-2 has resulted in significant global morbidity, mortality, and societal disruption. A better understanding of virus-host interactions may potentiate therapeutic insights toward limiting this infection. Here, we investigated the dynamics of the systemic response to SARS-CoV-2 in hamsters by histological analysis and transcriptional profiling.

Infection resulted in consistently high levels of virus in both the upper and lower respiratory tracts and sporadic occurrences in other distal tissues. A longitudinal cohort revealed a wave of inflammation including a Type-I interferon (IFNI) response that was evident in all tissues regardless of viral presence, but was insufficient to prevent disease progression. Bolstering the antiviral response with intranasal administration of recombinant IFN-I reduced viral disease, prevented transmission, and lowered inflammation in vivo. This study defines the systemic host response to SARS-CoV-2 infection and supports use of intranasal IFN-I as an effective means of early treatment.

20. 针对早期 Spike 蛋白开发的疫苗所产生的中和抗体仍具有中和 SARS-CoV-2 病毒变种 B.1.1.7 的能力

SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines

来源：bioRxiv

发布时间：2021-01-29

链接：https://www.biorxiv.org/content/10.1101/2021.01.27.428516v2

第一作者：Xiaoying Shen

通讯作者：David C. Montefiori

通讯作者单位：Department of Surgery, Duke University School of Medicine, Durham, NC, USA

DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

SARS-CoV-2 病毒的 Spike 糖蛋白能够介导病毒侵入细胞，是中和抗体的主要靶点。目前所有的疫苗都是针对早期的 Spike 蛋白开发的，其目的是产生保护性的中和抗体反应。然而，近期已经出现了几种 SARS-CoV-2 病毒的新变种，其 Spike 蛋白携带多个突变。由于这些病毒变种的传播速度快，并可能产生免疫逃逸，因此引起了人们的广泛担忧。病毒的新变种之一是首先在英国发现的 B.1.1.7(也被称为 VUI202012/01)，其 Spike 蛋白包含 8 个突变。这些突变可能会影响抗体治疗和疫苗的效果，增加再次被感染的风险。本文中，作者进行了基于慢病毒的假病毒试验。结果表明，无论是在 COVID-19 康复期患者的血清中，还是分别接种了基于原始 Spike 蛋白开发的两种不同疫苗：mRNA-1273 (Moderna)或蛋白纳米颗粒 NVX-CoV2373 (Novavax)的受试者的血清样本中，病毒变体 B.1.1.7 对抗体的中和作用仍然敏感，只是抗体的中和能力有一定的下降（约 2 倍）。一些针对 Spike 蛋白受体结合结构域(RBD)的单克隆抗体对该病毒变体的效果较差，而另一些则基本不受影响。这些发现表明，B.1.1.7 病毒变体不会发生免疫逃逸，不必对目前的疫苗或增加再感染的风险产生担忧。

Abstract:

The SARS-CoV-2 Spike glycoprotein mediates virus entry and is a major target for neutralizing antibodies. All current vaccines are based on the ancestral Spike with the goal of generating a protective neutralizing antibody response. Several novel SARS-CoV-2 variants with multiple Spike mutations have emerged, and their rapid spread and potential for immune escape have raised concerns. One of these variants, first identified in the United Kingdom, B.1.1.7 (also called VUI202012/01), contains eight Spike mutations with potential to impact antibody

therapy, vaccine efficacy and risk of reinfection. Here we employed a lentivirus-based pseudovirus assay to show that variant B.1.1.7 remains sensitive to neutralization, albeit at moderately reduced levels (~2-fold), by serum samples from convalescent individuals and recipients of two different vaccines based on ancestral Spike: mRNA-1273 (Moderna), and protein nanoparticle NVX-CoV2373 (Novavax). Some monoclonal antibodies to the receptor binding domain (RBD) of Spike were less effective against the variant while others were largely unaffected. These findings indicate that B.1.1.7 is not a neutralization escape variant that would be a major concern for current vaccines, or for an increased risk of reinfection.

21. 关于病毒突变体的标题报道

SARS-CoV-2 Y453F 水貂突变显著增强了 ACE-2 的亲和力（4 倍），但是不改变（针对野生型 RBD 或者 S 蛋白）抗体的中和能力

The SARS-CoV-2 Y453F mink variant displays a striking increase in ACE-2 affinity but does not challenge antibody neutralization

发表日期：2021-01-29

链接：https://www.biorxiv.org/content/10.1101/2021.01.29.428834v1

SARS-CoV-2 S 蛋白的 E484K 突变降低但是并没有消除康复病人或者免疫后血清的中和活性

The E484K mutation in the SARS-CoV-2 spike protein reduces but does not abolish neutralizing activity of human convalescent and post-vaccination sera.

发表日期：2021-01-29

链接：https://www.medrxiv.org/content/10.1101/2021.01.26.21250543v1

流行中的 SARS-CoV-2 突变株 B.1.1.7， 501Y.V2， and P.1 已经获得利用小鼠和大鼠 ACE2 的能力，在体外系统中改变了中和抗体和 ACE2-Ig 的敏感性

发表日期：

Circulating SARS-CoV-2 variants B.1.1.7, 501Y.V2, and P.1 have gained ability to utilize rat and mouse Ace2 and altered in vitro sensitivity to neutralizing antibodies and ACE2-Ig

发表日期：2021-01-31

链接：https://www.biorxiv.org/content/10.1101/2021.01.27.428353v2

22. 抗 SARS-CoV-2 记忆 B 细胞反应的成熟和持续性

Maturation and persistence of the anti-SARS-CoV-2 memory B cell response

来源：Cell

发布时间：2021-02-02

链接：https://www.cell.com/cell/fulltext/S0092-8674(21)00093-3#%20

第一作者：Aurélien Sokal, Pascal Chappert,

通讯作者：Matthieu Mahévas

通讯作者单位：Institut Necker Enfants Malades (INEM), INSERM U1151/CNRS UMS 8253, Université de Paris, Paris, France

DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2021.01.050

编译者：王玮

中文摘要：

记忆 B 细胞在宿主抵抗病毒的过程中起着基础性的作用，但迄今为止，对它们在 SARS-CoV-2 中的作用了解还很少。该研究报告了轻度和重度 COVID-19 患者长达 6 个月的纵向的 B 细胞单细胞测序分析。独特的 SARS-CoV-2 S 蛋白特异性激活的 B 细胞克隆促进了早期抗体分泌细胞的爆发以及持久的同步生发中心的反应。虽然高度突变的记忆 B 细胞，包括预先存在的交叉反应性季节性 β-冠状病毒特异性克隆，在应答早期被招募，但中和 SARS-CoV-2 RBD 特异性克隆会随着时间的推移而积累，并在很大程度上有助于后期非常稳定的记忆 B 细胞池。随着时间的推移，这些细胞在其可变区基因中表现出明显的体细胞突变积累，从而突出了生发中心的成熟。总的来说，这些发现表明抗原驱动的激活在 SARS-CoV-2 感染后持续并成熟到 6 个月，并可能提供长期的保护。

Abstract:

Memory B cells play a fundamental role in host defenses against viruses, but to date, their role has been relatively unsettled in the context of SARS-CoV-2. We report here a longitudinal single-cell and repertoire profiling of the B cell response up to 6 months in mild and severe COVID-19 patients. Distinct SARS-CoV-2 spike-specific activated B cell clones fueled an early antibody-secreting cell burst as well as a durable synchronous germinal center response. While highly mutated memory B cells, including pre-existing cross-reactive seasonal Betacoronavirus-specific clones, were recruited early in the response, neutralizing SARS-CoV-2 RBD-specific clones accumulated with time and largely contributed to the late remarkably stable memory B-cell pool. Highlighting germinal center maturation, these cells displayed clear accumulation of somatic mutations in their variable region genes over time. Overall, these findings demonstrate that an antigen-driven activation persisted and matured up to 6 months after SARS-CoV-2 infection and may provide long-term protection.

23. 由 BBIBP-CorV 灭活疫苗和重组二聚 RBD ZF2001 疫苗诱导产生的人源抗血清对 SARS-CoV-2 VOC 501Y.V2 的中和作用

Neutralization of SARS-CoV-2 VOC 501Y.V2 by human antisera elicited by both inactivated BBIBP-CorV and recombinant dimeric RBD ZF2001 vaccines

来源：bioRxiv

发布时间：2021-02-02

链接：https://www.biorxiv.org/content/10.1101/2021.02.01.429069v1

第一作者：Baoying Huang, Lianpan Dai

通讯作者：Wenjie Tan, George F. Gao

通讯作者单位：NHC Key Laboratory of Biosafety, National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, 102206, China

DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

近期出现并迅速传播的 SARS-CoV-2 病毒新变种 501Y.V2 引起了人们的担忧(VOC)。501Y.V2 变种的 Spike 蛋白携带 10 个氨基酸突变，因而能够逃避由感染或接种疫苗引起的

宿主免疫。由于病毒新变体可能会影响疫苗的效果，因此受到了全球的关注。本文中，作者对两种我国研发的疫苗对 501Y.V2 变体的中和活性进行了评估。两种疫苗分别是：获得许可的灭活疫苗 BBIBP-CorV，和重组二聚受体结合结构域(RBD)疫苗 ZF2001。令人鼓舞的是，与原始 SARS-CoV-2 病毒和当前流行的 D614G 病毒相比，两种疫苗对 501Y.V2 的中和滴度基本没有变化，只是略有下降。这些数据表明，基于全病毒或 RBD 开发的疫苗所引起的免疫反应仍对 501Y.V2 病毒变种有效。

编者注：

BBIBP-CorV 是国药北京生物的灭活疫苗,在国内已经获得附条件上市

ZF2001 是智飞生物（300122）与中国科学院微生物所联合开发的疫苗，目前正在进行三期临床试验

Abstract:

Recently, the emerged and rapidly spreading SARS-CoV-2 variant of concern (VOC) 501Y.V2 with 10 amino acids in spike protein were found to escape host immunity induced by infection or vaccination. Global concerns have been raised for its potential to affect vaccine efficacy. Here, we evaluated the neutralization activities of two vaccines developed in China against 501Y.V2. One is licensed inactivated vaccine BBIBP-CorV and the other one is recombinant dimeric receptor-binding domain (RBD) vaccine ZF2001. Encouragingly, both vaccines largely preserved neutralizing titres, with slightly reduction, against 501Y.V2 authentic virus compare to their titres against both original SARS-CoV-2 and the currently circulating D614G virus. These data indicated that 501Y.V2 variant will not escape the immunity induced by vaccines targeting whole virus or RBD.

24. 控制新型 SARS-CoV-2 变种的公共卫生行动

Public health actions to control new SARS-CoV-2 variants

来源：cell

发布时间：2021-01-29

链接：https://www.cell.com/action/showPdf?pii=S0092-8674%2821%2900087-8

第一作者：Nathan D. Grubaugh

通讯作者：Emma B. Hodcroft[4], Joseph R. Fauver[1], Alexandra L. Phelan[5]

通讯作者单位：1 Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT USA; 4 Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland; 5 Center for Global Health Science and Security, Georgetown University, Washington, DC, USA.

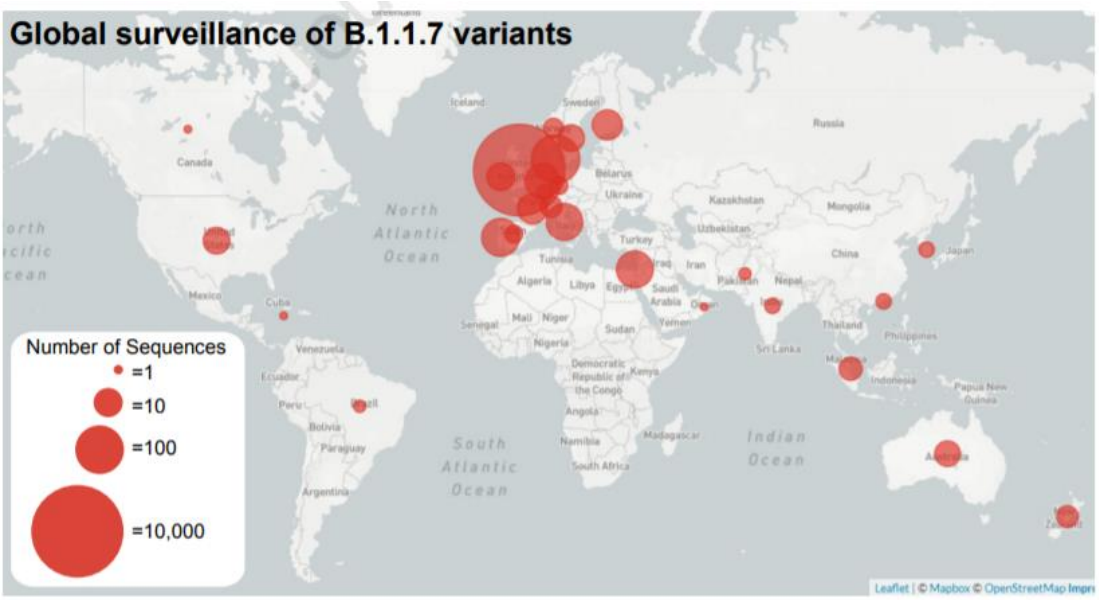
DOI 或 PUBMED ID：https://doi.org/10.1016/j.cell.2021.01.044

编译者：宋张悦

中文摘要：

近期报告提示，部分 SARS-CoV-2 基因变异，如 B.1.1.7，可能具有更强的传染性，正在全球快速传播。由于更具传染性的变异病毒的出现可能加剧大流行，我们为加强监测和采取措施减少社区传播提供公共卫生指南。

虽然本文的大部分内容都以 B.1.1.7 变种为例，但类似的原则也适用于其他值得关注的 SARS-CoV-2 变种，包括在南非发现的 B.1.351 变种和在巴西发现的 P.1 变种。



Abstract:
Recent reports suggest that some SARS-CoV-2 genetic variants, such as B.1.1.7, may be more transmissible, and are quickly spreading around the world. As the emergence of more transmissible variants may exacerbate the pandemic, we provide public health guidance for increased surveillance and measures to reduce community transmission.

25. 科学家对免疫护照的意见、态度和共识

Scientists' opinion, attitudes, and consensus towards immunity passports

来源：medRxiv

发布时间：2021-02-03

链接：https://www.medrxiv.org/content/10.1101/2021.02.02.21250796v1

第一作者：Iván Aranzales

通讯作者：David Stadelmann

通讯作者单位：Centre for Behavioural Economics, Society and Technology (BEST), Brisbane, Queensland, Australia

DOI 或 PUBMED ID：preprint

编译者：宋张悦

中文摘要：

目的：我们实测了众多科学家在 COVID-19 背景下对“免疫护照”（immunity passports）的态度。评估了科学家对免疫护照不同方面的共识意见。

方法：我们设计并实施了一项调查，以捕获来自世界各地和不同科学背景的科学家对免疫认证的看法。2020 年 5 月至 6 月，该调查将发送给在过去 5 年里发表在 27 个学科领域中排名前 20 的期刊上的学术文章的通信作者。研究人员收集了 12,738 名科学家的回答，并将他们的分布情况按健康科学和其他领域的参与者分类制成表格。采用适合于顺序响应变量的香农熵（Shannon Entropy）变量，计算响应一致性。

结果：无论学术背景如何，接受调查的科学家中**有一半都同意潜在的免疫护照计划将有利于公共健康(50.2%)和经济(54.4%)，分别有 19.1%和 15.4%的参与者不同意**。相当一部分科学

家提出了对免疫认证的担忧，理由是对他人的公平性(36.5%)和社会不平等(45.5%)。科学家对免疫护照的不同方面几乎没有共识。总的来说，有健康背景的科学家对免疫认证持比较保守的观点。

结论：**我们的研究结果表明，科学界对免疫认证项目的潜在健康和经济利益、社会成本和伦理问题缺乏普遍共识。**鉴于免疫护照由于疫苗供应和效力的增加而产生的相关和重要影响，应更加重视对设计和实施免疫认证计划的讨论。

Abstract:

Objectives: We measured attitudes towards "immunity passports" in the context of COVID-19 of a large sample of scientists. Consensus of scientists' opinions on a different aspect of immunity passports was assessed.

Methods: We designed and implemented a survey to capture what scientists from around the world and different scientific background think about immunity certification. The survey was sent to the corresponding authors of scholarly articles published in the last five years in the top 20-ranked journals in each of the 27 subject areas between May and June 2020. Responses from 12,738 scientists were captured, and their distribution was tabulated by participants in health science and other fields. Consensus of responses was calculated using a variant of Shannon Entropy, made suitable for the ordinal response variables.

Results: Half of the scientists surveyed, regardless of academic background agree that a potential immunity passport program will be good for public health (50.2%) and the economy (54.4%), with 19.1% and 15.4% of participants disagree, respectively. A significant proportion of scientists raised concerns about immunity certification over fairness to others (36.5%) and social inequality (45.5%). There is little consensus in the different aspects of immunity passport among scientists. Overall, scientists with health background hold a more conservative view towards immunity certification.

Conclusions: Our findings suggest a lack of general agreement regarding the potential health and economic benefits, societal costs, and ethical issues of an immunity certification program within the scientific community. Given the relevant and important implications of immunity passport due to the increasing vaccine availability and efficacy, more attention should be given to the discussion of the design and implementation of immunity certification program.