新型冠状病毒信息简报

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上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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1. 2020 年 9 月 10 日疫情

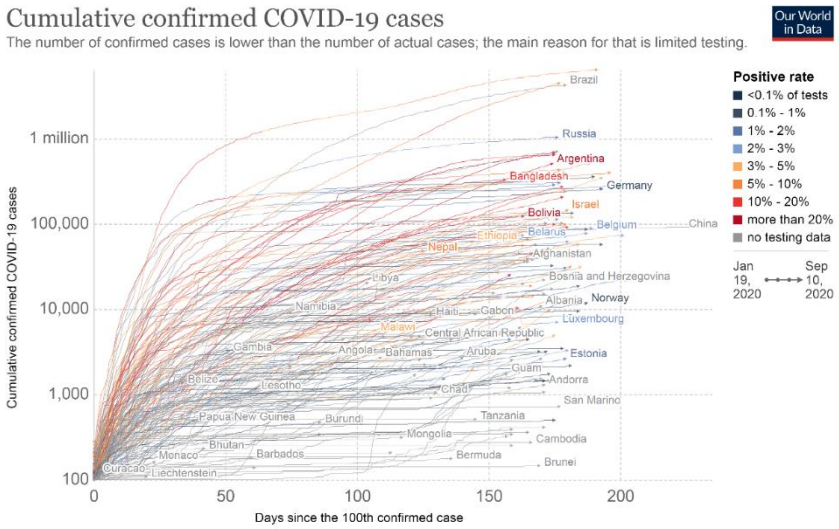
数据来源：WHO

发布时间：2020 年 9 月 10 日北京时间下午 4 点

链接：https://covid19.who.int/

根据 WHO 提供的数据，2020 年 9 月 10 日全球累计确诊新型冠状病毒病人 **27,738,179** 例，当日新增确诊 **250,003** 例，累计死亡 **899,916** 例，当日新增死亡 **4,880**。

中国累计确诊 90,595 例，累计死亡 4,740 例，当日新增确诊 13 例，新增死亡 0 例。



Source: European CDC – Situation Update Worldwide – Last updated 10 September, 15:05 (London time), Official data collated by Our World in Data
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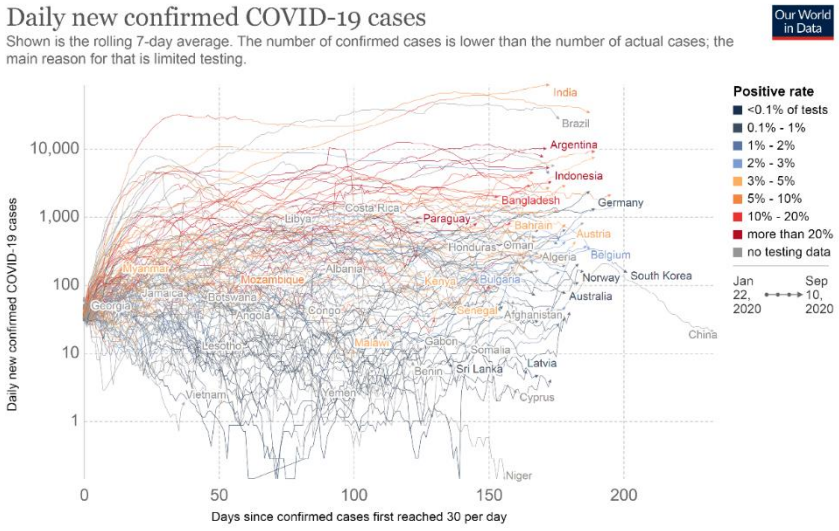
重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



Source: European CDC – Situation Update Worldwide – Last updated 10 September, 15:05 (London time), Official data collated by Our World in Data
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重点国家每日新增确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）

全国新型冠状病毒肺炎新增确诊病例分布图（9 月 10 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 新冠病毒再感染：科学家提出三个问题

Coronavirus reinfections: three questions scientists are asking

来源：Nature

发布时间：2020-09-04

链接：https://www.nature.com/articles/d41586-020-02506-y

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编译者：王玮

中文摘要：

二次感染引发了对 COVID-19 的长期免疫和疫苗前景的疑问。

上周，有消息传出，一名居住在香港的男子再次感染冠状病毒，几个月后，免疫学家 Akiko Iwasaki 说。“这是一个很好的教科书式的例子，说明了免疫反应是如何工作的。”

Iwasaki 一直在耶鲁大学研究 SARS-CoV-2 病毒的免疫反应，对他来说，这个病例令人鼓舞，因为第二次感染并没有引起症状。她说，这表明，这名男子的免疫系统可能已经记住了它以前与病毒的接触，并采取行动，在病毒可能造成严重损害之前抵御了反复感染。

但不到一周后，内华达州的公共卫生工作者报告了另一个再次感染事件，这次症状更严重。有没有可能免疫系统不仅没能抵御病毒，反而让事情变得更糟？Iwasaki 说。

Iwasaki 知道她不能从几个病例中得出关于 SARS-CoV-2 的长期免疫反应的确切结论。但在接下来的几周和几个月里，岩崎和其他人预计会看到更多的再感染报告，并且，随着时间的推移，世界是否可以依靠免疫系统来结束这场大流行的图景可能会浮出水面。

随着数据的不断流入，研究人员试图回答有关再次感染的关键问题。

再次感染有多普遍？

关于可能再次感染的报道已经流传了几个月，但最近的研究结果首次排除了第二次感染仅仅是第一次感染的延续的可能性。

为了确定每一个人中的两种感染是独立的事件，香港和内华达州团队都测序了来自第一和第二次感染的病毒基因组。两人都发现了足够的差异，确定是病毒的不同变种在起作用。

目前只有两个例子，仍然不清楚再次感染发生的频率。德克萨斯大学加尔维斯顿医学分校的病毒学家 Thomas Geisbert 说，到目前为止，全世界已知有 2600 万冠状病毒感染，一些再次感染可能还不值得担心。他说：“我们需要更多的信息来了解这种现象的流行程度。”

一些地区正在经历新的疫情暴发，为人们再次接触病毒提供了机会。测试也变得更快和更容易。这些因素将使得在不久的将来更容易发现和验证再次感染。

再次感染是否比第一次严重？

与 Iwasaki 不同的是，伦敦弗兰西斯克里克研究所的病毒学家 Jonathan Stoye 认为，COVID-19 的严重程度因人而异，可能因同一人的不同感染而有所不同。诸如病毒初始剂量、SARS-CoV-2 变异株之间可能存在的差异以及一个人整体健康状况的变化等变量都可能影响再感染的严重程度。他说：“关于再感染的未知数几乎和本案之前一样多。”。

弄清楚“免疫记忆”是否会影响第二次感染时的症状是至关重要的，尤其是对于疫苗的研发。如果第二次症状像香港二次感染病人一样减少，这表明免疫系统应该做出反应。

但是，如果在第二次 COVID-19 中症状持续恶化，就像内华达州病人一样，免疫系统可能会使事情变得更糟，澳大利亚的免疫学家 Gabrielle Belz 说。例如，一些严重的 COVID-19 病例由于免疫反应破坏健康组织而恶化。Belz 说，那些在第一次感染中经历过这种情况的人，其免疫细胞可能会在第二次感染时以不相称的方式再次做出反应。

另一种可能是，在第二次感染期间，对 SARS-CoV-2 产生的抗体有助于而不是对抗病毒。这种被称为抗体依赖性增强的现象很少见，但研究人员在试图开发针对相关冠状病毒的疫苗时发现了令人担忧的迹象。

再次感染对疫苗前景有什么影响？

马萨诸塞州波士顿儿童医院儿科传染病专家 Richard Malley 说，从历史上看，最容易制造的疫苗是针对那些原发性感染导致持久免疫的疾病。例如麻疹和风疹。

但他补充说，再次感染并不意味着抗 SARS-CoV-2 的疫苗不会有效。例如，有些疫苗需要“加强”注射来维持保护。Malley 说，“这不应该意味着疫苗不可能研制出来，也不意味着对这种病毒的自然免疫力无法产生。”

Poovorawan 说，了解更多关于再次感染的知识可以帮助研究人员开发疫苗，教会他们哪些免疫反应对维持免疫力很重要。例如，研究人员可能会发现，当抗体下降到一定水平以下时，人们很容易再次感染。可以设计疫苗接种策略来应对，可能可以通过注射强化疫苗来维持抗体水平。

Malley 担心疫苗只会在第二次感染时减轻症状，而不是完全预防这种感染。这提供了一些好处，但它可以有效地将接种疫苗的人变成无症状的 SARS-CoV-2 携带者，使脆弱人群处于危险之中。例如，老年人是受 COVID-19 感染最严重的人群之一，但往往对疫苗反应不好。

基于这个原因，Malley 很想知道当人们再次感染 SARS-CoV-2 时，会“释放”多少病毒。如果我们想摆脱这种混乱，我们需要更好地理解自然感染和疫苗接种之后的情况。”

Abstract:
Although Africa reported its millionth official COVID-19 case last week, it seems to have weathered the pandemic relatively well so far, with fewer than one confirmed case for every thousand people and just 23,000 deaths so far. Yet several antibody surveys suggest far more Africans have been infected with the coronavirus—a discrepancy that is puzzling scientists around the continent.

“We do not have an answer,” says immunologist Sophie Uyoga at the Kenya Medical Research Institute–Wellcome Trust Research Programme…

3. 4℃条件下三文鱼附着的 SARS-CoV-2 长期存活，是海产品市场的潜在传播源

Long-term survival of salmon-attached SARS-CoV-2 at 4° C as a potential source of transmission in seafood markets

来源：bioRxiv

发布时间：2020-09-06

链接：https://www.biorxiv.org/content/10.1101/2020.09.06.284695v1

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编译者：宋张悦

中文摘要：

COVID-19 的几次暴发都与海产品市场有关，这使人们担心鱼类附着的 SARS-CoV-2 可能在低温环境中存活较长时间。在这里，我们发现在 4℃的温度下，三文鱼附着的 SARS-CoV-2 可以保持感染性超过一周，这表明鱼附着的 SARS-CoV-2 可能是一个传播源。

Figure A

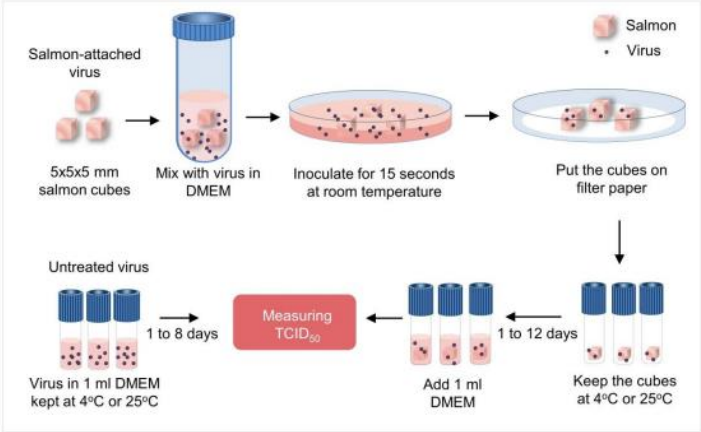
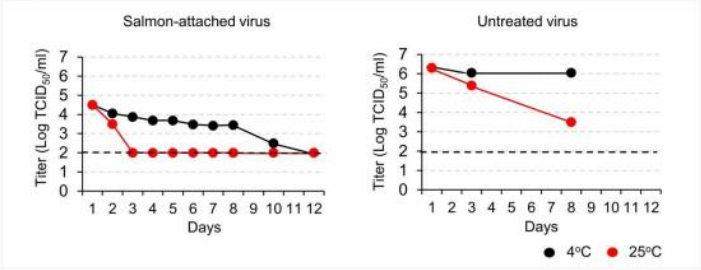


Figure B



Fiugre A and B. Viability of salmon-attached and untreated SARS-CoV-2 in culture medium at 4°C and 25°C. Panel A is the overview of the study design and experimental procedure. In panel B, the titer of SARS-CoV-2 was quantified by end-point titration on Vero E6 cells and is expressed as log10 TCID50 /mL. Plots show the means of data from two or three samples. The dashed lines indicate the limit of detection, which were 10^2 TCID50 /mL.

Abstract:
Several outbreaks of COVID-19 were associated with seafood markets, raising concerns that fish-attached SARS-CoV-2 may exhibit prolonged survival in low-temperature environments. Here we showed that salmon-attached SARS-CoV-2 at 4℃ could remain infectious for more than one week, suggesting that fish-attached SARS-CoV-2 may be a source of transmission.

4. 罹患 COVID-19 的儿童中多系统炎症综合征（MIS-C）的免疫学

The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19
7 月 10 日简报第 15 条报告过该研究的预印本。
链接: https://www.cell.com/cell/fulltext/S0092-8674(20)31157-0

5. 在重症 COVID-19 病人中，SARS-CoV-2 诱导了长期的 TGF-β 为主的适应性免疫反应

In severe COVID-19, SARS-CoV-2 induces a chronic, TGF-β-dominated adaptive immune response
来源：medrxiv
发布时间：2020-09-09
链接：https://www.medrxiv.org/content/10.1101/2020.09.04.20188169v2
第一作者：Marta Ferreira-Gomes
通讯作者： Mir-Farzin Mashreghi
通讯作者单位：德国风湿病研究中心-DRFZ
DOI 或 PUBMED ID：preprint
编译者：蒋立春
中文摘要：
作者们通过在单细胞水平研究激活的 B 细胞如何进入血液，分析了重症 COVID-19 病人中由 SARS-CoV-2 引起的适应性免疫反应的动力学。在早期，在发生针对 SARS-CoV-2 刺突蛋白血清转换之前，激活的外周 B 细胞呈现出一型干扰素诱导的基因表达特征。发生了血清转化之后，活化的 B 细胞失去了这个特征，开始表达 IL-21 以及 TGF-β 诱导的基因表达特征，以及主要表达 IgG1 和 IgA1。在持续有免疫反应的 COVID-19 病人中，直到第 59 天，激活的外周 B 细胞转变为表达 IgA2,反映了 TGF-β 的指向。在病故的 COVID-19 病人中，尽管有持续产生的活化 B 细胞，在这些病人肺部既没有找到活化 B 细胞，IgA2 也不和最主要的抗原结合。在重症 COVID-19 病人中，SARS-CoV-2 激发了长期的免疫反应，但是该免疫反应并不是集中于病毒自身，而是被 TGF-β 所指引。

Abstract:
Here we have analyzed the dynamics of the adaptive immune response triggered by SARS-CoV-2 in severely affected COVID-19 patients, as reflected by activated B cells egressing into the blood, at the single cell level.
Early on, before seroconversion in response to SARS-CoV-2 spike protein, activated peripheral B cells displayed a type 1 interferon-induced gene expression signature. After seroconversion, activated B cells lost this signature, expressed IL-21- and TGF-β-induced gene expression signatures, and mostly IgG1 and IgA1. In the sustained immune reaction of the COVID-19 patients, until day 59, activated peripheral B cells shifted to expression of IgA2, reflecting instruction by TGF-β. Despite the continued generation of

activated B cells, those cells were not found in the lungs of deceased COVID-19 patients, nor did the IgA2 bind to dominant antigens of SARS-CoV-2. In severe COVID-19, SARS-CoV-2 thus triggers a chronic immune reaction distracted from itself and instructed by TGF-β.

6. Moderna 的 COVID-19 疫苗在老年人中可能比其它竞争产品的效果更好

Moderna's COVID-19 vaccine may work better in the elderly than competitors'
来源：biocentury
发表日期：2020-08-27
链接：
https://www.biocentury.com/article/629786?editionId=ckef4n5jk0heb0179cdty9krg&editionType=weekly
作者：SANDI WONG（助理编辑）
编译者：雷颖
中文摘要：
鉴于疫苗需要免疫功能来诱导针对病原体的保护，因此老年人的免疫系统减弱一直是疫苗开发人员关注的问题。新的临床 I 期数据表明，Moderna 的 COVID-19 疫苗在老年人中的免疫原性也许比其它两种领先的疫苗更好。假设中和抗体是保护的关键决定因素，并且早期结果成立，这可能意味着 mRNA-1273 将在保护高危人群方面做得更好。在 Moderna 的研究中，年龄在 71 岁及以上人群的抗体滴度仅比 18-55 岁人群少一点，比 56-70 岁人群少约 25%。与 mRNA-1273 在高年龄组的抗体反应下降最小相反，另外两种疫苗在早期临床研究中显示出更急剧的下降。由 Pfizer 和 BioNTech 研发的 BNT162b2 诱导的中和效价在 18-55 岁年龄组中下降了约 60%。CanSino 的 Ad5-nCoV 最初产生的滴度较弱，但从 18-44 岁组到 55 岁以上组仅下降了 36%。另一个悬而未决的问题是，不同的 T 细胞群体在保护中是否以及有多少贡献。目前，在非人类灵长类动物中进行病毒攻击研究为此类保护相关因素提供了最佳线索。其中几项研究（包括 mRNA-1273 研究）表明，即使在没有明显 T 细胞活化的情况下，高中和滴度也可能足以提供保护。动物数据并不排除 T 细胞的保护作用，Moderna 还报告说，在第一阶段研究的三个年龄段中，100 μg mRNA-1273 诱导了 Th1 偏向的 CD4 + T 细胞反应。CanSino 还显示出其腺病毒载体疫苗可刺激 T 细胞反应，但未按年龄分层数据报告。BioNTech 和 Pfizer 在他们的研究中未评估 T 细胞反应。
Abstract
The weakening immune systems in older individuals have been a concern for vaccine developers, given that immune function is needed for vaccines induce protection against pathogens. New Phase I data suggest Moderna's COVID-19 vaccine maintains its immunogenicity in elderly individuals better than two other leading vaccines. Assuming neutralizing antibodies are key determinants of protection, and that the early results hold up, that could mean mRNA-1273 will do a better job of protecting the high-risk population. The 71 and older group in Moderna's study had titers that were just a hair less than those in the 18-55 group, and about 25% less than those in the 56-70 group. In contrast to what appears to be a minimal decline in the antibody response to mRNA-1273, two other vaccines have shown steeper declines in early clinical studies. Neutralizing titers induced by BNT162b2 from Pfizer Inc. (NYSE:PFE) and BioNTech SE (NASDAQ:BNTX) fell by about 60% in subjects aged 65-85 years

compared with 18-55 year-olds. Ad5-nCoV from CanSino Biologics Inc. (HKEX:6185; Shanghai:688185), which produced somewhat weaker titers to begin with, showed a drop of 36% from 18-44 years to age 55 and up. Another open question is whether and how much different T cell populations contribute to protection. For now, viral challenges studies in non-human primates offer the best clues to such correlates of protection. Several of these studies, including of mRNA-1273, suggest high neutralizing titers may be sufficient to confer protection, even in the absence of appreciable T cell activation (see "Non-human Primate Data Shed Light on Correlates of Protection"). The animal data do not rule out protective contributions from T cells though, and Moderna also reported that 100 μg of mRNA-1273 induced Th1-biased CD4+ T cell responses that were consistent across the three age groups in the Phase I study. CanSino has also shown its adenovirus vector vaccine stimulates T cells responses but did not stratify the data report by age. BioNTech and Pfizer did not evaluate T cell responses in their study.

7. 新冠肺炎疫苗发展概述

Evolution of the COVID-19 vaccine development landscape

来源：Nature Reviews Drug Discovery

发布时间：2020-09-04

链接：https://www.nature.com/articles/d41573-020-00151-8

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DOI 或 PUBMED ID：10.1038/d41573-020-00151-8

编译者：孔娟

中文摘要：

文中总结了截止到 2020 年 9 月 2 日全球 COVID-19 疫苗研发概况。已有 321 种候选疫苗，其中 33 种疫苗正在进行临床试验，11 个疫苗由中国组织研发。并且已有研究显示，疫苗诱导出令人鼓舞的中和抗体和 T 细胞应答。这些候选疫苗研究计划从 34 个不同国家的至少 470 个研究中心招募 280,000 多名受试者。疫苗研究的主要技术平台如图 1 所示，既包括传统方法，也包括 mRNA 疫苗和 DNA 疫苗这些新的方法。目前候选疫苗多以棘突（S）蛋白及其变异体为靶点，针对其他或多种抗原的候选疫苗正在开发中，包括针对 N 蛋白的候选疫苗、减毒疫苗、灭活疫苗和肽疫苗。文中同时对新冠肺炎候选疫苗临床开发的一些最重要的考虑因素进行了简述，其中包括试用设计、临床终点、保护性免疫的相关因素、疫苗的目标人群及安全考虑。应当鼓励充分代表面临传染性非典型肺炎-冠状病毒-2 感染风险和/或严重后果的人群，如一线保健工作者、老年人和有潜在健康问题的人，因为他们可能从安全有效的疫苗中受益最多。在定义终点时，应考虑终点在所考虑人群中的发生率、疫苗对终点影响的重要性以及测量终点的可靠性。在涉及新病原体的大流行情况下，保持临床终点定义的灵活性非常重要。同时开发一个充分的安全数据库对于任何新疫苗的监管批准和公众接受都是至关重要的。在许可前试验中，样本量、随访时间和研究人群异质性的传统标准可能需要与监管机构密切合作进行调整，以确保安全性和有效性，从而满足新冠肺炎疫苗快速发展的前所未有的需求。笔者认为尽管领先的新冠肺炎候选疫苗已经以惊人的速度发展到临床开发的高级阶段，但由于迄今为止缺乏可靠的临床数据，仍存在许多不确定性。

Abstract:
In this updated overview, we focus on candidates in clinical trials and provide some initial perspectives on their clinical development. As of 3 September 2020, the global COVID-19 vaccine R&D landscape includes 321 vaccine candidates, Of these, 33 vaccine candidates are in clinical trials, with plans to enrol more than 280,000 participants from at least 470 sites in 34 different countries. Technology platforms and targets. The current COVID-19 vaccine pipeline comprises a broad range of technology platforms, including both traditional and novel approaches. At the same time, some of the most important considerations in the clinical development of candidate vaccines for COVID-19 are briefly described, including trial design, clinical endpoint, Correlates of protection, target population and safety considerations. Although the leading COVID-19 vaccine candidates have progressed to advanced stages of clinical development at exceptional speed, many uncertainties remain given the lack of robust clinical data so far.

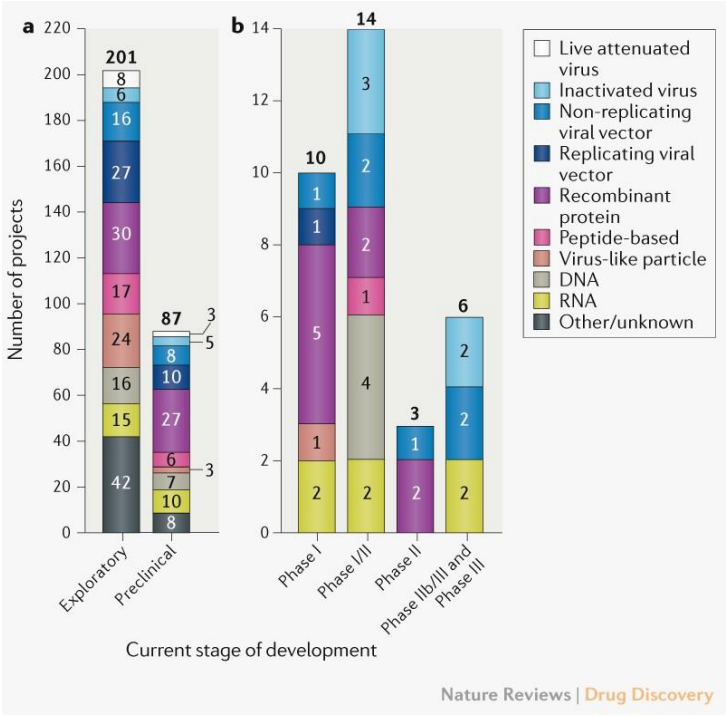

Fig. 1 | Pipeline of COVID-19 vaccine candidates by phase of development and technology platform. a | Exploratory and preclinical pipeline. b | Clinical pipeline. Traditional approaches include live attenuated and inactivated; novel approaches include viral vector, RNA, DNA, recombinant protein, peptide-based, virus-like particle. See Supplementary Box 1 for details of the data set and analysis.

8. 一项领先的冠状病毒疫苗试验暂停:科学家做出反应

A leading coronavirus vaccine trial is on hold: scientists react

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第一作者：Nicky Phillips 新闻编辑
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编译者：孔娟
中文摘要：
9 月 8 日，阿斯利康宣布，由于一名参加试验疫苗接种的志愿者出现无法解释的疾病，该公司将暂停正在进行的一项全球性的新冠疫苗试验。该疫苗由阿斯利康与牛津大学研究人员合作，这是处于测试的最后“第三阶段”的九种冠状病毒疫苗之一。其不良事件的细节，包括其严重程度和发生时间均未报道。这一消息突显了在批准疫苗广泛使用之前，等待大型、设计合理的试验结果以评估安全性的重要性。阿斯利康在一份声明中承诺“我们致力于参与者的安全和我们试验中的最高行为标准。”“如果这一事件与疫苗有明确的联系，甚至可能有联系，那么对这种特定的候选疫苗来说，这可能是一个决定性的打击。如果不相关，搁置可能会在几周内解除，”基尼说。 但是科学家们说，如果没有关于这一不良事件的更多细节，包括它有多严重以及何时发生，就很难评估它对试验的影响以及疫苗批准的时间表。这是英国第二次暂停疫苗的给药。目前，这款由牛津团队研发、阿斯利康负责发行的新冠候选疫苗，到上个月底，各国已经订购了至少 29.4 亿剂——比任何其他候选冠状病毒疫苗都多。澳大利亚墨尔本莫纳什大学的医生和生物伦理学家保罗·科梅萨罗夫说，不良事件并不罕见，但考虑到开发一种安全有效的疫苗的利害关系，这项研究的所有细节都应该公开。他说:“这些试验都是公开支持的，这种疾病对人类构成了 100 年来最大的威胁，药物开发过程高度政治化，只有在公众信任能够得到保证和维护的情况下，结果才会是成功的。”研究人员尤其担心，当接种疫苗的人随后暴露于病毒时，新冠肺炎疫苗可能会导致“增强性疾病”。包括牛津/阿斯利康候选疫苗在内的新冠肺炎疫苗的动物研究和早期人体试验，迄今为止没有报告疾病加重的迹象。几十个团体表示，他们正在研究冠状病毒的病毒载体疫苗，包括强生公司开发的一种候选疫苗，以及由中国军方和总部位于中国天津的加拿大生物制品公司共同开发的另一种疫苗。
Abstract:
Researchers at the University of Oxford, UK, in collaboration with the pharmaceutical company AstraZeneca, are developing the vaccine, which is one of nine coronavirus vaccines in the final, ‘phase III’ stage of being tested.
Details of the adverse event, including how serious it is and when it happened, have not been reported by Oxford or AstraZeneca. We are committed to the safety of our participants and the highest standards of conduct in our trials,” the statement notes. “If the event is linked definitively, or even probably, to the vaccine, it could be a definitive blow to this particular vaccine candidate. If unrelated, the hold might be lifted in a matter of weeks,” says Kieny. But without more details of the adverse event, including how serious it is and when it happened, it is difficult to assess the impact it will have on the trials and the timeline for the vaccine’s approval, say scientists. Many countries have pre-ordered millions of doses of the Oxford vaccine in the hope that it will be successful. By late last month, countries had ordered at least 2.94 billion doses

— more than any other coronavirus-vaccine candidate. That is not unusual, but given the stakes involved in the development of a safe, effective vaccine, all of the study's details should be made public, says Paul Komesaroff, a physician and bioethicist at Monash University in Melbourne, Australia. "The trials are all publicly supported, the disease is posing the greatest threat to humanity in a hundred years, the drug-development processes are highly politicized, and the outcome will only be a successful one if public trust can be secured and maintained," he says. Researchers have been especially worried that COVID-19 vaccines could cause an 'enhanced disease' when people who receive the vaccine are exposed to the virus subsequently. Animal studies and early-phase human trials of COVID-19 vaccines, including the Oxford/AstraZeneca candidate, have so far reported no signs of enhanced disease. The Oxford vaccine is a viral-vector vaccine that harnesses a cold-causing 'adenovirus' isolated from chimpanzees. The chimpanzee adenovirus has been modified such that it can no longer replicate in cells, and it expresses the 'spike' protein that the coronavirus uses to infect human cells. Dozens of groups say they are working on viral-vector vaccines for coronavirus, including a candidate developed by US drug maker Johnson & Johnson, and another co-developed by the Chinese military and CanSino Biologics, based in Tianjin, China.

9. 科兴生物在巴西的临床试验结果'非常乐观'，巴西可能会会在 12 月发布中国疫苗

'Extremely Positive' Results Point to December Launch of Chinese Coronavirus Vaccine in Brazil

根据位于澳门的中葡简讯，中国科兴生物的灭活疫苗在巴西进行的临床中显示出'非常乐观的'结果，圣保罗州的州长说巴西可能会在早至 12 月开始大规模的免疫。在巴西一共有 6 个州在帮助科兴生物进行临床试验。这个疫苗在 98%的 60 岁以上人群中激发了免疫反应，目前还没有报道引发副作用。

巴西总统对该疫苗持有反对意见。他规划了 3.6 亿美金购买由阿斯利康公司和牛津大学开发的疫苗。

链 接 :https://www.clbrief.com/extremely-positive-results-point-to-december-launch-of-chinese-coronavirus-vaccine-in-brazil/

以下是英文报道部分摘录:

Clinical trials in Brazil of a Chinese-made vaccine against Covid-19 have shown "extremely positive" results, and a widespread vaccination campaign could begin as early as December, the governor of São Paulo state said.

"The results have been extremely positive," Governor Joao Doria told a news conference, quoted by AFP. "We will soon be able to immunise Brazilians in São Paulo and across the country with the CoronaVac vaccine … The projected delivery date is in December this year."

São Paulo, the epicentre of the coronavirus pandemic in Brazil, is one of six states helping to test the CoronaVac vaccine developed by Sinovac Biotech.

The vaccine produced an immune response in 98 per cent of recipients over 60 years old, with no adverse side-effects reported so far, Governor Joao Doria said Wednesday.

Brazilian President Jair Bolsonaro has criticised the vaccine, and lashed out at Doria, a leading opponent, for supposedly backing it.
Bolsonaro instead allocated 1.9 billion reals (US$360 million) to purchase another vaccine candidate, developed by Oxford University and pharmaceutical firm AstraZeneca.

10. 两种剂型中基于 rAd26 和 rAd5 载体的异源 prime boost COVID-19 疫苗的安全性和免疫原性：来自俄罗斯的两项开放的、非随机的 1/2 阶段研究

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia
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编译者：刘焕珍
中文摘要：

背景：我们开发了一种异源 COVID-19 疫苗，该疫苗由两个部分组成，分别是 26 型重组腺病毒（rAd26）载体和 5 型重组腺病毒（rAd5）载体，两者均携带 SARS-CoV-2 刺突糖蛋白（rAd26-S 和 rAd5-S）的基因。 我们旨在评估该疫苗的两种制剂（冷冻和冻干）的安全性和免疫原性。

方法：我们在俄罗斯的两家医院进行了两项开放的、非随机的 1/2 期研究。我们招募了 18-60 岁的健康成年志愿者（男性和女性）参与这两项研究。在每项研究的第一阶段，我们在第 0 天肌肉注射一剂 rAd26-S 或一剂 rAd5-S，并评估这两种成分 28 天的安全性。在第二阶段的研究中，我们在第一阶段疫苗接种后不早于 5 天开始，我们肌肉注射一种主要的增强型疫苗，第 0 天注射 rAd26-S，第 21 天注射 rAd5-S。主要观察指标为抗原特异性体液免疫（第 0 天、第 14 天、第 21 天、第 28 天和第 42 天通过 ELISA 测定 SARS-CoV-2 特异性抗体）和安全性（在整个研究过程中监测不良事件的参与者人数）。次要观察指标是抗原特异性细胞免疫（T 细胞反应和干扰素-γ 浓度）和中和抗体的变化（用 SARS-CoV-2 中和试验检测）。这些试验已在 ClinicalTrials.gov 上注册，NCT04436471 和 NCT04437875。

研究结果：在 2020 年 6 月 18 日至 8 月 3 日期间，我们招募了 76 名参与者参与这两项研究（每个研究 38 名）。在每项研究中，有 9 名志愿者在第 1 阶段接受 rAd26-S 的治疗，有 9 名志愿者在第 1 阶段接受 rAd5-S 的治疗，20 名志愿者在第 2 阶段接受 rAd26-S 和 rAd5-S 的治疗。两种疫苗制剂都是安全的，并且耐受性良好。最常见的不良反应是注射部位疼痛（44 例[58%]），高热（38 例[50%]），头痛（32 例[42%]），乏力（21 例[28%]），以及肌肉和关节疼痛（18 例[24%]）。大多数不良事件为轻度，未发现严重不良事件。所有参与者都产生了抗 SARS-CoV-2 糖蛋白的抗体。第 42 天，冷冻制剂和冻干制剂的受体结合域特异性 IgG 滴度分别为 14 703 和 11 143，冷冻制剂的中和抗体为 49.25，冻干制剂为 45.95，血清转化率为 100%。所有受试者在第 28 天检测到细胞介导的反应，冷冻制剂的细胞增殖中值为 2.5%CD4+和 1.3%CD8+，冻干制剂的中位数细胞增殖率为 1.3%CD4+和 1.1%CD8+。

解释：异源 rAd26 和 rAd5 载体的 COVID-19 疫苗具有良好的安全性，并在参与者中引起强烈的体液和细胞免疫反应。该疫苗预防 COVID-19 的有效性有待进一步研究。

Abstract:

Background: We developed a heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein (rAd26-S and rAd5-S). We aimed to assess the safety and immunogenicity of two formulations (frozen and lyophilised) of this vaccine.

Methods: We did two open, non-randomised phase 1/2 studies at two hospitals in Russia. We enrolled healthy adult volunteers (men and women) aged 18–60 years to both studies. In phase 1 of each study, we administered intramuscularly on day 0 either one dose of rAd26-S or one dose of rAd5-S and assessed the safety of the two components for 28 days. In phase 2 of the study, which began no earlier than 5 days after phase 1 vaccination, we administered intramuscularly a prime-boost vaccination, with rAd26-S given on day 0 and rAd5-S on day 21. Primary outcome measures were antigen-specific humoral immunity (SARS-CoV-2-specific antibodies measured by ELISA on days 0, 14, 21, 28, and 42) and safety (number of participants with adverse events monitored throughout the study). Secondary outcome measures were antigen-specific cellular immunity (T-cell responses and interferon-γ concentration) and change in neutralising antibodies (detected with a SARS-CoV-2 neutralisation assay). These trials are registered with ClinicalTrials.gov, NCT04436471 and NCT04437875.

Findings: Between June 18 and Aug 3, 2020, we enrolled 76 participants to the two studies (38 in each study). In each study, nine volunteers received rAd26-S in phase 1, nine received rAd5-S in phase 1, and 20 received rAd26-S and rAd5-S in phase 2. Both vaccine formulations were safe and well tolerated. The most common adverse events were pain at injection site (44 [58%]), hyperthermia (38 [50%]), headache (32 [42%]), asthenia (21 [28%]), and muscle and joint pain (18 [24%]). Most adverse events were mild and no serious adverse events were detected. All participants produced antibodies to SARS-CoV-2 glycoprotein. At day 42, receptor binding domain-specific IgG titres were 14 703 with the frozen formulation and 11 143 with the lyophilised formulation, and neutralising antibodies were 49.25 with the frozen formulation and 45.95 with the lyophilised formulation, with a seroconversion rate of 100%. Cell-mediated responses were detected in all participants at day 28, with median cell proliferation of 2.5% $CD4^+$ and 1.3% $CD8^+$ with the frozen formulation, and a median cell proliferation of 1.3% $CD4^+$ and 1.1% $CD8^+$ with the lyophilized formulation.

Interpretation: The heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has a good safety profile and induced strong humoral and cellular immune responses in participants. Further investigation is needed of the effectiveness of this vaccine for prevention of COVID-19.

11. 不用打针！全球首个鼻喷新冠疫苗获批开展临床试验

No injections!The world's first nasal spray vaccine has been approved for clinical trials
文章链接：https://mp.weixin.qq.com/s/gsh89cAqIlzmWKgzchtA6w
编译者：张怡
中文摘要：
全球首个鼻喷新冠肺炎疫苗已通过国家药品监督管理局的应急审批，获准开展临床试验，并于日前在江苏东台启动Ⅰ期临床试验。该疫苗是在双重减毒的普通季节性流感病毒载体内，插入新冠病毒刺突蛋白基因片段研发而成的活病毒载体疫苗，是目前已获准开展临床试验的新冠肺炎候选疫苗中唯一采用鼻腔喷雾接种方式的疫苗，通过模拟呼吸道病毒天然感染途径激活局部免疫应答和全身性免疫应答发挥保护作用。

12. SARS-CoV-2 候选疫苗可能与目前流行的所有变种相匹配

A SARS-CoV-2 vaccine candidate would likely match all currently circulating variants
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第一作者：Bethany Dearlove
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DOI 或 PUBMED ID：https://doi.org/10.1073/pnas.2008281117
编译者：张鹏伟
中文摘要：
在这里，我们研究了严重急性呼吸综合征冠状病毒 2（SARS-CoV-2）序列的多样性，并将其与大多数候选疫苗所依据的序列进行了比较。使用 18,514 个序列，我们进行系统发育，群体遗传和结构生物信息学分析。我们发现 SARS-CoV-2 基因组的多样性有限：只有 11 个位点在>5%的序列中显示多态性；然而两个突变，包括 Spike 中的 D614G 突变，已经成为共识。由于 SARS-CoV-2 的传播速度比进化速度快，病毒的数量也越来越均匀，基因组之间的平均核苷酸替换量为 7 个。有纯化选择的证据，但几乎没有多样化选择的证据，在结构基因和非结构基因之间的替代率相当。最后，作为不同疫苗候选物基础的 Spike 蛋白的武汉-Hu-1 参考序列与优化的疫苗插入片段匹配，与原始序列相同，并且与共有序列相距一个突变。虽然 D614G 突变的迅速传播需要进一步的研究，但我们的结果表明漂移和瓶颈事件可以解释 SARS-CoV-2 序列之间的最小差异。这些发现表明，单一的候选疫苗应该对目前流行的变种有效。
Abstract
The magnitude of the COVID-19 pandemic underscores the urgency for a safe and effective vaccine. Many vaccine candidates focus on the Spike protein, as it is targeted by neutralizing antibodies and plays a key role in viral entry. Here we investigate the diversity seen in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) sequences and compare it to the sequence on which most vaccine candidates are based. Using 18,514 sequences, we perform phylogenetic, population genetics, and structural bioinformatics analyses. We find limited diversity across SARS-CoV-2 genomes: Only 11 sites show polymorphisms in >5% of sequences;

yet two mutations, including the D614G mutation in Spike, have already become consensus. Because SARS-CoV-2 is being transmitted more rapidly than it evolves, the viral population is becoming more homogeneous, with a median of seven nucleotide substitutions between genomes. There is evidence of purifying selection but little evidence of diversifying selection, with substitution rates comparable across structural versus nonstructural genes. Finally, the Wuhan-Hu-1 reference sequence for the Spike protein, which is the basis for different vaccine candidates, matches optimized vaccine inserts, being identical to an ancestral sequence and one mutation away from the consensus. While the rapid spread of the D614G mutation warrants further study, our results indicate that drift and bottleneck events can explain the minimal diversity found among SARS-CoV-2 sequences. These findings suggest that a single vaccine candidate should be efficacious against currently circulating lineages.

13. 预融合 SARS-CoV-2 spike RNA 疫苗具有高度免疫原性，可防止非人灵长类动物的肺部感染

A prefusion SARS-CoV-2 spike RNA vaccine is highly immunogenic and prevents lung infection in non-human primates

来源：bioRxiv

发布时间：2020-09-08

链接：https://www.biorxiv.org/content/10.1101/2020.09.08.280818v1

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中文摘要：

在这项研究中，我们报告了 BNT162b2 候选疫苗在猕猴中的设计、临床前开发、免疫原性和抗病毒保护作用。BNT162b2 包含经 LNP 配制的核苷修饰的 mRNA，该 mRNA 编码以其融合前构象捕获的 spike 糖蛋白。在细胞中表达 BNT162b2 编码序列后，大约 20％的 spike 分子处于一 RBD 向上，两 RBD 向下状态。用单剂量的 BNT162b2 免疫小鼠后，假病毒中和效价会出现剂量水平依赖性的增加。恒河猴的初免-加强疫苗接种引起了 SARS-CoV-2 中和几何平均效价为 SARS-CoV-2 恢复期人血清组的 10.2 至 18.0 倍。BNT162b2 在小鼠和恒河猴中产生强烈的 TH1 型 CD4 +和 IFNγ+ CD8 + T 细胞反应。BNT162b2 候选疫苗可完全保护免疫恒河猴的肺免受传染性 SARS-CoV-2 攻击。BNT162b2 目前正在一项全球关键的 2/3 期临床试验（NCT04368728）中进行评估。

Abstract:

To contain the coronavirus disease 2019 (COVID-19) pandemic, a safe and effective vaccine against the new severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is urgently needed in quantities sufficient to immunise large populations. In this study, we report the design, preclinical development, immunogenicity and anti-viral protective effect in rhesus macaques of the BNT162b2 vaccine candidate. BNT162b2 contains an LNP-formulated nucleoside-modified mRNA that encodes the spike glycoprotein captured in its prefusion conformation. After expression of

the BNT162b2 coding sequence in cells, approximately 20% of the spike molecules are in the one-RBD up, two-RBD down state. Immunisation of mice with a single dose of BNT162b2 induced dose level-dependent increases in pseudovirus neutralisation titers. Prime-boost vaccination of rhesus macaques elicited authentic SARS-CoV-2 neutralising geometric mean titers 10.2 to 18.0 times that of a SARS-CoV-2 convalescent human serum panel. BNT162b2 generated strong TH1 type CD4+ and IFNγ+ CD8+ T-cell responses in mice and rhesus macaques. The BNT162b2 vaccine candidate fully protected the lungs of immunised rhesus macaques from infectious SARS-CoV-2 challenge. BNT162b2 is currently being evaluated in a global, pivotal Phase 2/3 trial (NCT04368728).

14. SARS-CoV-2 重组刺突蛋白纳米颗粒疫苗的 1-2 期试验

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

来源：NEJM

发布时间：2020-09-02

链接：

https://www.nejm.org/doi/full/10.1056/NEJMoa2026920?query=C19&cid=DM98059_NEJM_Registered_Users_and_InActive&bid=253678107

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DOI 或 PUBMED ID：10.1056/NEJMoa2026920

编译者：张丽双

中文摘要：

NVX-CoV2373 是重组三重全长 SARS-CoV-2 刺突糖蛋白和 Matrix-M1 佐剂组成的 rSARS-CoV-2 纳米颗粒疫苗。启动了一项随机，安慰剂对照的 1–2 期试验，以评估 rSARS-CoV-2 疫苗（5μg 和 25μg 剂量，有/无 Matrix-M1 佐剂）的安全性和免疫原性。两次肌肉注射，相隔 21 天。在第 35 天时，NVX-CoV2373 似乎是安全的，并且引发的免疫反应超过了 Covid-19 康复期血清中的水平。Matrix-M1 佐剂诱导的 CD4 + T 细胞反应偏向 Th1 表型。

Abstract:

BACKGROUND: NVX-CoV2373 is a recombinant severe acute respiratory syndrome coronavirus 2 (rSARS-CoV-2) nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant.

METHODS: We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-μg and 25-μg doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. In phase 1, vaccination comprised two intramuscular injections, 21 days apart. The primary outcomes were reactogenicity; laboratory values (serum chemistry and hematology), according to Food and Drug Administration toxicity scoring, to assess safety; and IgG anti–spike protein response (in enzyme-linked immunosorbent assay [ELISA] units). Secondary outcomes included unsolicited adverse events, wild-type virus neutralization (microneutralization assay), and T-cell responses (cytokine staining). IgG and microneutralization assay results were compared with 32 (IgG)

and 29 (neutralization) convalescent serum samples from patients with Covid-19, most of whom were symptomatic. We performed a primary analysis at day 35.
RESULTS: After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced immune responses, was antigen dose-sparing, and induced a T helper 1 (Th1) response. The two-dose 5-μg adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients (8344 and 983, respectively).
CONCLUSIONS: At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype. (Funded by the Coalition for Epidemic Preparedness Innovations; ClinicalTrials.gov number, NCT04368988. opens in new tab).

15. 用口炎病毒（VSV）假病毒应对 SARS-CoV-2

Snatching the Crown from SARS-CoV-2
来源：Cell Host Microbe
发布时间：2020-09-09
链接：https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30462-5#%20
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通讯作者：Lynda Coughlan
通讯作者单位：美国马里兰大学
DOI 或 PUBMED ID：https://doi.org/10.1016/j.chom.2020.08.007
编译者：张丽双
中文摘要：
在本期《Cell Host & Microbe》杂志上，有三篇文章描述了表达 SARS-CoV-2 刺突蛋白的口炎病毒（VSV）假病毒。该 VSV-CoV-2-S 平台允许在 BSL-2 上进行病毒中和测定，并且还可以作为候选载体疫苗来诱导针对 SARS-CoV-2 的保护性免疫。
Abstract：
In this issue of Cell Host & Microbe, three papers describe the pseudotyping of vesicular stomatitis virus (VSV) with the SARS-CoV-2 spike. This VSV-CoV-2-S platform allows virus neutralization assays to be performed at BSL-2 and also has applications as a candidate vectored vaccine to elicit protective immunity against SARS-CoV-2.

16. 基于 SARS-CoV-2 核糖体框架位移的药物筛选工具包

A drug screening toolkit based on the -1 ribosomal frameshifting of SARS-CoV-2
来源：Heliyon

发布时间：2020.08.26
文章链接：https://www.cell.com/heliyon/fulltext/S2405-8440(20)31636-4
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DOI：https://doi.org/10.1016/j.heliyon.2020.e04793
编译者：张怡
中文摘要：
SARS-CoV-2 中核糖体移码对于中开放阅读框架(ORF)1b 的翻译至关重要。ORF1b 的产物参与病毒复制。因此，改变移码的频率会降低病毒的存活率。这项研究的目的是成功地开发一个筛选抗病毒药物的工具包。最后，筛选了 FDA 批准的药物库，发现伊伐卡托和(-)-石杉碱 A 在改变 SARS-CoV-2 的- 1 核糖体框架位移方面效果良好。
Abstract
The －1 ribosomal frameshifting is vital for the translation of the open reading frame (ORF)1b in SARS-CoV-2. The products of ORF1b participate in viral replication. Therefore, changing the frameshift frequency reduces the survival of the virus. This study aimed to successfully develop a toolkit for screening antiviral drugs. Finally, the FDA-approved drug library was screened, revealing that ivacaftor and (－)-Huperzine A worked well in changing the －1 ribosomal frameshifting of SARS-CoV-2 in vitro.

17. 从头设计 SARS-CoV-2 微蛋白抑制剂

De novo design of picomolar SARS-CoV-2 miniprotein inhibitors
来源：science
发布时间：2020-09-09
链接：https://science.sciencemag.org/content/early/2020/09/08/science.abd9909
第一作者：Longxing Cao
通讯作者：David Baker
通讯作者单位：美国华盛顿大学
DOI 或 PUBMED ID：10.1126/science.abd9909
编译者：刘焕珍
中文摘要：
靶向 SARS-CoV-2 Spike 蛋白和人类 ACE2 受体之间的相互作用是一种有前途的治疗策略。我们使用两种从头设计方法设计抑制剂。计算机生成的支架要么围绕与 Spike 受体结合域（RBD）相互作用的 ACE2 螺旋构建，要么靠着 RBD 对接以鉴定新的结合模式，其氨基酸序列设计用于优化靶标结合，折叠和稳定性。10 种设计以 100pM 至 10nM 的亲和力结合 RBD，并阻断了 IC 50 值为 24 pM 至 35 nM 的 Vero E6 细胞的 ARS-CoV-2 感染；最有效的新结合模式是 56 和 64 个残基蛋白（IC 50∽0.16 ng/ml）。 这些微型粘合剂与 SARS-CoV-2 spike 胞外域三聚体结合并结合所有三个 RBD 的低温电子显微镜结构与计算模型几乎相同。这些超稳定的微型粘合剂为 SARS-CoV-2 治疗提供了起点。
Abstract:
Targeting the interaction between the SARS-CoV-2 Spike protein and the human

ACE2 receptor is a promising therapeutic strategy. We designed inhibitors using two de novo design approaches. Computer generated scaffolds were either built around an ACE2 helix that interacts with the Spike receptor binding domain (RBD), or docked against the RBD to identify new binding modes, and their amino acid sequences designed to optimize target binding, folding and stability. Ten designs bound the RBD with affinities ranging from 100pM to 10nM, and blocked ARS-CoV-2 infection of Vero E6 cells with IC 50 values between 24 pM and 35 nM; The most potent, with new binding modes, are 56 and 64 residue proteins (IC 50 ~ 0.16 ng/ml). Cryo-electron microscopy structures of these minibinders in complex with the SARS-CoV-2 spike ectodomain trimer with all three RBDs bound are nearly identical to the computational models. These hyperstable minibinders provide starting points for SARS-CoV-2 therapeutics.

18. 恢复期血浆在印度抗新冠肺炎治疗中的应用：一项开放、平行临床 II 期多中心随机对照试验

Convalescent plasma in the management of moderate COVID-19 in India: An open-label parallel-arm phase II multicentre randomized controlled trial (PLACID Trial)

来源：medRxiv

发布时间：2020-09-08

链接：https://www.medrxiv.org/content/10.1101/2020.09.03.20187252v1

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通讯作者：Aparna Mukherjee

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DOI 或 PUBMED ID：preprint

编译者：孔娟

中文摘要：

目的：文中研究了恢复期血浆(CP)作为中和抗体治疗新冠肺炎的有效性。设计：开放、平行、第二阶段多中心随机对照试验。背景：印度 39 家医院参与其中。参与者：住院、确诊的新冠肺炎中度疾病患者(血氧饱和度：200-300 或呼吸频率>24/分钟，室内空气中血氧饱和度 ≤ 93%)。干预：参与者被随机分为对照组(最佳护理标准)或干预组(恢复期血浆+最佳护理标准)。在干预组中，每隔 24 小时输入两剂 200 毫升的氯吡格雷。主要观察指标：注射后 28 天发展为严重疾病(PaO2/FiO2<100)或全因死亡率的综合指标。结果：2020 年 4 月 22 日至 7 月 14 日，共招募 464 名参与者其中干预组 235 名，对照组 229 名。干预组的 44 名(18.7%)和对照组的 41 名(17.9%)获得了综合主要结果 [aOR: 1.09; 95% CI: 0.67, 1.77]。死亡率干预组 34 名(13.6%)和对照组 31 名[aOR) 1.06 95% CI: -0.61 to 1.83]。解释：恢复期血浆与死亡率降低或发展为严重新冠肺炎病无关。该试验具有很高的普遍性，并且在实验室能力有限的情况下，接近康复期血浆疗法的真实环境。对献血者和受试者中和抗体滴度的先验测量可以进一步阐明恢复期血浆在新冠肺炎管理中的作用。

Abstract

Objectives: Convalescent plasma (CP) as a passive source of neutralizing antibodies and immunomodulators is a century-old therapeutic option used for the management of viral diseases. We investigated its effectiveness for the treatment

of COVID-19. Design: Open-label, parallel-arm, phase II, multicentre, randomized controlled trial. Setting: Thirty-nine public and private hospitals across India. Participants: Hospitalized, moderately ill confirmed COVID-19 patients (PaO2/FiO2: 200-300 or respiratory rate > 24/min and SpO2 ≤ 93% on room air). Intervention: Participants were randomized to either control (best standard of care (BSC)) or intervention (CP + BSC) arm. Two doses of 200 mL CP was transfused 24 hours apart in the intervention arm. Main Outcome Measure: Composite of progression to severe disease (PaO2/FiO2<100) or all-cause mortality at 28 days post-enrolment. Results: Between 22 nd April to 14 th July 2020, 464 participants were enrolled; 235 and 229 in intervention and control arm, respectively. Composite primary outcome was achieved in 44 (18.7%) participants in the intervention arm and 41 (17.9%) in the control arm [aOR: 1.09; 95% CI: 0.67, 1.77]. Mortality was documented in 34 (13.6%) and 31 (14.6%) participants in intervention and control arm, respectively [aOR) 1.06 95% CI: -0.61 to 1.83]. Interpretation: CP was not associated with reduction in mortality or progression to severe COVID-19. This trial has high generalizability and approximates real-life setting of CP therapy in settings with limited laboratory capacity. A priori measurement of neutralizing antibody titres in donors and participants may further clarify the role of CP in management of COVID-19.

19. SARS-CoV-2 的蛋白编码能力

The coding capacity of SARS-CoV-2

来源：nature

发布时间：2020-09-09

链接：https://www.nature.com/articles/s41586-020-2739-1

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DOI 或 PUBMED ID：10.1038/s41586-020-2739-1

编译者：蒋立春

中文摘要：

SARS-CoV-2 蛋白编码图谱目前是基于和其他冠状病毒的同源性的计算机预测。因为冠状病毒可能在特别是附属蛋白的蛋白组上面有差异，无偏好性地对 SARS-CoV-2 的蛋白进行研究非常必要。用翻译组测序技术，作者们呈现了一个高精度的 SARS-CoV-2 的表达区域，准确定量了典型的病毒开放读码框，另外也鉴定到 23 个没有注释的病毒开放读码框。这些开放读码框包括可能是起到调节功能的基因上游开放读码框，几个在已有开放读码框内部的同框开放读码框一会产生 N 端截断的多肽，以及在已有开放读码框内部的移框开放读码框一会产生全新的多肽。病毒 mRNAs 的翻译并没有比宿主的 mRNAs 翻译效率更高，病毒的翻译胜过额宿主的翻译原因是因为病毒的转录水平高。该工作为将来的功能性研究提供了丰富的资源。

Abstract:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the ongoing Coronavirus disease 19 (COVID-19) pandemic1. In order to understand

SARS-CoV-2 pathogenicity and antigenic potential, and to develop therapeutic tools, it is essential to portray the full repertoire of its expressed proteins. The SARS-CoV-2 coding capacity map is currently based on computational predictions and relies on homology to other coronaviruses. Since coronaviruses differ in their protein array, especially in the variety of accessory proteins, it is crucial to characterize the specific collection of SARS-CoV-2 proteins in an unbiased and open-ended manner. Using a suite of ribosome profiling techniques, we present a high-resolution map of the SARS-CoV-2 coding regions, allowing us to accurately quantify the expression of canonical viral open reading frames (ORFs) and to identify 23 unannotated viral ORFs.These ORFs include upstream ORFs (uORFs) that are likely playing a regulatory role, several in-frame internal ORFs lying within existing ORFs, resulting in N-terminally truncated products, as well as internal out-of-frame ORFs, which generate novel polypeptides. We further show that viral mRNAs are not translated more efficiently than host mRNAs; rather, virus translation dominates host translation due to high levels of viral transcripts. Our work provides a rich resource, which will form the basis of future functional studies.

20. 一种人源二价抗体 V_H结构域在 SARS-CoV-2 动物模型中具有很好的效果

High potency of a bivalent human V_H domain in SARS-CoV-2 animal models

来源：Cell

发布时间：2020-09-04

链接：https://www.cell.com/cell/fulltext/S0092-8674(20)31148-X

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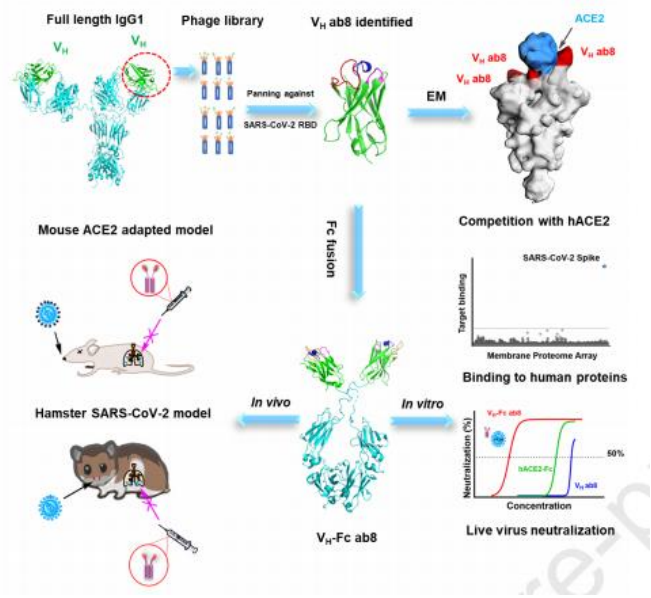
DOI 或 PUBMED ID：10.1016/j.cell.2020.09.007

编译者：宋珂

中文摘要：

目前，开发针对 COVID-19 的新颖治疗药物的需求十分迫切。本文中，作者利用噬菌体展示技术构建了人源抗体 V_H结构域文库，并从中鉴别出了具有高亲和力的 V_H蛋白 ab8。二价 V_H，V_H-Fc ab8 与膜结合相关的 S 糖蛋白，以及患者中发现的 S 糖蛋白突变体的结合能力都很强。在野生型小鼠中，其对适应小鼠的 SARS-CoV-2 病毒的有效中和滴度低至 2 mg/kg，并且在仓鼠模型中表现出较好的预防和治疗 SARS-CoV-2 感染的功效。当然，也可能是由于其相对较小的体型而增强了效果。作者结合电子显微镜与突变扫描技术，发现 ab8 与所有三个 S 蛋白原体间均存在相互作用，并显示了 ab8 如何通过直接干扰 ACE2 的结合从而中和病毒感染。V_H-Fc ab8 不发生聚集，并且不与 5300 人源膜结合蛋白结合。结合 V_H-Fc ab8 的有效中和活性与良好的可开发性，以及与 SARS-CoV-2 突变体的交叉反应性，为评估其作为

COVID-19 治疗药物的潜力提供了有力的依据。



Abstract:
Novel COVID-19 therapeutics are urgently needed. We generated a phage-displayed human antibody VH domain library from which we identified a high-affinity VH binder ab8. Bivalent VH, VH-Fc ab8 bound with high avidity to membrane-associated S glycoprotein and to mutants found in patients. It potently neutralized mouse adapted SARS-CoV-2 in wild type mice at a dose as low as 2 mg/kg and exhibited high prophylactic and therapeutic efficacy in a hamster model of SARS-CoV-2 infection, possibly enhanced by its relatively small size. Electron microscopy combined with scanning mutagenesis identified ab8 interactions with all three S protomers and showed how ab8 neutralized the virus by directly interfering with ACE2 binding. VH-Fc ab8 did not aggregate and did not bind to 5300 human membrane-associated proteins. The potent neutralization activity of VH-Fc ab8 combined with good developability properties and cross-reactivity to SARS-CoV-2 mutants provide a strong rationale for its evaluation as a COVID-19 therapeutic.

21. 妊娠期间通过 JAK/STAT 依赖的增强子激活了 SARS-CoV-2 的受体 Ace2

Activation of the SARS-CoV-2 receptor Ace2 through JAK/STAT-dependent enhancers during pregnancy

来源：Cell Reports

发布时间：2020-09-06

链接：https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31188-8

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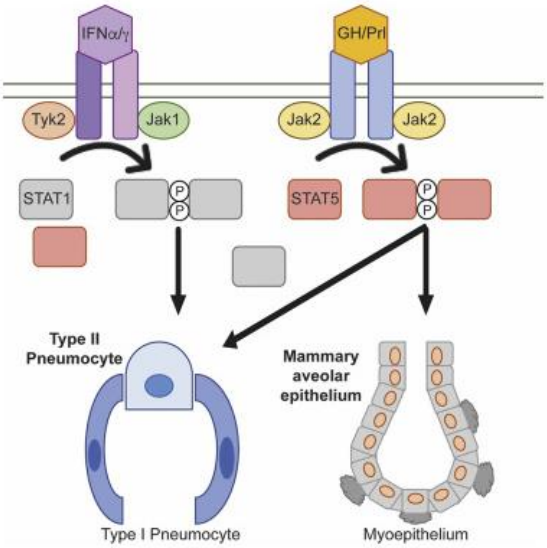
DOI 或 PUBMED ID：10.1016/j.celrep.2020.108199
编译者：宋珂
中文摘要：

ACE2 是 SARS-CoV-2 病毒的受体，并介导病毒侵入细胞。干扰素能够激活 ACE2 在肺泡细胞中的表达，揭示出细胞因子在 SARS-CoV-2 的靶细胞中起到了至关重要的作用。目前至少有七项研究指出，在母乳中检测到了病毒 RNA。这说明在哺乳期内 ACE2 在乳腺组织中表达的可能性比较高。本文中，作者发现在怀孕和哺乳期内，小鼠乳腺组织中 Ace2 被诱导表达，这与内含子中增强子被激活相吻合。这些增强子被催乳激素激活的转录因子 STAT5 以及其他调控因子（包括 Polymerase II）占据。敲除 Stat5a 能造成增强子失效，Ace2 mRNA 下降 83%。作者还发现，哺乳期内肺中 Ace2 的表达量增高，但在肾脏和肠中却没有增加。JAK/STAT 组分在一系列 SARS-CoV-2 靶细胞中均有分布，从而引出了细胞因子对病毒载量和肺外病理生理影响的可能性。



Abstract:
ACE2 binds the coronavirus SARS-CoV-2 and facilitates its cellular entry. Interferons activate ACE2 expression in pneumocytes, suggesting a critical role of cytokines in SARS-CoV-2 target cells. Viral RNA was detected in breast milk in at least seven studies, raising the possibility that ACE2 is expressed in mammary tissue during lactation. Here we show that Ace2 expression in mouse mammary tissue is induced during pregnancy and lactation, which coincides with the activation of intronic enhancers. These enhancers are occupied by the prolactin-activated transcription factor STAT5 and additional regulatory factors, including Polymerase II. Deletion of Stat5a results in decommissioning of the enhancers and an 83% reduction of Ace2 mRNA. We also demonstrate that Ace2 expression increases during lactation in lung, but not in kidney and intestine. JAK/STAT components are present in a range of SARS-CoV-2 target cells opening the possibility that cytokines contribute to the viral load and extrapulmonary pathophysiology.

22. 许多蝙蝠不是 SARS-CoV 和 SARS-CoV-2 的潜在宿主：证据来源于 ACE2 受体的使用

Many bat species are not potential hosts of SARS-CoV and SARS-CoV-2: Evidence from ACE2 receptor usage

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中文摘要：

蝙蝠是 SARS-CoV 和 SARS-CoV-2 的天然宿主，后者导致了 COVID-19 的大流行。病毒刺突蛋白与宿主 ACE2 的相互作用是潜在宿主和跨物种传播的关键决定因素。该研究使用病毒-宿主受体结合和感染分析表明，来自 46 种系统发育不同的蝙蝠物种（包括与人类有近距离和远距离接触的蝙蝠）中的 24 种、21 种和 16 种，它们的 ACE2 同源序列不支持 SARS-CoV、SARS-CoV-2 和这两种冠状病毒的进入。此外，该研究利用基因和功能分析来确定与病毒进入限制相关的 bat ACE2 受体的基因变化。研究表明，即使不是大多数，许多蝙蝠物种也不是 SARS-CoV 和 SARS-CoV-2 的潜在宿主，这为大流行控制和野生动物保护提供了重要的见解。

Abstract:

Bats are the suggested natural hosts for severe acute respiratory syndrome coronavirus (SARS-CoV) and SARS-CoV-2, the latter of which caused the coronavirus disease 2019 (COVID-19) pandemic. The interaction of viral Spike proteins with their host receptor angiotensin-converting enzyme 2 (ACE2) is a critical determinant of potential hosts and cross-species transmission. Here we use virus-host receptor binding and infection assays to show that ACE2 orthologs from 24, 21, and 16 of 46 phylogenetically diverse bat species, including those in close and distant contact with humans, do not support entry of SARS-CoV, SARS-CoV-2, and both of these coronaviruses, respectively. Furthermore, we used genetic and functional analyses to identify genetic changes in bat ACE2 receptors associated with viral entry restrictions. Our study demonstrates that many, if not most, bat species are not potential hosts of SARS-CoV and SARS-CoV-2, and provides important insights into pandemic control and wildlife conservation.

23. 全球疫苗分配的伦理框架

An ethical framework for global vaccine allocation

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中文摘要：

公平优先模式（The Fair Priority Model）主要针对三个群体，一个是由全球免疫联盟、世界卫生组织（WHO）和流行病防范创新联盟(CEPI)领导的 COVAX 机构，该机构打算购买疫苗，以便在各国间公平分配。第二个群体是疫苗生产商。值得庆幸的是,许多生产商致力于广泛的公开和公平的国际分配疫苗。最后一个群体是国家政府,他们中的一些人也公开承诺公平分配。

这些组织需要一个清晰的框架，协调竞争价值，他们和其他人将欣然接受的，而不仅仅是一种权力的主张。公平优先模式规定了公平分配疫苗所需要的条件，并为它们的承诺提供内容。此外，接受这一共同道德框架将减少重复和浪费，减轻公平分配的努力。这反过来又将增强生产者的信心，使他们相信疫苗将被公平地分配给造福于人民的人，从而促进增加国际分配的疫苗供应。

公平优先模式是限制伤害、惠及弱势群体、承认平等关注等伦理价值观的最佳体现。执行这一模式的责任在于各国、国际组织和疫苗生产商。他们需要使用已经建立的应对大流行的合作机制，如 COVAX 设施。各组织还在实证评估疫苗分配实际上如何根据 SEYLL、贫困和 GNI 等指标影响国家方面发挥着不可或缺的作用。最终，该模式为各国政府、国际组织和疫苗生产商提供了一种切实可行的方式，以履行其公平公正地分配疫苗的承诺，并使其承诺成为现实。

Abstract:

The Fair Priority Model offers a practical way to fulfill pledges to distribute vaccine fairly and equitably