新型冠状病毒信息简报

第 97 期（2021 年 3 月 20-26 日报）

上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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1. 2021 年 3 月 25 日疫情

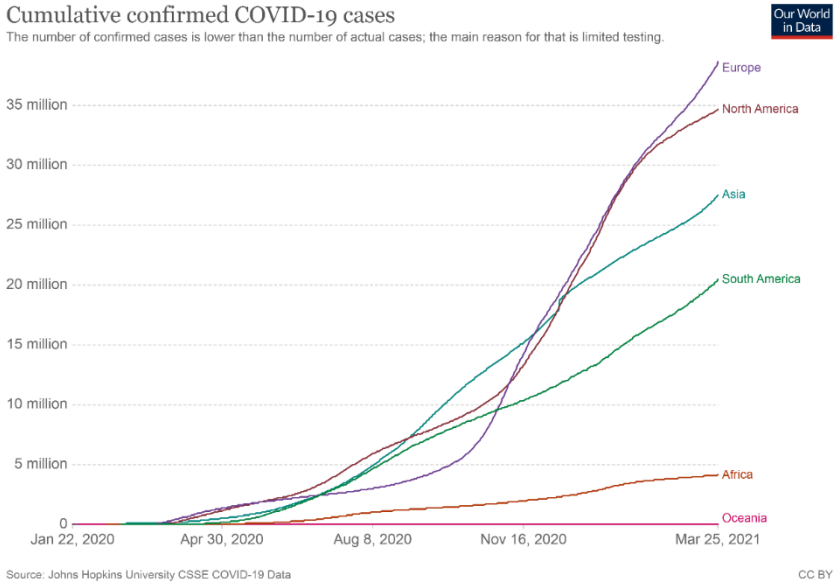
数据来源：WHO

发布时间：2021 年 3 月 25 日北京时间下午 4 点

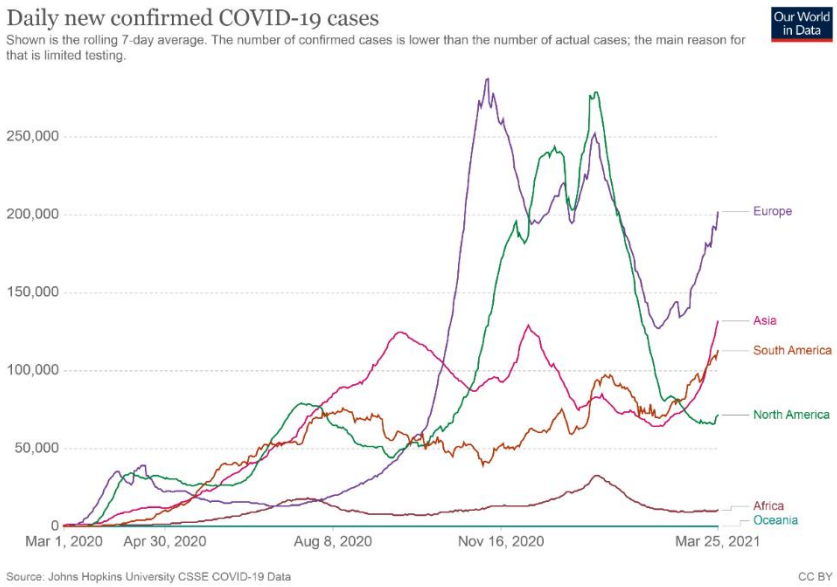
链接：https://covid19.who.int/

根据 WHO 提供的数据，2021 年 3 月 25 日全球累计确诊新型冠状病毒病人 **124,535,520** 例，当日新增确诊 **575,191** 例，累计死亡 **2,738,876** 例，当日新增死亡 **10,421**。

中国累计确诊 102,612 例，累计死亡 4,850 例，当日新增确诊 23 例，新增死亡 0 例。



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



世界各洲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（3 月 25 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 凌晨通报，新增 1 例本土确诊病例

来源：央视网

发布时间:2021-03-27

链接：https://mp.weixin.qq.com/s/Tdg47_B3Akco8rnG8huYuA

摘要：江西省卫健委 27 日凌晨发布通报称，**此前江西省新增的 1 例本土新冠肺炎无症状**感染者转为确诊病例。

流调显示，**该确诊病例张某某**曾与境外输入确诊病例吴某乘坐同一趟火车同一个车厢从南京抵达南昌。

3. 斯洛伐克人群快速抗原检测对 SARS-CoV-2 流行的影响

The impact of population-wide rapid antigen testing on SARS-CoV-2 prevalence in Slovakia

来源：science

发布时间：2021-03-23

链接：https://science.sciencemag.org/content/early/2021/03/22/science.abf9648

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DOI 或 PUBMED ID：

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中文摘要：

斯洛伐克在 2020 年末进行了多轮针对 SARS-CoV-2 的全人群快速抗原检测，并实施了一段时间的社交限制。在接受两轮大规模检测的 45 个县中，观察到的患病率在一周内下降了 58%

（95% CI:57-58%），这一估计在调整多个潜在混杂因素时仍然是可靠的。根据大规模检测活动前每天 4.4%（1.1-6.9%）的流行性增长进行调整，与未开展限制措施相比，估计流行率下降了 70%（67-73%）。模型表明，这一减少不能仅仅来自感染控制措施，还有对检测呈阳性的家庭成员进行隔离和检疫的影响。

Abstract:
Slovakia conducted multiple rounds of population-wide rapid antigen testing for SARS-CoV-2 in late 2020, combined with a period of additional contact restrictions. Observed prevalence decreased by 58% (95% CI: 57-58%) within one week in the 45 counties that were subject to two rounds of mass testing, an estimate that remained robust when adjusting for multiple potential confounders. Adjusting for epidemic growth of 4.4% (1.1-6.9%) per day preceding the mass testing campaign, the estimated decrease in prevalence compared to a scenario of unmitigated growth was 70% (67-73%). Modelling indicated that this decrease could not be explained solely by infection control measures, but required the additional impact of isolation and quarantine of household members of those testing positive.

4. 使用串联 CRISPR 核酸酶加速 RNA 检测

Accelerated RNA detection using tandem CRISPR nucleases

来源：medrxiv
发布时间：2021-03-24
文章链接：https://www.medrxiv.org/content/10.1101/2021.03.19.21253328v1

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doi: https://doi.org/10.1101/2021.03.19.21253328

编译者：张怡

中文摘要：
直接、无扩增的 RNA 检测具有改变分子诊断的潜力，可以实现对人类或环境样本的简单现场分析。CRISPR-Cas 核酸酶提供可设计的 RNA 引导的 RNA 识别，从而触发荧光报告分子的切割和释放，但当应用于医护点检测时，长时间的反应阻碍了灵敏度和速度。本研究表明，不相关的 CRISPR 核酸酶可以串联部署，提供直接 RNA 检测和快速信号生成，从而能够在 20 分钟内对每微升约 30 个 RNA 拷贝进行检测。将 RNA 引导的 Cas13 和 Csm6 与化学稳定的激活剂相结合，创建了一种一步法检测方法，使用一种紧凑的成像系统，在微流控芯片中使用 PCR 衍生 Ct 值高达 29 的微流控芯片，检测鼻咽样本中的 SARS-CoV-2 RNA。这种快速集成的串联核酸酶检测(FIND-IT)方法使得在医疗点的感染诊断、以及其他广泛的诊断和研究应用中能够直接进行 RNA 检测。

Abstract
Direct, amplification-free detection of RNA has the potential to transform molecular diagnostics by enabling simple on-site analysis of human or environmental samples. CRISPR-Cas nucleases offer programmable RNA-guided recognition of RNA that triggers cleavage and release of a fluorescent reporter molecule, but long reaction times hamper sensitivity and speed when applied to point-of-care testing. Here we show that unrelated CRISPR nucleases can be

deployed in tandem to provide both direct RNA sensing and rapid signal generation, thus enabling robust detection of ~30 RNA copies/microliter in 20 minutes. Combining RNA-guided Cas13 and Csm6 with a chemically stabilized activator creates a one-step assay that detected SARS-CoV-2 RNA from nasopharyngeal samples with PCR-derived Ct values up to 29 in microfluidic chips, using a compact imaging system. This Fast Integrated Nuclease Detection In Tandem (FIND-IT) approach enables direct RNA detection in a format amenable to point-of-care infection diagnosis, as well as to a wide range of other diagnostic or research applications.

5. 江苏硕世生物科技股份有限公司对新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）主动召回

来源：国家药监局

发布时间：2021-03-22

链接：

https://www.nmpa.gov.cn/xxgk/chpzhh/ylqxzhh/ylqxzhhdf/20210323020147417.html

编译者：宋张悦

中文摘要：

江苏硕世生物科技股份有限公司报告，该企业的新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）在运输过程中存在某些时间点温度异常的情况，其研发部门充分验证对产品质量无影响，但考虑到潜在的风险，现主动召回，召回级别为三级。注册证编码：国械注准 20203400384，共召回 20 个批次 13990 盒检测产品，涉及产品的具体信息见《医疗器械召回事件报告表》（请点击上述链接查看详情。）

6. 表位分辨的血清学检测可区分 COVID-19 的临床结果，并能识别 SARS-CoV-2 变异株的抗体响应缺陷

Epitope-resolved serology test differentiates the clinical outcome of COVID-19 and identifies defects in antibody response in SARS-CoV-2 variants

来源：medRxiv

发布时间：2021-03-20

链接：https://www.medrxiv.org/content/10.1101/2021.03.16.21253716v1

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DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

背景 体液免疫在 COVID-19 患者体内的作用尚不完全清楚，这在很大程度上是由于感染 SARS-CoV-2 后产生的抗体组分非常复杂。当前，对患者进行血清学检测的需求十分迫切，能够据此评估患者的特异性抗体反应并预测临床治疗结果。

方法 利用 SARS-CoV-2 蛋白质组和肽段芯片技术，对 146 例 COVID-19 患者的血浆样本进行了抗原和表位鉴定。作者据此开发出了一个主要表位阵列和一个表位特异性凝聚检测方法，能够以较高的分辨率系统性地测量抗体响应。

结果 作者从 Spike(S)蛋白和 Nucleocapsid(N)蛋白中鉴别出了 54 个线性表位，而且发现这些表位比蛋白抗原具有更高的抗体特征分辨率。具体而言，作者发现对 S(811-825)、S(881-895)和 N(156-170)表位的抗体响应与患者的临床严重程度呈负相关，而与患者的存活率呈正相关。此外，作者还发现，与冠状病毒 B.1.1.7 型相关的 P681H 和 S235F 突变改变了相应表位的特异性。

结论 表位分辨抗体检测，不仅提供了一种可替代传统免疫分析方法，并可以以更高的分辨率来表征感染 SARS-CoV-2 后的复杂体液免疫反应，而且能够区分中和性和非中和性抗体，同时其还可以作为预测临床结果的指标。肽段阵列和乳胶凝聚的格式中的表位肽很容易被修改，从而可以检测针对病毒变异株的抗体。

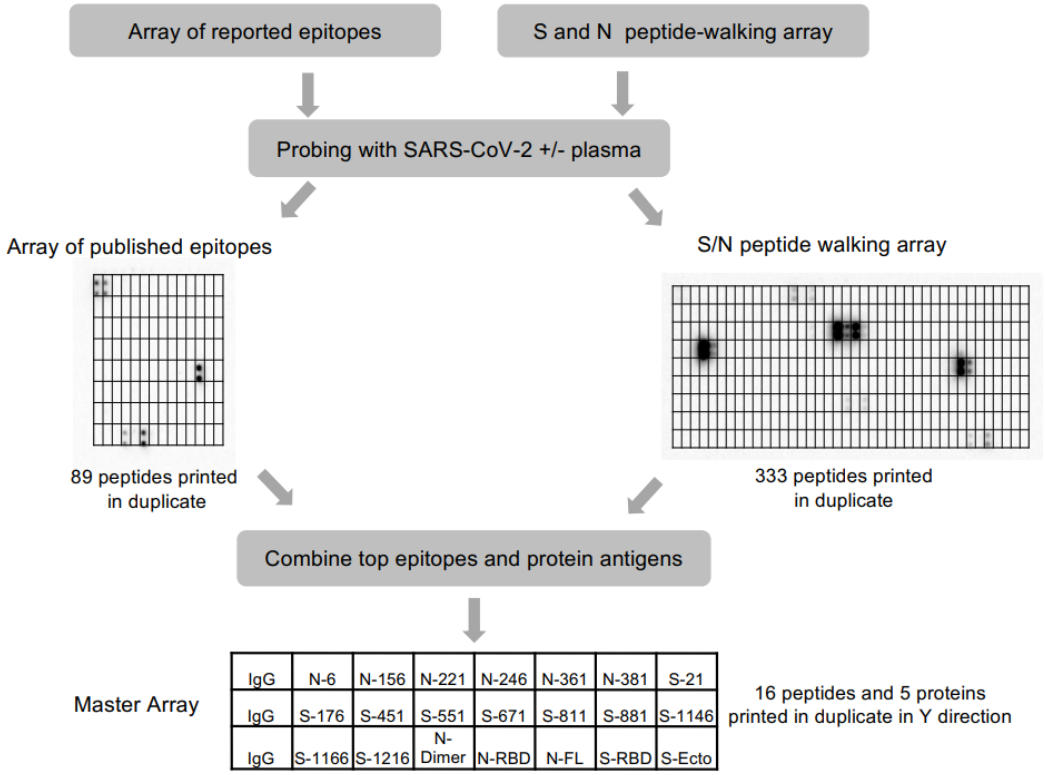

Fig2 A. Workflow for identifying antigenic epitopes by peptide arrays and the layout of a master array for SARS-CoV-2 antibody profiling

基金 Ontario Research Fund (ORF)-COVID-19 Rapid Research Fund, the Toronto COVID-19 Action Fund, Western University, the Lawson Health Research Institute, the London Health Sciences Foundation, and the AMOSO Innovation Fund.

Abstract:

BACKGROUND The role of humoral immunity in the coronavirus disease 2019 (COVID-19) is not fully understood owing, in large part, to the complexity of antibodies produced in response to the SARS-CoV-2 infection. There is a pressing need for serology tests to assess patient-specific antibody response and predict clinical outcome.

METHODS Using SARS-CoV-2 proteome and peptide microarrays, we screened 146 COVID-19 patients plasma samples to identify antigens and epitopes. This enabled us to develop a master epitope array and an epitope-specific agglutination assay to

gauge antibody responses systematically and with high resolution.
RESULTS We identified 54 linear epitopes from the Spike (S) and Nucleocapsid (N) protein and showed that epitopes enabled higher resolution antibody profiling than protein antigens. Specifically, we found that antibody responses to the S(811-825), S(881-895) and N(156-170) epitopes negatively or positively correlated with clinical severity or patient survival. Moreover, we found that the P681H and S235F mutations associated with the coronavirus variant B.1.1.7 altered the specificity of the corresponding epitopes.
CONCLUSIONS Epitope-resolved antibody testing not only offers a high-resolution alternative to conventional immunoassays to delineate the complex humoral immunity to SARS-CoV-2 and differentiate between neutralizing and non-neutralizing antibodies, it may also be used as predictor of clinical outcome. The epitope peptides can be readily modified to detect antibodies against variants in both the peptide array and latex agglutination formats.
FUNDING Ontario Research Fund (ORF)-COVID-19 Rapid Research Fund, the Toronto COVID-19 Action Fund, Western University, the Lawson Health Research Institute, the London Health Sciences Foundation, and the AMOSO Innovation Fund.

7. COVID-19 后遗症

Post-acute COVID-19 syndrome
来源：nature
发布时间：2021-03-22
链接：https://www.nature.com/articles/s41591-021-01283-z
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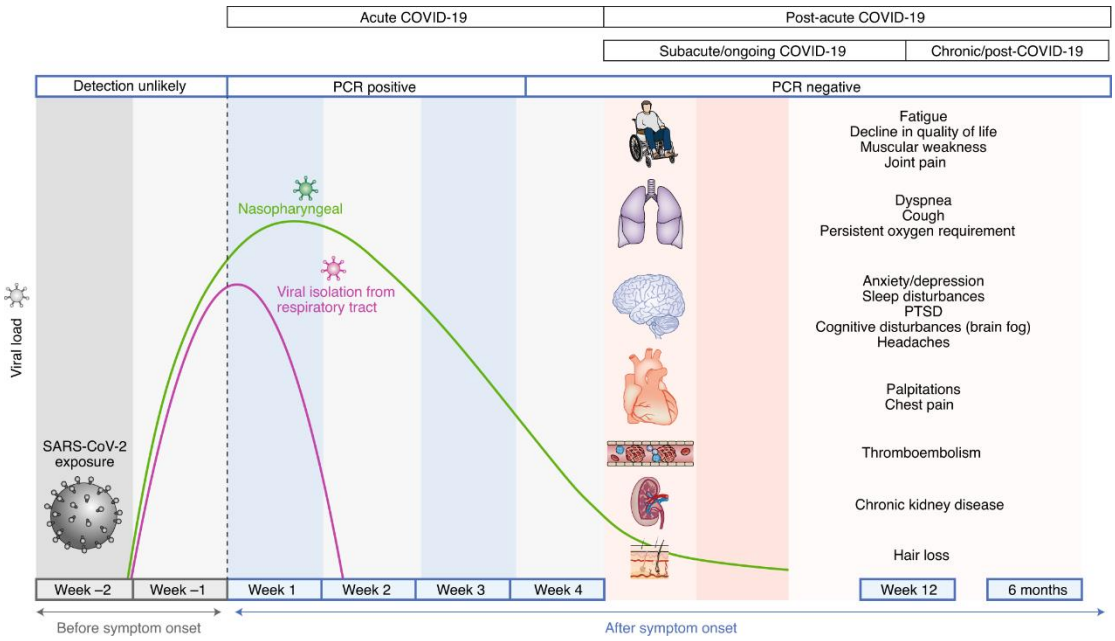
DOI 或 PUBMED ID：https://doi.org/10.1038/s41591-021-01283-z
编译者：宋张悦
中文摘要：
严重急性呼吸系统综合征冠状病毒 2 (SARS-CoV-2)是导致 2019 冠状病毒病(COVID-19)大流行的病原体，导致全球医疗危机和卫生资源紧张。随着 COVID-19 患者康复人数的增长，对相关医疗保健问题的了解是至关重要的。COVID-19 现在被确认为是一种具有广泛表现的多器官疾病。与其他强毒性冠状病毒流行的幸存者描述的后遗症类似，COVID-19 急性感染期后，出现持续和长期影响的报告越来越多。患者宣传团体（Patient advocacy groups，其中许多成员自称为长途搬运工）帮助识别了急性后 COVID-19，这是一种以持续症状和/或出现症状 4 周后的延迟或长期并发症为特征的综合征。在此，我们对当前关于 COVID-19 急性后、病理生理学及其器官特异性后遗症的文献进行了全面综述。最后，我们讨论了 COVID-19 幸存者多学科护理的相关考虑因素，还提出一个框架，用于识别急性后 COVID-19 高危人群，并通过专门的 COVID-19 诊所对其进行协调管理。

Fig.1 Timeline of post-acute COVID-19.



Abstract:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for the coronavirus disease 2019 (COVID-19) pandemic, which has resulted in global healthcare crises and strained health resources. As the population of patients recovering from COVID-19 grows, it is paramount to establish an understanding of the healthcare issues surrounding them. COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations. Similarly to post-acute viral syndromes described in survivors of other virulent coronavirus epidemics, there are increasing reports of persistent and prolonged effects after acute COVID-19. Patient advocacy groups, many members of which identify themselves as long haulers, have helped contribute to the recognition of post-acute COVID-19, a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. Here, we provide a comprehensive review of the current literature on post-acute COVID-19, its pathophysiology and its organ-specific sequelae. Finally, we discuss relevant considerations for the multidisciplinary care of COVID-19 survivors and propose a framework for the identification of those at high risk for post-acute COVID-19 and their coordinated management through dedicated COVID-19 clinics.

8. 哥伦比亚大学欧文医学中心/纽约长老会医院进行的新冠肺炎神经病理学的相关研究

COVID-19 Neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital

来源：medrxiv

发布时间：2021-03-20

链接：https://www.medrxiv.org/content/10.1101/2021.03.16.21253167v1

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许多 SARS-CoV-2 感染患者会出现神经系统体征和症状，但迄今为止，几乎没有证据表明原发性脑感染是一个重要的促发因素。研究中介绍了接受尸检的 41 例 SARS-CoV-2 感染患者的临床、神经病理学和分子学发现。患者平均年龄为 74 岁(38-97 岁)，27 名患者(66%)为男性，34 名(83%)为西班牙裔/拉丁裔。24 名患者(59%)入住重症监护室(ICU)。常见医院相关并发症，包括 8 例(20%)深静脉血栓形成/肺栓塞(DVT/PE)，7 例(17%)急性肾损伤需要透析，10 例(24%)入院时血培养阳性。8 例(20%)患者在入院 24 小时内死亡，11 例(27%)在入院 4 周后死亡。研究者对每例脑的 20-30 个区域进行神经病理学检查，结果显示所有脑(包括全脑和局灶)均出现缺氧/缺血性变化;不同程度的梗塞和伴随神经嗜食的小胶质结节的小胶质细胞活化，最显著地在脑干中。在血管周围区域或脑实质中观察到稀疏的 T 淋巴细胞积聚。许多大脑都存在大动脉粥样硬化和小动脉硬化，18 例(44%)含有神经退行性疾病的病理特征。研究者使用定量逆转录酶 PCR (qRT PCR)、RNAscope 以及针对 S 蛋白区域的引物、探针和抗体免疫，对 28 例的多个新鲜冷冻和固定组织中是否存在病毒 RNA 和蛋白进行了检测。qRT-PCR 显示，尽管病毒 RNA 水平远低于鼻上皮，但在大多数大脑中存在可以检测到较低水平的病毒 RNA。RNAscope 和免疫法未能检测出大脑中的病毒 RNA 或蛋白。研究表明，新冠肺炎脑中可检测病毒的水平非常低，与组织病理学改变无关。在多数大脑中观察到的小胶质细胞活化、结节和神经嗜食不是由脑实质的直接病毒感染引起的，而可能由全身炎症引起的，可能与缺氧/缺血的协同作用有关。需要进一步研究以确定这些病理是否可能导致慢性神经系统问题。

Abstract

Many patients with SARS-CoV-2 infection develop neurological signs and symptoms, though, to date, little evidence exists that primary infection of the brain is a significant contributing factor. We present the clinical, neuropathological, and molecular findings of 41 consecutive patients with SARS-CoV-2 infections who died and underwent autopsy in our medical center. The mean age was 74 years (38-97 years), 27 patients (66%) were male and 34 (83%) were of Hispanic/Latinx ethnicity. Twenty-four patients (59%) were admitted to the intensive care unit (ICU). Hospital-associated complications were common, including 8 (20%) with deep vein thrombosis/pulmonary embolism (DVT/PE), 7 (17%) patients with acute kidney injury requiring dialysis, and 10 (24%) with positive blood cultures during admission. Eight (20%) patients died within 24 hours of hospital admission, while 11 (27%) died more than 4 weeks after hospital admission. Neuropathological examination of 20-30 areas from each brain revealed hypoxic/ischemic changes in all brains, both global and focal; large and small infarcts, many of which appeared hemorrhagic; and microglial activation with microglial nodules accompanied by neuronophagia, most prominently in the brainstem. We observed sparse T lymphocyte accumulation in either perivascular regions or in the brain parenchyma. Many brains contained atherosclerosis of large arteries and

arteriolosclerosis, though none had evidence of vasculitis. Eighteen (44%) contained pathologies of neurodegenerative diseases, not unexpected given the age range of our patients. We examined multiple fresh frozen and fixed tissues from 28 brains for the presence of viral RNA and protein, using quantitative reverse-transcriptase PCR (qRTPCR), RNAscope, and immunocytochemistry with primers, probes, and antibodies directed against the spike and nucleocapsid regions. qRT-PCR revealed low to very low, but detectable, viral RNA levels in the majority of brains, although they were far lower than those in nasal epithelia. RNAscope and immunocytochemistry failed to detect viral RNA or protein in brains. Our findings indicate that the levels of detectable virus in COVID-19 brains are very low and do not correlate with the histopathological alterations. These findings suggest that microglial activation, microglial nodules and neuronophagia, observed in the majority of brains, do not result from direct viral infection of brain parenchyma, but rather likely from systemic inflammation, perhaps with synergistic contribution from hypoxia/ischemia. Further studies are needed to define whether these pathologies, if present in patients who survive COVID-19, might contribute to chronic neurological problems.

9. NEJM：医护人员接种新冠疫苗后患病率骤降，但仍有感染

来源：NEJM 医学前沿公众号

发布时间：2021-03-24

链接:https://mp.weixin.qq.com/s/7yLZqKK03zKwqSCIiNJsqQ

转载摘要：

上周，西安一家医院检验师在接种 2 剂新冠疫苗后仍然成为 Covid-19 确诊病例。这则消息被广为报道，一时间让人们对新冠疫苗的保护率产生疑虑。其实，从今年 1 月新冠疫情小规模复燃被扑灭以来，我国 Covid-19 的本地传播基本绝迹，因此这个孤立事件除了再次证明没有保护率 100%的疫苗以外，并不能给我们带来更多启示。

然而，在新冠疫情仍未得到有效控制的美国等国家，新冠疫苗对一线医护人员的真实世界保护率就显得尤为重要。美国当地时间 3 月 23 日，《新英格兰医学杂志》（NEJM）发表 3 篇真实世界研究，分别统计了美国和以色列共 4 家医疗系统医务人员从去年 12 月中旬至今年 2 月初接种 SARS-CoV-2 疫苗后的感染情况，而 12 月前后正是美国 Covid-19 患病激增的时期其中，对于美国得克萨斯大学西南医学中心的一线医护人员，8969 名未接种疫苗的员工中有 234 人感染（2.61%），8121 名接种全部疫苗的员工中只有 4 人感染（0.05%），而加利福尼亚州研究也得到了类似结果。在耶路撒冷的一家医院接种两剂疫苗的医护人员中，新发 Covid-19 病例在 B.1.1.7 变异株突增（见于多达 80%的病例）的情况下仍大幅减少。这些数据无一例外都表明，辉瑞-BioNTech 的 BNT162b2 和 Moderna 的 mRNA-1273 这两款 mRNA 疫苗在高风险的一线医务人员中也达到了高保护率。

美国加州数据还显示，真实世界医务人员接种疫苗后 SARS-CoV-2 阳性的绝对危险数值要高于去年 11 月公布的两个 3 期临床试验结果。作者推测，这与医疗机构更频繁的核酸检测（因而检测出更多无症状感染）、与疫苗接种同期剧增的病例数量以及医务人员平均年龄小于临床试验入组人群且有更高暴露风险等因素有关。

我们在此发布这 3 篇论文的全文翻译。

10. 2.54 亿老龄人口有望接种新冠疫苗，产量完全可满足接种需求

来源：第一财经
发布时间：2021-03-22
链接:https://news.cctv.com/2021/03/22/ARTIagMhoqiOC6PkXJwdLdEp210322.shtml
摘要：
我国将大规模开展 60 岁以上老年人群的新冠疫苗接种，这一消息意味着，2.54 亿 60 岁以上的老龄人口有望纳入新冠疫苗接种群体。

3 月 21 日，国务院联防联控机制召开新闻发布会，介绍新冠病毒疫苗安全性有效性有关情况。会上，国家卫生健康委疾控局一级巡视员贺青华介绍，关于 60 岁以上人群接种，部分地区在充分评估健康状况的情况下和被感染风险的前提下，**已经开始为 60 岁以上身体条件比较好的老人开展接种新冠疫苗**。

同时，疫苗研发单位也在加快推进研发，在临床试验取得足够安全性、有效性数据以后，我们将大规模开展 60 岁以上老年人群的疫苗接种。

11. AZD1222 的美国 III 期试验中期分析数据符合预防新冠肺炎的主要疗效终点

AZD1222 US Phase III trial met primary efficacy endpoint in preventing COVID-19 at interim analysis
来源：AstraZeneca
发布时间：2021-03-22
链接：https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/astrazeneca-us-vaccine-trial-met-primary-endpoint.html
第一作者：Adrian Kemp Company Secretary AstraZeneca PLC
编译者：孔娟
中文摘要：
近日，阿斯利康（AstraZeneca）公布了该公司与牛津大学开发的腺病毒疫苗 COVID-19 Vaccine AstraZeneca（前称 AZD1222）的美国 III 期临床试验（D8110C000011）的中期分析数据。该临床实验是一项 III 期随机、双盲、安慰剂对照多中心研究，在美国、秘鲁和智利 88 个试验中心开展，包括 32449 名受试者。包括不同种族和年龄段人群，受试者中 65 岁以上占比 20%。结果显示，这款疫苗在预防有症状的 COVID-19 方面的有效率为 79%、在预防严重或重症疾病和住院方面的有效率为 100%，在 65 岁及以上人群中的有效率为 80%，疫苗的效力在各个种族和年龄上是一致的，数据具有统计学意义。此外，AZD1222 具有良好的反应性和整体安全性。现在，阿斯利康和 SII 将与 COVAX Facility 合作，开始在世界各地供应疫苗，其中大部分将尽快运往中低收入国家。
Abstract:
The AstraZeneca US Phase III trial of AZD1222 demonstrated statistically significant vaccine efficacy of 79% at preventing symptomatic COVID-19 and 100% efficacy at preventing severe disease and hospitalisation. This interim safety and efficacy analysis was based on 32,449 participants accruing 141 symptomatic cases of COVID-19. Vaccine efficacy was consistent across ethnicity and age. Notably, in participants aged 65 years and over, vaccine efficacy was 80%. Approximately 20% of participants were 65 years and over, and approximately 60% had co-morbidities associated with an increased risk for progression of severe COVID-19, such as diabetes, severe obesity or cardiac disease. AstraZeneca continues to engage with governments, multilateral organisations and collaborators around the world to ensure broad and equitable access to the

vaccine at no profit for the duration of the pandemic.

12. 智飞龙科马生物制药有限公司研发的重组蛋白亚单位疫苗（ZF2001）1 期和 2 期临床试验结果

Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials

来源：The Lancet

发布时间：2021-03-24

链接:

http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00127-4/fulltext#%20

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编译者：孔娟

中文摘要：

背景：开发范围更广、作用机制不同的疫苗，有助于控制 SARS-CoV-2 在全球的传播。研究者使用 SARS-CoV-2 S 蛋白的受体结合结构域(RBD)二聚体形式作为抗原，开发了一种抗新冠肺炎病毒的蛋白亚单位疫苗 ZF2001。研究中评估了 ZF2001 的安全性和免疫原性，并对接种剂量和效力进行了研究。

方法:研究者进行了两项随机、双盲、安慰剂对照的 1 期和 2 期试验。共招募 950 名、18 至 59 岁的健康成年人，采用了随机、双盲和安慰剂对照的试验方案。试验在重庆医科大学第二附属医院、首都医科大学北京朝阳医院和湖南省湘潭疾控中心完成。。在第 1 阶段，参与者被随机分配(2:2:1)接受三剂疫苗(25μg 或 50μg)或安慰剂肌肉注射，间隔 30 天。在 2 期，参与者被随机分配至 25μg、50μg 或安慰剂肌肉注射，间隔 30 天，分两次给药和三次给药。试验对疫苗的安全性和免疫原性进行评估，包括不良事件和严重不良事件、抗体滴度、中和抗体滴度以及血清阳转率。这些试验在 ClinicalTrials.gov 注册(NCT04445194 和 NCT04466085)，参与者随访正在进行中。

结果：该疫苗具有良好的耐受性和免疫原性。大多数入组者没有观察到不良反应或者为轻度或中度的不良反应，主要是红肿、注射部位疼痛、骚痒等，为重组蛋白疫苗接种后常见反应。没有疫苗相关的严重不良事件发生。在两次给药方案中，第二次给药后 14 天中和抗体的血清转换率在 25μg 组为 76%(114/150 参与者)，在 50μg 组为 72%(108/150 参与者)；在三剂量方案中，第三剂量后 14 天中和抗体的血清转换率在 25 μg 组为 97 %(148 名参与者中的 143 名),在 50 μg 组为 93 %(148 名参与者中的 138 名)。抗体的几何平均滴度（GMT）达到 102.5，超过 89 份新冠康复病人血清中和抗体水平（GMT, 51）。此外，疫苗能产生适度和平衡的 Th1/Th2 细胞免疫应答。

解释： ZF2001 具有良好的耐受性和免疫原性。1 期和 2 期试验的安全性和免疫原性数据支持在正在进行的 3 期试验中以三剂量方案使用 25μg 剂量，以大规模评估 ZF2001 的安全性和疗效。

Abstract：

Methods：We did two randomised, double-blind, placebo-controlled, phase 1 and phase 2 trials. Phase 1 was done at two university hospitals in Chongqing and Beijing, China, and phase 2 was done at the Hunan Provincial Center for Disease

Control and Prevention in Xiangtan, China. Healthy adults aged 18–59 years, without a history of SARS-CoV or SARS-CoV-2 infection, an RT-PCR-positive test result for SARS-CoV-2, a history of contact with confirmed or suspected COVID-19 cases, and severe allergies to any component of the vaccine were eligible for enrolment. In phase 1, participants were randomly assigned (2:2:1) to receive three doses of the vaccine (25μg or 50μg) or placebo intramuscularly, 30 days apart. In phase 2, participants were randomly assigned (1:1:1:1:1:1) to receive the vaccine (25μg or 50μg) or placebo intramuscularly, 30 days apart, in either a two-dose schedule or a three-dose schedule. Investigators, participants, and the laboratory team were masked to group allocation. For phase 1, the primary outcome was safety, measured by the occurrence of adverse events and serious adverse events. For phase 2, the primary outcome was safety and immunogenicity (the seroconversion rate and the magnitude, in geometric mean titres [GMTs], of SARS-CoV-2-neutralising antibodies).

Findings: Between June 22 and July 3, 2020, 50 participants were enrolled into the phase 1 trial and randomly assigned to receive three doses of placebo (n=10), the 25μg vaccine (n=20), or the 50μg vaccine (n=20). The mean age of participants was 32.6 (SD 9.4) years. Between July 12 and July 17, 2020, 900 participants were enrolled into the phase 2 trial and randomly assigned to receive two doses of placebo (n=150), 25μg vaccine (n=150), or 50μg vaccine (n=150), or three doses of placebo (n=150), 25μg vaccine (n=150), or 50μg vaccine (n=150). The mean age of participants was 43.5 (SD 9.2) years. In both phase 1 and phase 2, adverse events reported within 30 days after vaccination were mild or moderate (grade 1 or 2) in most cases (phase 1: six [60%] of ten participants in the placebo group, 14 [70%] of 20 in the 25μg group, and 18 [90%] of 20 in the 50 μg group; phase 2: 37 [25%] of 150 in the two-dose placebo group, 43 [29%] of 150 in the two-dose 25μg group, 50 [33%] of 150 in the two-dose 50μg group, 47 [31%] of 150 in the three-dose placebo group, 72 [48%] of 150 in the three-dose 25μg group, and 65 [43%] of 150 in the three-dose 50μg group). In phase 1, two (10%) grade 3 or worse adverse events were reported in the 50μg group. In phase 2, grade 3 or worse adverse events were reported by 18 participants (four [3%] in the two-dose 25μg vaccine group, two [1%] in the two-dose 50μg vaccine group, two [1%] in the three-dose placebo group, four [3%] in the three-dose 25 μg vaccine group, and six [4%] in the three-dose 50 μg vaccine group), and 11 were considered vaccine related (two [1%] in the two-dose 25μg vaccine group, one [1%] in the two-dose 50μg vaccine group, one [1%] in the three-dose placebo group, two [1%] in the three-dose 25 μg vaccine group, and five [3%] in the three-dose 50 μg vaccine group); seven participants reported serious adverse events (one [1%] in the two-dose 25μg vaccine group, one [1%] in the two-dose 50μg vaccine group, two [1%] in the three-dose placebo group, one [1%] in the three-dose 25 μg vaccine group, and two [1%] in the three-dose 50μg vaccine group), but none was considered vaccine related. In phase 2, on the two-dose schedule, seroconversion rates of neutralising antibodies 14 days after the second dose were 76% (114 of 150 participants) in the 25μg group and

72% (108 of 150) in the 50μg group; on the three-dose schedule, seroconversion rates of neutralising antibodies 14 days after the third dose were 97% (143 of 148 participants) in the 25 μg group and 93% (138 of 148) in the 50 μg group. In the two-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the second dose were 17.7 (95% CI 13·6–23·1) in the 25μg group and 14.1 (10.8–18.3) in the 50μg group. In the three-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the third dose were 102.5 (95% CI 81.8–128.5) in the 25μg group and 69.1 (53.0–90.0) in the 50μg group. Interpretation: The protein subunit vaccine ZF2001 appears to be well tolerated and immunogenic. The safety and immunogenicity data from the phase 1 and 2 trials support the use of the 25μg dose in a three-dose schedule in an ongoing phase 3 trial for large-scale evaluation of ZF2001's safety and efficacy.

13. 评估 CpG 佐剂的 S-2P 亚单位疫苗对 SARS-CoV-2 相关变种的中和能力

Evaluating the neutralizing ability of a CpG-adjuvanted S-2P subunit vaccine against SARS-CoV-2 Variants of Concern

来源：medrxiv

发布时间：2021-03-22

链接：https://www.medrxiv.org/content/10.1101/2021.03.19.21254000v1

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DOI 或 PUBMED ID：https://doi.org/10.1101/2021.03.19.21254000

编译者：刘焕珍

中文摘要：

目前，接种疫苗是控制 COVID-19 大流行的最佳武器。但是，数量惊人的称为关注变异（VoC）的新变异具有隐藏的突变，这些变异削弱了疫苗引发的抗体的中和能力。我们研究了用 MVC-COV1901 疫苗免疫的人和大鼠血清抗体的中和滴度。接种了两剂佐剂 S-2P 的大鼠保留了针对 B.1.351 变体的中和活性，尽管与野生型相比略有降低。接种 1 期疫苗的受试者对 B.1.351 变体的中和能力降低了更多。据我们所知，该研究是首次在亚单位蛋白 COVID-19 疫苗的临床试验中，证明不同剂量抗原针对 VoC（尤其是针对 B.1.351）的剂量依赖性中和反应。疫苗逃逸变体的出现是当前许多当前 COVID-19 疫苗和治疗剂所面临的日益关注的问题。应针对这些变体的不断变化的性质采取策略。这项研究的观察结果使我们对针对当前和将来的变体的先发制人的攻击有宝贵的见解。

Abstract:

Vaccination is currently the best weapon to control the COVID-19 pandemic. However, an alarming number of novel variants termed Variants of Concern (VoC) were found to harbor mutations that diminished the neutralizing capacity of antibodies elicited by the vaccines. We have investigated the neutralizing titers of antibodies from sera of humans and rats immunized with the MVC-COV1901 vaccine against pseudoviruses coated with the wildtype, D614G, B.1.1.7, or B.1.351 spike proteins. Rats vaccinated with two doses of adjuvanted S-2P retained neutralization activities against the B.1.351 variant, albeit with a slight reduction compared to wildtype. Phase 1 vaccinated subjects showed more reduced

neutralization abilities against the B.1.351 variant. The study is among the first, to our knowledge, to demonstrate dose-dependent neutralizing responses against VoCs, particularly against B.1.351, from different doses of antigen in a clinical trial for a subunit protein COVID-19 vaccine. The appearance of vaccine escape variants is a growing concern facing many current COVID-19 vaccines and therapeutics. Strategies should be adopted against the ever-changing nature of these variants. The observations of this study grant us valuable insight into preemptive strikes against current and future variants.

14. 科兴生物：新冠疫苗在儿童中产生的抗体水平更高

来源：新浪新闻中心

发布时间：2021-03-23

链接：https://news.sina.com.cn/c/2021-03-23/doc-ikkntiam6633446.shtml

责任编辑：贾楠

整理者：刘焕珍

中文摘要：

彭博 3 月 23 日消息，科兴生物医学总监曾刚周一在一个论坛上表示，该公司的新冠疫苗在儿童和青少年中产生的新冠病毒抗体水平高于成年人。在 3 至 17 岁受试者组别中，科兴生物的新冠疫苗显示出良好的安全性。有关该年龄段的数据已提交给中国监管机构。3 月 21 日，国务院联防联控机制召开新闻发布会，介绍新冠病毒疫苗安全性有效性有关情况。北京科兴公司品牌与公共关系总监刘沛诚在会上表示，科兴中维新冠灭活疫苗克尔来福自去年 12 月以来，已经陆续在中国、智利、巴西、土耳其等近 30 个国家获批使用，包括紧急使用、附条件上市或正式上市，并且陆续启动了大规模接种工作。刘沛诚表示：“截至目前，包括中国在内，我们在全球已经累计接种了超过 7000 万剂克尔来福。”

15. 科学家对牛津－阿斯利康 COVID 疫苗知多少

What scientists do and don’t know about the Oxford–AstraZeneca COVID vaccine

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中文摘要：

牛津大学和阿斯利康制药公司公布 COVID-19 疫苗试验的早期阳性结果后，一家监督试验的美国官员对疫苗效力的说法提出了质疑。与许多昂贵且必须在极低温度下保存的疫苗不同，牛津-阿斯利康疫苗可以保存在普通冰箱中，每剂花费几美元。澳大利亚国家免疫研究和监测中心主任说，这种疫苗已经在 100 多个国家获得监管部门的批准，应该放心使用。但目前美国尚未批准。3 月 22 日，阿斯利康初步分析发现，在美国、秘鲁和智利对 32449 名成年人进行的一项试验中，两种剂量对预防 COVID-19 的有效率为 79%。第二天，美国国家过敏和传染病研究所（NIAID）表示，一个监督试验的独立数据安全监测委员会（DSMB）担心阿斯利康可能提供了“过时的信息”，对疫苗的疗效提供了不完整的看法。阿斯利康在随后的一份声明中说，其 79%的疗效数据是基于截至 2 月 17 日的早期数据的中期分析，目前尚未公布试验的最终结果。该公司补充称，这些结果将“与中期分析一致”。（3 月 25 日，阿斯

利康新闻发布了最新的试验结果，报告总体疗效为 76%）。这个问题在欧洲引起了广泛关注，当时有 20 多个国家在零星报道了罕见的凝血情况后暂停了推广，这些情况大多发生在 55 岁或更年轻的女性身上。最初的研究中，55 岁以上的受试者太少，研究人员无法知道疫苗对老年人和年轻人是否有同样的保护作用。格里芬说：“这是一个相当大的数据漏洞。阿斯利康的中期试验数据表明，疫苗在 65 岁或以上人群中预防 COVID-19 的有效率为 80%，这些人群占试验参与者的 20%。早期的试验最初是为单剂量方案设计的，但数据显示单剂量不能产生足够强的免疫反应后，研究人员决定添加一种增强剂。他们尝试了一系列的剂量间隔，从 4 到 12 周。英国一项阿斯利康疫苗试验的初步分析发现，阿斯利康疫苗对英国首次发现的 B.1.1.7 变种具有与先前存在的变种相似的保护水平，但它不能抵抗来自南非首次发现的 B.1.351 的轻度到中度 COVID-19。阿斯利康负责生物制药研发的执行副总裁梅内•潘加洛斯（Mene Pangalos）在 3 月 23 日的线上新闻发布会上说，阿斯利康很快将开始下一代疫苗的试验，这些疫苗将对目前所有的 SARS-CoV-2 变种有效。他补充说，他希望它们能在 2021 年底投入使用。

Abstract:

Less than a day after the University of Oxford and the pharmaceutical firm AstraZeneca reported positive early results from the largest trial so far of their COVID-19 vaccine, officials at a US government agency overseeing the trial questioned claims about the vaccine’s efficacy. Unlike many of the vaccines, which are expensive and must be stored at very low temperatures, the Oxford-AstraZeneca vaccine can be kept in an ordinary fridge and costs a few dollars per dose. The vaccine has received regulatory approval in more than 100 countries and should be used with confidence, Kristine Macartney, director of Australia’s National Centre for Immunisation Research and Surveillance in Sydney, said on Monday. But it has not yet been approved in the United States. On 22 March, the company said in a press release that a preliminary analysis had found two doses to be 79% effective at preventing COVID-19 in a trial of 32,449 adults across the United States, Peru and Chile. The following day, the US National Institutes of Allergy and Infectious Diseases (NIAID) said that an independent data safety monitoring board (DSMB) overseeing the trial had concerns that AstraZeneca could have presented “outdated information” that provided an incomplete view of the vaccine’s efficacy. In a subsequent statement, AstraZeneca said that its 79% efficacy figure had been based on an interim analysis of early data up to 17 February, and that it has yet to issue the trial’s final results. Those results, the company added, would be “consistent with the interim analysis”. (On 25 March, AstraZeneca press released updated trial results reporting an overall efficacy of 76%).So far, there has been no evidence of differences in efficacy and safety in people of different ethnicities. This question loomed large over the past week in Europe, when more than 20 countries paused the roll-out after scattered reports of rare blood-clotting conditions, mostly in women aged 55 or younger. This was despite the vaccine having been approved and rolled out to millions in the United Kingdom, and the WHO continuing to recommend its use, saying that the benefits outweighed the risks. The first studies included too few participants aged over 55 for researchers to know whether the vaccine offers the same protection for older people as for younger people. “That was a pretty

big hole in the data," says Griffin. AstraZeneca's interim trial data suggests that the vaccine is 80% effective at preventing COVID-19 among those aged 65 or older, who made up 20% of trial participants. Early trials were originally designed for a one-dose regimen, but researchers decided to add a booster after data showed that a single dose didn't produce a strong enough immune response. They tried a range of intervals between doses, from 4 to 12 weeks. Stephen Evans, a biostatistician at the London School of Hygiene & Tropical Medicine, hopes that the FDA will put the vaccine's reputation back on track. In contrast to other regulators, the FDA uses raw trial data to conduct its own analysis. "I think the way that the ship will be righted is by having the FDA's scrutiny," says Evans, who expects it to eventually authorize the vaccine. Preliminary analysis in one UK trial of the AstraZeneca vaccine found that it provided a similar level of protection against the B.1.1.7 variant, first detected in the United Kingdom, as it did against pre-existing variants. But the situation with B.1.351, first detected in South Africa, is more complicated. A small study there, of some 2,000 adults aged under 65, found that it didn't protect against mild-to-moderate COVID-19 from that variant. South Africa has suspended roll-out of the AstraZeneca vaccine, but the WHO still recommends its use in regions where variants of concern are circulating. Soon, AstraZeneca will start trials on next-generation vaccines that will work against all current SARS-CoV-2 variants, said Mene Pangalos, the company's executive vice-president of biopharmaceuticals research and development, at a virtual press briefing on 23 March. He added that he hopes they will become available for use in late 2021.

16. 疫苗和新冠病毒变异株：急需相应的免疫保护性

Vaccines and SARS-CoV-2 variants: the urgent need for a correlate of protection

来源：the LANCET

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中文摘要：

随着世界范围内接种新冠疫苗导致病毒变异体出现从而降低疫苗免疫效果。新冠疫苗在之前的临床试验中有高达 95%的功效，并对之前出现的变异株有 100%预防效果。新出现的病毒变异株，尤其是 501Y，可以逃避天然或疫苗免疫所产生的免疫力，并引发对现存疫苗能否有效预防轻度和重度新冠肺炎病讨论。初步研究数据显示，新冠病毒 501Y 变异株对南非康复患者血清有完全免疫逃逸能力， 四种试验疫苗的血清样本对该变异株的中和能力降低。令人担忧的是，在英国和巴西 AZD1222 的临床保护效果为 70%，但在南非仅为 22%。英国疫苗 NVX-CoV237 的保护效果为 89%，而在南非为 49%，美国疫苗 Ad26COV2-S 的保护效果为 72%，但在南非仅为 57%。

疫苗对之前的变异株和新型变异株的保护效率可能会被严重误判。为应对不断出现的

新冠病毒变异体挑战，需要对其进行基因组监测、命名以及变异体和疫苗血清样本储备，但最迫切是根据现有的变异体和疫苗建立保护相关性从而预测可能出现的新病毒变异体，目前无法实现对每株变异体均进行临床试验。此外，临床试验耗时长且试验中有可能会再出现新的变异体。

因为预防轻度和重度感染所需的免疫保护力不同，保护效果判断需要对新冠肺炎的严重程度进行划分。而达到该目标需四个必要条件：首先，所有疫苗开发商应透明，开放和共享临床数据。其次，应指定专家委员会审查分析现有疫苗临床数据，以确定疫苗有效保护因素。第三，应启动多疫苗免疫研究计划，快速确定动物模型、检测方法和标记分子作为保护效果参考指标，从而弥补不同疫苗间的研究差距。最后，建立中央数据库以有效分析疫苗临床数据，从而有更多数据评估多变量保护因素，确定相关保护因素的普遍性。因为疫苗保护相关因素确定非常重要和紧迫，不应由个人或疫苗开发单位独力完成。变异株501Y传播期间，南非被推至疫苗推广的最前沿。必须在无充分数据情况下做出疫苗免疫决策。疫苗对轻度和重度新冠感染的保护效率是作为疫苗选取重要参考依据，同时广泛有效的疫苗接种可清除全球控制新冠病毒变异体的障碍。

Abstract:

Immune-escape variants have raised concerns about the effectiveness of vaccines as the world scales up SARS-CoV-2 immunisation. COVID-19 vaccines have shown up to 95% efficacy in preventing clinical cases and up to 100% efficacy in preventing severe disease or admission to hospital in settings with pre-existing variants. New variants, especially 501Y.V2, which escape natural-induced and vaccine-induced immunity, have created uncertainty on whether the vaccines are effective in preventing both mild and severe COVID-19. Preliminary reports show that the 501Y.V2 variant has complete immune-escape in South African convalescent serum samples,

and reductions in neutralising activity in vaccinee serum samples for all four vaccines tested.Concerningly, the clinical trial efficacy of AZD1222 was 70% in the UK and Brazil,but 22% according to preliminary data from South Africa.For NVX-CoV237 the efficacy was 89% in the UK but 49% in South Africa,whereas for Ad26.COV2-S the efficacy was 72% in the USA but 57% in South Africa.

Extrapolating vaccine efficacy against pre-existing variants to new variants could be seriously misleading.Adequate genomic surveillance, standardised variant nomenclature, and a repository of variants and vaccinee serum samples are needed to deal with the challenges of repeatedly emerging new SARS-CoV-2 variants, but there is a particularly pressing need to establish a correlate of protection so that vaccine efficacy results obtained with pre-existing variants can be translated to newly emerging variants, Furthermore, repeating clinical trials for each variant might take so long that even newer variants could emerge while these clinical trials are underway.

Because the immune responses required to prevent mild disease might be different to severe disease, correlates of protection might need to be stratified on the basis of disease severity. There are four key requirements to achieve this aim. First, all SARS-CoV-2 vaccine developers should commit to transparency and open data sharing. Second, an expert committee should be appointed to review existing and planned analyses to identify correlates of protection for each efficacious

vaccine. Third, studies with multiple vaccines to fast-track the identification of an animal model, assay, or marker as a correlate of protection should be initiated to address gaps in the correlate research plans. Finally, a central database should be created to collate data for each of the efficacious vaccines, thereby providing larger sample sizes to assess multiple variables as correlates of protection and to test if a correlate identified in one trial is valid in other trials.The identification of a correlate of protection is too important and urgent to be left to uncoordinated separate studies by individual investigators or vaccine developers. South Africa, at the forefront of dealing with the challenge of its vaccine roll-out during the spread of a predominant 501Y.V2 variant, has to make vaccine decisions without adequate efficacy data. A correlate of protection for mild and severe SARS-CoV-2 infection will go a long way to providing an evidence base for these decisions and overcome the obstacles that new variants are placing on the vision of global SARS-CoV-2 control with the widespread implementation of effective immunisation.

17. CVnCoV 保护 human ACE2 转基因小鼠免受 ancestral B BavPat1 和新兴 B.1.351 SARS-CoV-2 的侵害

CVnCoV protects human ACE2 transgenic mice from ancestral B BavPat1 and emerging B.1.351 SARS-CoV-2

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中文摘要：

最近，出现了被称为“关注变异”（VOC）的病毒突变体，具有逃避宿主免疫力的潜力。VOC B.1.351 于 2020 年底在南非首次发现，由于中和性差且有逃避祖传菌株免疫力的能力，引起了全球关注。我们在 K18-hACE2 转基因小鼠模型中测试了针对原始菌株 BavPat1 和新型 VOC B.1.351 的 spike 码编码 mRNA 疫苗（CVnCoV）的功效。首次接受实验的小鼠和用福尔马林灭活的 SARS-CoV-2 制剂免疫的小鼠用作对照。mRNA 免疫的小鼠开发出升高的 SARS-CoV-2 RBD 特异性抗体以及针对祖传菌株 BavPat1 的中和效价。与 VOC B.1.351 的中和效价很容易检测到，但与 BavPat1 相比显着降低。感染了 VOC B.1.351 的对照动物的病程延迟，但是几乎所有 SARS-CoV-2 攻击的首次接受实验的小鼠都死于病毒传播和高病毒载量。CVnCoV 疫苗完全保护了动物免受任何病毒株引起的疾病和死亡。此外，在这些组的口腔拭子，肺或脑中未检测到 SARS-CoV-2。在接受福尔马林灭活病毒制剂的小鼠中仅观察到部分保护作用。尽管与祖传菌株 BavPat1 相比，中和抗体的效价更低，但在我们的研究中，CVnCoV 表现出了针对新型 VOC B.1.351 的完全疾病防护。

编者注：本文多名作者为 CureVac 公司员工

Abstract:

The ongoing severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic necessitates the fast development of vaccines as the primary control option. Recently, viral mutants termed “variants of concern” (VOC) have emerged with the potential to escape host immunity. VOC B.1.351 was first discovered in South Africa in late 2020, and causes global concern due to poor neutralization with propensity to evade preexisting immunity from ancestral strains. We tested the efficacy of a spike encoding mRNA vaccine (CVnCoV) against the ancestral strain BavPat1 and the novel VOC B.1.351 in a K18-hACE2 transgenic mouse model. Naive mice and mice immunized with formalin-inactivated SARS-CoV-2 preparation were used as controls. mRNA-immunized mice developed elevated SARS-CoV-2 RBD-specific antibody as well as neutralization titers against the ancestral strain BavPat1. Neutralization titers against VOC B.1.351 were readily detectable but significantly reduced compared to BavPat1. VOC B.1.351-infected control animals experienced a delayed course of disease, yet nearly all SARS-CoV-2 challenged naïve mice succumbed with virus dissemination and high viral loads. CVnCoV vaccine completely protected the animals from disease and mortality caused by either viral strain. Moreover, SARS-CoV-2 was not detected in oral swabs, lung, or brain in these groups. Only partial protection was observed in mice receiving the formalin-inactivated virus preparation. Despite lower neutralizing antibody titers compared to the ancestral strain BavPat1, CVnCoV shows complete disease protection against the novel VOC B.1.351 in our studies.

18. 辉瑞 Comirnaty 疫苗仅在第二剂后才能达到针对 COVID19 的抗体反应的人群内同质性

Population homogeneity for the antibody response to COVID19 Comirnaty vaccine is only reached after the second dose

来源：medRxiv

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中文摘要：

虽然授权用于紧急用途的 mRNA 疫苗在全球范围内试图遏制 COVID19 危机，但对其诱导的免疫反应的异质性知之甚少。在这里，我们报告了一项纵向研究的前 6 周，该研究在 1245 个医疗服务提供者 Lx1000HCW-PZF 队列中量化了对 BNT162b2 mRNA COVID-19（辉瑞/BioNTech，Comirnaty）的体液免疫应答。首次给药后 3 周，我们发现了一个惊人的个体间差异，该差异仅部分与年龄和性别有关。在第 2 剂给药后,IgG 反应达到了人群同质性，但 IgM 和 IgA 的水平仍然很低且异质。我们对 Comirnaty 的同型和异源抗体反应的研究结果突显了需要评估 COVID-19 mRNA 疫苗在预防感染以外的疾病方面的功效，并且-与提出的建议相反-提倡不延长两次剂量之间的间隔 。

Abstract:

While mRNA vaccines authorised for emergency use are administrated worldwide in an effort to contain the COVID19 crisis, little is known about the heterogeneity of the immune response they induce. Here, we report the first 6 weeks of a longitudinal study that quantifies the humoral immune response to BNT162b2 mRNA COVID-19 (Pfizer/BioNTech, Comirnaty) in 1245 health care providers, the Lx1000HCW-PZF cohort. We reveal a striking inter-individual variation 3 weeks after the 1st dose administration that only in part related to age and sex. While population homogeneity in robust IgG responses was reached upon 2nd dose administration, IgM and IgA levels remain low and heterogenous. Our findings of isotypic and heterogenous antibody responses to Comirnaty highlight the need for evaluating the efficacy of COVID-19 mRNA vaccine in preventing infection aside disease, and - contrary to what has been proposed - advocate for the interval between the two doses not to be extended.

19. 未接触 SARS-CoV-2 的疗养院居民的 BNT162b2 mRNA 疫苗应答降低

Reduced BNT162b2 mRNA vaccine response in SARS-CoV-2-naive nursing home residents

来源：medrxiv

发布时间：2021.03.22

文章链接：https://www.medrxiv.org/content/10.1101/2021.03.19.21253920v1

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doi: https://doi.org/10.1101/2021.03.19.21253920

编译者：张怡

摘要

SARS-CoV-2 大流行对疗养院(NH)居民的影响促使他们优先进行早期接种。为了填补疗养院居民疫苗免疫原性的数据空白，研究者们在 149 名疗养院居民和 111 名卫生保健工作者对照中检测了 BNT162b2 mRNA 疫苗对刺突蛋白、受体结合域(RBD)和病毒中和后的抗体水平。与未接触 SARS-CoV-2 的医疗工作者相比，未接触 SARS-CoV-2 的疗养院居民的抗体应答中位中和滴度低近 4 倍，抗尖峰水平是前者的一半。相比之下，SARS-CoV-2 恢复的疫苗接种的疗养院居民的中和性、抗刺突蛋白和抗 RBD 滴度与 SARS-CoV-2 恢复的疫苗接种的医护人员相似。疗养院居民的钝化抗体反应对于新抗原疫苗提供的保护的质量和持久性具有重要意义。我们迫切需要针对疗养院居民人群的疫苗有效性的更好的纵向证据，以便为疗养院居民感染控制措施、疫情预防和疫苗增强的潜在迹象提供最佳方案。

Abstract

The SARS-CoV-2 pandemic impact on nursing home (NH) residents prompted their prioritization for early vaccination. To fill the data gap for vaccine immunogenicity in NH residents, we examined antibody levels after BNT162b2 mRNA vaccine to spike, receptor binding domain (RBD) and for virus neutralization in 149 NH residents and 111 health care worker controls. SARS-CoV-2-naive NH residents mount antibody responses with nearly 4-fold lower median neutralization titers and half the anti-spike level compared to SARS-CoV-2-naive healthcare workers. By contrast, SARS-CoV-2-recovered vaccinated NH

residents had neutralization, anti-spike and anti-RBD titers similar to SARS-CoV-2-recovered vaccinated healthcare workers. NH residents blunted antibody responses have important implications regarding the quality and durability of protection afforded by neoantigen vaccines. We urgently need better longitudinal evidence on vaccine effectiveness specific to NH resident populations to inform best practices for NH infection control measures, outbreak prevention and potential indication for a vaccine boost.

20. 康希诺生物：不用打针！吸入用重组新型冠状病毒疫苗获得 NMPA 药物临床试验批件

来源：药创客

发布时间：2021-3-22

链接：https://mp.weixin.qq.com/s/MED42uicy1K-l2zcLsXu8A

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中文摘要：

3 月 22 日，康希诺生物在港交所发布公告称，其吸入用重组新型冠状病毒疫苗获得了国家药品监督管理局的药物临床试验批件。

这次康希诺生物在港交所发布的公告称，其与中国人民解放军军事科学院军事医学研究院生物工程研究所合作开发的吸入用重组新型冠状病毒疫苗(5 型腺病毒载体)已获得国家药品监督管理局的药物临床试验批件。

21. Oramed 组建了一家合资公司 Oravax Medical Inc.，以开发新型口服 COVID-19 疫苗

Oramed Forms a Joint Venture, Oravax Medical Inc., for the Development of Novel Oral COVID-19 Vaccines

来源：Biospace

发布时间：2021-3-19

链 接 ： https://www.biospace.com/article/releases/oramed-forms-a-joint-venture-oravax-medical-inc-for-the-development-of-novel-oral-covid-19-vaccines/

编译者：雷颖

中文摘要：

Oramed Pharmaceuticals Inc.是一家专注于开发口服药物递送系统的临床阶段制药公司，今天宣布已达成最终协议，以形成一项合资公司专注于新型口服 COVID-19 疫苗的开发。新公司 Oravax Medical Inc.基于 Oramed 专有的 POD ™ 口服给药技术和 Premas Biotech Pvt 有限公司的新型疫苗技术。Oravax 的 COVID-19 疫苗候选物得益于针对三种结构蛋白的类病毒颗粒（VLP）的三抗原疫苗，这将使其成为更好的对冠状病毒新突变提供保护的候选物。疫苗的口服给药可以允许大规模接种，并且无需注射即可更容易地分发疫苗。在一项先导动物研究中，口服 COVID-19 疫苗通过免疫球蛋白 G（IgG）和免疫球蛋白 A（IgA）促进了全身免疫，其中免疫球蛋白 G（IgG）是血液和体液中最常见的可防止病毒感染的抗体。Oravax 预计将于 2021 年第二季度开始一项临床研究。

Abstract

Oramed Pharmaceuticals Inc. (Nasdaq: ORMP) (TASE: ORMP) (www.oramed.com), a

clinical-stage pharmaceutical company focused on the development of oral drug delivery systems, announced today that it has entered into definitive agreements to form a joint venture focused on the development of novel oral COVID-19 vaccines. The new company, Oravax Medical Inc., is based on Oramed's proprietary POD™ oral delivery technology and Premas Biotech Pvt. Ltd.'s novel vaccine technology.
Oravax's COVID-19 vaccine candidate benefits from being a virus like particle (VLP) triple antigen vaccine that targets three structural proteins, which should make it a better candidate for protection across emerging mutations of the coronavirus. The oral delivery of the vaccine should allow for widescale inoculation and easier distribution of the vaccine without requiring an injection.
In a pilot animal study, the oral COVID-19 vaccine promoted both systemic immunity through Immunoglobulin G (IgG), the most common antibody in blood and bodily fluids that protects against viral infections, and Immunoglobulin A (IgA).
Oravax anticipates commencing a clinical study during the second quarter of 2021.
"An oral COVID-19 vaccine would eliminate several barriers to rapid, widescale distribution, potentially enabling people to take the vaccine themselves at home. While ease of administration is critical today to accelerate inoculation rates, an oral vaccine could become even more valuable in the case that a COVID-19 vaccine may be recommended annually like the standard flu shot," said Nadav Kidron, CEO of Oramed.

22. Spike 蛋白的 N501Y 突变能够增强 SARS-CoV-2 病毒的传播能力

The N501Y spike substitution enhances SARS-CoV-2 transmission
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中文摘要：

自 2020 年夏季开始，造成 COVID-19 疫情的 SARS-CoV-2 病毒的一个变种在英国出现。由于其感染和/或传播的效率更高，B.1.1.7 变种在各已测序的病毒株中的流行率迅速上升。英国发现的病毒变种的基因组中存在 19 个非同义突变，其中包括在 spike 蛋白上的 8 个取代或缺失突变。病毒的 spike 蛋白能够与细胞受体相互作用，介导病毒的感染和趋向性。在本文中，作者利用反向遗传学方法发现，在 8 种 spike 蛋白的单点变体中，只有 N501Y 突变体的复制能力在模型仓鼠的上呼吸道和人类主气管上皮细胞中表现出了一致的适应性提高。单独的 N501Y 突变体就能够重现出同时具有在英国发现的 8 个突变位点的 spike 蛋白所表

现出的病毒传播能力增强的表型特征，证明 N501Y 是该变异株传播能力增强的主要决定因素。机理上的解释为，N501Y 突变提高了病毒 spike 蛋白与细胞受体的亲和力。根据巴西和南非发现的病毒的趋同进化现象，作者的结果表明 N501Y 突变是一个需要重点关注的主要的 spike 蛋白自适应突变。

Abstract:
Beginning in the summer of 2020, a variant of SARS-CoV-2, the cause of the COVID-19 pandemic, emerged in the United Kingdom (UK). This B.1.1.7 variant increased rapidly in prevalence among sequenced strains, attributed to an increase in infection and/or transmission efficiency. The UK variant has 19 nonsynonymous mutations across its viral genome including 8 substitutions or deletions in the spike protein, which interacts with cellular receptors to mediate infection and tropism. Here, using a reverse genetics approach, we show that, of the 8 individual spike protein substitutions, only N501Y exhibited consistent fitness gains for replication in the upper airway in the hamster model as well as primary human airway epithelial cells. The N501Y substitution recapitulated the phenotype of enhanced viral transmission seen with the combined 8 UK spike mutations, suggesting it is a major determinant responsible for increased transmission of this variant. Mechanistically, the N501Y substitution improved the affinity of the viral spike protein for cellular receptors. As suggested by its convergent evolution in Brazil and South Africa, our results indicate that N501Y substitution is a major adaptive spike mutation of major concern.

23. 急性 COVID-19 后的异质性免疫恢复轨迹

Heterogeneous immunological recovery trajectories revealed in post-acute COVID-19

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中文摘要：

关于不同患者如何从 COVID-19 中恢复，以及这些恢复轨迹如何受感染严重程度影响的免疫学景象尚不清楚。该研究利用临床资料、病毒载量评估、血浆和循环免疫细胞的多组学分析，调查了 140 例 COVID-19 患者从诊断到康复的全过程。免疫表型动力学解决了四个恢复轨迹。一个轨迹标志着恢复到感染前的健康基线，而另三个轨迹的特征是持续性细胞毒性和增殖性 T 细胞的不同比例、不同的 B 细胞成熟过程和记忆样先天免疫。分离出一小部分血浆蛋白，在诊断时进行测量，可以预测患者的生存和恢复轨迹。该研究为可能影响长期不良后遗症的 COVID-19 急性后免疫结果提供了新的见解。

Abstract:
The immunological picture of how different patients recover from COVID-19, and

how those recovery trajectories are influenced by infection severity, remain unclear. We investigated 140 COVID-19 patients from diagnosis to convalescence using clinical data, viral load assessments, and multi-omic analyses of blood plasma and circulating immune cells. Immune-phenotype dynamics resolved four recovery trajectories. One trajectory signals a return to pre-infection healthy baseline, while the other three are characterized by differing fractions of persistent cytotoxic and proliferative T cells, distinct B cell maturation processes, and memory-like innate immunity. We resolve a small panel of plasma proteins that, when measured at diagnosis, can predict patient survival and recovery-trajectory commitment. Our study offers novel insights into post-acute immunological outcomes of COVID-19 that likely influence long-term adverse sequelae.

24. COVID-19 不可能群体免疫的 5 个原因

Five reasons why COVID herd immunity is probably impossible

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中文摘要：

即使全力接种疫苗，战胜 COVID-19 的理论门槛似乎仍遥不可及。随着全球 COVID-19 疫苗接种率的提高，人们有理由开始问：这场大流行还会持续多久？这是一个充满不确定性的问题。但一度流行的想法是，有足够多的人最终会获得对 SARS-CoV-2 的免疫力，从而阻止大多数传播——一个“群体免疫阈值”——开始看起来不太可能。

这一阈值一般只有在高接种率的情况下才能达到，许多科学家曾认为，一旦人们开始集体免疫，群体免疫将使社会恢复正常。大多数估计认为，通过接种疫苗或过去接触病毒，获得免疫力的人口的阈值为 60%至 70%。但随着疫情进入第二个年头，人们的想法开始转变。今年 2 月，独立数据科学家顾悠扬将其广受欢迎的 COVID-19 预测模型的名字从“路径到群体免疫”改为“路径到常态化”。他说，由于疫苗接种的犹豫、新的变异的出现以及儿童疫苗的延迟到位等因素，达到群体免疫阈值看起来是不可能的。

1. 目前还不清楚疫苗是否能预防传播
2. 疫苗的推广参差不齐
3. 新的变种改变了群体免疫方程式
4. 免疫力可能不会永远持续
5. 疫苗可能会改变人类的行为

Abstract:

Even with vaccination efforts in full force, the theoretical threshold for vanquishing COVID-19 looks to be out of reach. As COVID-19 vaccination rates pick up around the world, people have reasonably begun to ask: how much longer will this pandemic last? It’s an issue surrounded with uncertainties. But the once-

popular idea that enough people will eventually gain immunity to SARS-CoV-2 to block most transmission — a ‘herd-immunity threshold’ — is starting to look unlikely.

That threshold is generally achievable only with high vaccination rates, and many scientists had thought that once people started being immunized en masse, herd immunity would permit society to return to normal. Most estimates had placed the threshold at 60–70% of the population gaining immunity, either through vaccinations or past exposure to the virus. But as the pandemic enters its second year, the thinking has begun to shift. In February, independent data scientist Youyang Gu changed the name of his popular COVID-19 forecasting model from ‘Path to Herd Immunity’ to ‘Path to Normality’. He said that reaching a herd-immunity threshold was looking unlikely because of factors such as vaccine hesitancy, the emergence of new variants and the delayed arrival of vaccinations for children.

Long-term prospects for the pandemic probably include COVID-19 becoming an endemic disease, much like influenza. But in the near term, scientists are contemplating a new normal that does not include herd immunity. Here are some of the reasons behind this mindset, and what they mean for the next year of the pandemic.

1. It’s unclear whether vaccines prevent transmission
2. Vaccine roll-out is uneven
3. New variants change the herd-immunity equation
4. Immunity might not last forever
5. Vaccines might change human behaviour