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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免责申明：

本简报仅作为科研参考之用，不构成医疗建议，如您怀疑自己感染新型冠状病毒，请去正规医院或者咨询医生。

1. 2020 年 12 月 3 日疫情

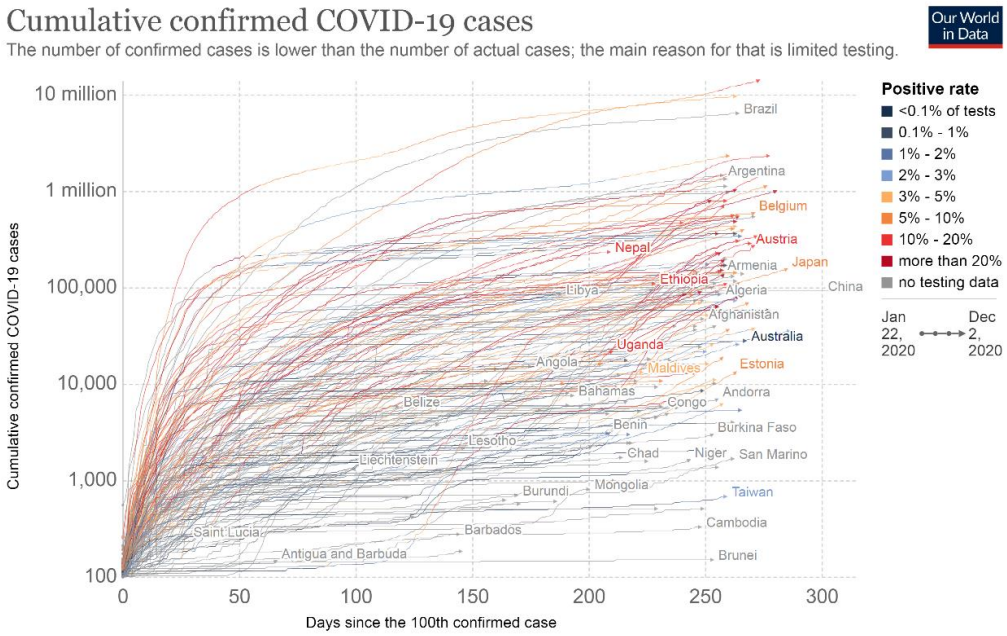
数据来源：WHO

发布时间：2020 年 12 月 3 日北京时间下午 4 点

链接：https://covid19.who.int/

根据 WHO 提供的数据，2020 年 12 月 3 日全球累计确诊新型冠状病毒病人 **63,965,092** 例，当日新增确诊 **591,432** 例，累计死亡 **1,488,120** 例，当日新增死亡 **11,741**。

中国累计确诊 93,797 例，累计死亡 4,751 例，当日新增确诊 129 例，新增死亡 1 例。



Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 3 December, 18:06 (London time), Official data collated by Our World in Data
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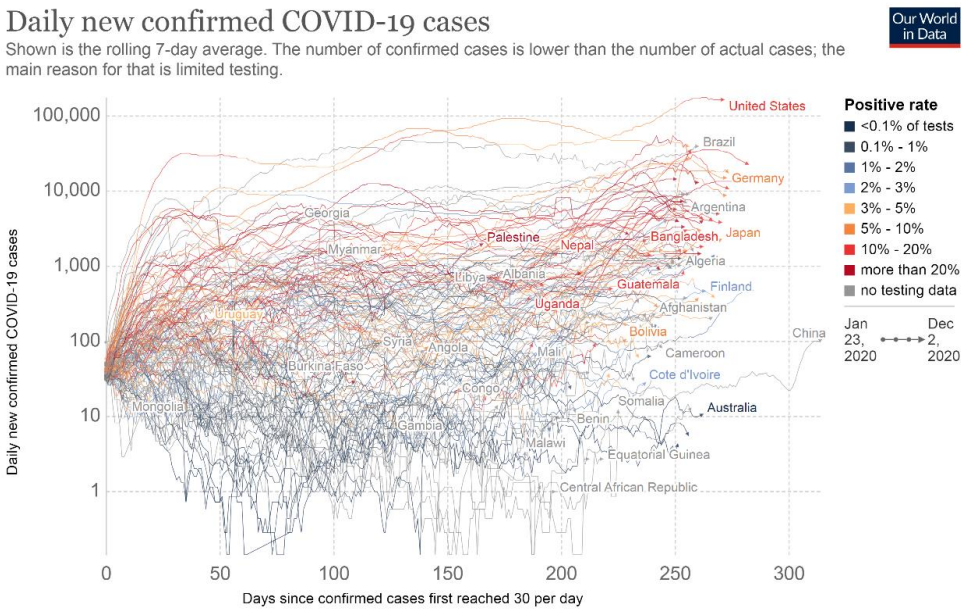
重点国家确诊数量曲线（https://ourworldindata.org/covid-cases?country=~OWID_WRL#what-is-the-daily-number-of-confirmed-cases）



Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 3 December, 18:06 (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（12 月 3 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 对美国 2019 年 12 月到 2020 年 1 月捐赠的血液进行 SARS-CoV-2 反应抗体的血清学检测

Serologic testing of U.S. blood donations to identify SARS-CoV-2-reactive antibodies: December 2019-January 2020

来源：

发布时间：2020-11-26

链接：https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1785/6012472

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DOI： https://doi.org/10.1093/cid/ciaa1785

中文摘要：

知识分子公众号文章：https://mp.weixin.qq.com/s/OZHaQrl7aKrTjbokBXn7sw

去年 12 月美国有无新冠病毒感染？美国疾控中心研究引发争论

Abstract:

Background

SARS-CoV-2, the virus that causes COVID-19 disease, was first identified in Wuhan, China in December 2019, with subsequent worldwide spread. The first U.S. cases were identified in January 2020.

Methods

To determine if SARS-CoV-2 reactive antibodies were present in sera prior to the

first identified case in the U.S. on January 19, 2020, residual archived samples from 7,389 routine blood donations collected by the American Red Cross from December 13, 2019 to January 17, 2020, from donors resident in nine states (California, Connecticut, Iowa, Massachusetts, Michigan, Oregon, Rhode Island, Washington, and Wisconsin) were tested at CDC for anti-SARS-CoV-2 antibodies. Specimens reactive by pan-immunoglobulin (pan Ig) enzyme linked immunosorbent assay (ELISA) against the full spike protein were tested by IgG and IgM ELISAs, microneutralization test, Ortho total Ig S1 ELISA, and receptor binding domain / Ace2 blocking activity assay.

Results

Of the 7,389 samples, 106 were reactive by pan Ig. Of these 106 specimens, 90 were available for further testing. Eighty four of 90 had neutralizing activity, 1 had S1 binding activity, and 1 had receptor binding domain / Ace2 blocking activity >50%, suggesting the presence of anti-SARS-CoV-2-reactive antibodies. Donations with reactivity occurred in all nine states.

Conclusions

These findings suggest that SARS-CoV-2 may have been introduced into the United States prior to January 19, 2020.

3. 近期地方性流行的冠状病毒感染与 COVID-19 症状更轻有关

Recent endemic coronavirus infection is associated with less severe COVID-19

来源：The Journal of Clinical Investigation

发布时间：2020-09-30

链接：https://www.jci.org/articles/view/143380

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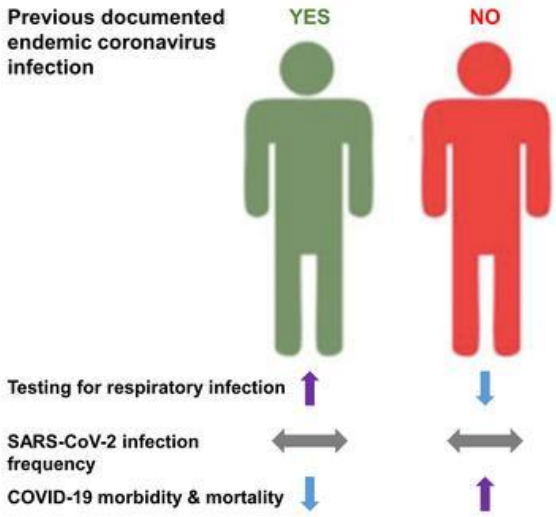
DOI 或 PUBMED ID：10.1172/JCI143380

编译者：宋珂

中文摘要：

四种不同的地方性冠状病毒（eCoV）是季节性“普通感冒”的病原体，而且这些 eCoV 与 SARS-CoV-2 病毒具有广泛的序列同源性。本文中，作者发现，与近期没有感染过 eCoV 的个体相比，相对最近一段时间内感染过 eCoV 的个体发生呼吸道感染的频率更高，但感染 SARS-CoV-2 病毒的比率却相近。重要的是，先前被检测到感染 eCoV 的患者也患有不太严重的 COVID-19。作者的观察结果表明，现有的针对地方性人类冠状病毒的免疫反应可以缓解 SARS-CoV-2 感染引起的临床症状。



Abstract:
Four different endemic coronaviruses (eCoVs) are etiologic agents for the seasonal "common cold," and these eCoVs share extensive sequence homology with human severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Here, we show that individuals with as compared to without a relatively recent documented eCoV were tested at greater frequency for respiratory infections but had similar rate of SARS-CoV-2 acquisition. Importantly, the patients with a previously detected eCoV had less severe coronavirus disease-2019 (COVID-19) illness. Our observations suggest that pre-existing immune responses against endemic human coronaviruses can mitigate disease manifestations from SARS-CoV-2 infection.

4. 新冠肺炎患者无症状密切接触者快速抗原检测(Panbio COVID-19 Ag 快速检测装置)的真实评估

Real-life evaluation of a rapid antigen test (Panbio COVID-19 Ag Rapid Test Device) for SARS-CoV-2 detection in asymptomatic close contacts of COVID-19 patients

来源：medRxiv

发布时间：2020-12-02

链接：https://www.medrxiv.org/content/10.1101/2020.12.01.20241562v1

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DOI 或 PUBMED ID：Preprint

编译者：宋张悦

中文摘要：

目的：目前关于快速抗原检测(RAD)用于识别感染 SARS-CoV-2 的无症状个体的信息有限。在

这项现场研究中，我们为此评估了 Panbio COVID-19 Ag 快速测试装置（雅培诊断，耶拿，德国）。

方法：共纳入 634 例个体，（女性 355 例；平均年龄为 37 岁；年龄范围：9-87 岁）。在索引病例诊断后，在中位数 2 天(范围 1-7)，对家庭接触者(n=338)进行了检测，在暴露后的中位数 6 天(范围 1-7)，对非家庭接触者(n=296)进行了检测。使用 RAD 测试进行了即时检测。RT-PCR 检测使用 TaqPath COVID-19 Combo 试剂盒（Thermo Fisher Scientific，马萨诸塞州，美国）。

结果：RT-PCR 检测 79 人(12.4%)呈阳性，其中 RAD 阳性 38 人(48.1%)。RAD 检测的总体灵敏度和特异性分别为 48.1% (95% CI: 37.4-58.9)和 100% (95% CI: 99.3-100)。灵敏度在家庭接触者中(50.8%;95%置信区间:38.9-62.5)高于非家庭接触者(35.7%;95%置信区间:16.3-61.2%)。RAD 测试呈阳性的个体比阴性的个体更有可能(P<0.001)出现症状。

结论：Panbio 检测对 COVID-19 患者无症状密切接触者敏感性较低，尤其是对非家庭接触者。尽管如此，在这一组中确定上呼吸道采集的最佳时机似乎是确定检测灵敏度的当务之急。

Abstract

Objectives: There is limited information on the performance of rapid antigen detection (RAD) tests to identify SARS-CoV-2-infected asymptomatic individuals. In this field study, we evaluated the Panbio COVID-19 Ag Rapid Test Device (Abbott Diagnostics, Jena, Germany) for the purpose.

Methods: A total of 634 individuals (355 female; median age, 37 years; range, 9-87) were enrolled. Household (n=338) contacts were tested at a median of 2 days (range, 1-7) after diagnosis of the index case and non-household contacts (n=296) at a median of 6 days (range, 1-7) after exposure. RAD testing was carried out at the point of care. The RT-PCR test used was the TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, Massachusetts, USA).

Results: In total, 79 individuals (12.4%) tested positive by RT-PCR, of whom 38 (48.1%) yielded positive RAD results. The overall sensitivity and specificity of the RAD test was 48.1% (95% CI: 37.4-58.9) and 100% (95% CI: 99.3-100), respectively. Sensitivity was higher in household (50.8%; 95% CI: 38.9-62.5) than in non-household (35.7%; 95% CI:16.3-61.2%) contacts. Individuals testing positive by RAD test were more likely (P<0.001) to become symptomatic than their negative counterparts.

Conclusion: The Panbio test displays low sensitivity in asymptomatic close contacts of COVID-19 patients, particularly in non-household contacts. Nonetheless, establishing the optimal timing for upper respiratory tract collection in this group seems imperative to pinpoint test sensitivity.

5. 在 COVID-19 患者中 SARS-CoV-2 经嗅粘膜入侵作为进入中枢神经系统的通道

Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19

简报 6 月 12 日第 16 条报道过该工作的预印本。

链接：https://www.nature.com/articles/s41593-020-00758-5

6. Nature 关注：新冠最可怕的后遗症来了，可致数年后痴呆症激增

Bio 生物世界公众号：https://mp.weixin.qq.com/s/tkME6kd8rwhJ6nLBlEoNlg

7. 黏膜相关恒定 T 细胞在不同性别的 COVID-19 病人中有所不同

Mucosal Associated Invariant T (MAIT) Cell Responses Differ by Sex in COVID-19

来源：biorxiv

发布时间：2020-12-01

链接：https://www.biorxiv.org/content/10.1101/2020.12.01.407148v1

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中文摘要：

免疫反应的性别差异对 COVID-19 病人的结局有影响，但是造成这种差异的机制我们了解得并不完全。

作者们对确诊的住院病人以及门诊病人、没有感染的密接、以及健康人进行性别平衡的采样，对他们的 PBMC 细胞进行了 36 色流式细胞分析以及单细胞 RNA 测序。作者们的研究结果显示在感染的女性中，循环的黏膜相关恒定 T 细胞显著降低。整合已发表的 COVID-19 气道组织数据，提示这个降低代表了在女性中感染早期黏膜相关恒定 T 细胞的渗出。该研究还显示女性中黏膜相关恒定 T 细胞呈现出免疫活化基因信号，而男性表现出促凋亡信号，可能提示女性为什么对 COVID-19 更不易感。

表一：研究中病人样本信息

Table 1. Summary of Patient Demographics and Sample Information

Group		healthy	exposed	infected	hospitalized	total
Age mean ± SD (range)		39.70 ± 13.68 (25-61)	42.57 ± 13.93 (17-60)	36.73 ± 13.88 (20-65)	59.44 ± 15.11 (31-76)	42.84 ± 16.06 (17-76)
# subjects (F:M ratio)		n = 10 (5:5)	n = 7 (3:4)	n = 19 (8:11)	n = 9 (4:5)	n = 45 (20:25)
Race n (%)	African American	3 (30.00%)	0	1 (5.26%)	5 (55.56%)	9 (20.00%)
	Asian	0	1 (14.29%)	2 (10.53%)	0	3 (6.67%)
	White	7 (70.00%)	5 (71.42%)	16 (84.21%)	3 (33.33%)	31(68.89%)
	Others/ unknown	0	1 (14.29%)	0	1 (11.11%)	2 (4.44%)
Days since onset when enrolled mean ± SD (range)		N/A	15.17 ± 11.25 (5-33)	11.18 ± 4.30 (3-19)	8.25 ± 6.14 (1-18)	11.19 ± 6.73 (1-33)
# samples of flow cytometry (F:M ratio)		n = 10 (5:5)	n = 20 (9:11)	n = 44 (21:23)	n = 9 (4:5)	n = 83 (39:44)
# samples of scRNA-seq (F:M ratio)		n = 5 (F:M = 3:2)	n = 8 (F:M = 3:5)	n = 29 (F:M = 12:17)	n = 6 (F:M = 1:5)	n = 48 (F:M = 19:29)
Days since onset when samples collected mean ± SD (range)		N/A	26.94 ± 14.94 (5-61)	18.27 ± 8.44 (3-40)	8.25 ± 6.14 (1-18)	19.32 ± 11.44 (1-61)

Abstract:

Sexual dimorphisms in immune responses contribute to coronavirus disease 2019 (COVID-19) outcomes, yet the mechanisms governing this disparity remain

incompletely understood. We carried out sex-balanced sampling of peripheral blood mononuclear cells from confirmed COVID-19 inpatients and outpatients, uninfected close contacts, and healthy controls for 36-color flow cytometry and single cell RNA-sequencing.

Our results revealed a pronounced reduction of circulating mucosal associated invariant T (MAIT) cells in infected females. Integration of published COVID-19 airway tissue datasets implicate that this reduction represented a major wave of MAIT cell extravasation during early infection in females. Moreover, female MAIT cells possessed an immunologically active gene signature, whereas male counterparts were pro-apoptotic. Collectively, our findings uncover a female-specific protective MAIT profile, potentially shedding light on reduced COVID-19 susceptibility in females.

8. 无症状 SARS-CoV-2 感染中的高功能病毒特异性细胞免疫应答

Highly functional virus-specific cellular immune response in asymptomatic SARS-CoV-2 infection

来源： bioRxiv

发布时间：2020-11-27

链接：https://www.biorxiv.org/content/10.1101/2020.11.25.399139v1

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DOI 或 PUBMED ID：

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中文摘要：

病毒特异性 T 细胞清除病原体的功效涉及其抗病毒和炎性特征之间的良好平衡。清除 SARS-CoV-2 感染而无症状或疾病的个体中的 SARS-CoV-2 特异性 T 细胞可能显示出非病理性但具有保护性的特征。因此，我们在抗体血清转化后的不同时间点，比较了无症状个体（n = 85）和有症状 COVID-19 患者（n = 76）人群中 SARS-CoV-2 特异性 T 细胞的数量和功能。我们使用 ELISpot 分析法对与结构蛋白（M，NP 和 Spike）反应的 T 细胞进行了定量，并测量了细胞因子分泌的量（IL-2，IFN-γ，IL-4，IL-6，IL-1β，TNF-α）T 细胞活化后，以 SARS-CoV-2 肽库作为功能性读数，检测全血。有症状的和有症状的个体在恢复的早期对不同的 SARS-CoV-2 蛋白具有特异性的 T 细胞的频率相似。但是，**与有症状的个体相比，血液中 SARS-CoV-2 特异性 T 细胞活化后，我们发现无症状的 IFN-γ 和 IL-2 产生增加**。仅在无症状感染中，这与 IL-10 和促炎细胞因子（IL-6，TNF-α 和 IL-1β）的比例分泌有关，而 SARS-CoV-2 触发了炎症细胞因子的过度分泌。 有症状的个体中特定的 T 细胞活化。因此，无症状的 SARS-CoV-2 感染者的特征不是抗病毒免疫力弱。相反，它们产生了强大而功能强大的病毒特异性细胞免疫应答。它们诱导成比例产生 IL-10 的能力可能有助于减少病毒清除过程中的炎症事件。

Abstract:

The efficacy of virus-specific T cells in clearing pathogens involves a fine balance between their antiviral and inflammatory features. SARS-CoV-2-specific T cells in individuals who clear SARS-CoV-2 infection without symptoms or disease

could reveal non-pathological yet protective characteristics. We therefore compared the quantity and function of SARS-CoV-2-specific T cells in a cohort of asymptomatic individuals (n=85) with that of symptomatic COVID-19 patients (n=76), at different time points after antibody seroconversion. We quantified T cells reactive to structural proteins (M, NP and Spike) using ELISpot assays, and measured the magnitude of cytokine secretion (IL-2, IFN-γ, IL-4, IL-6, IL-1β, TNF-α and IL-10) in whole blood following T cell activation with SARS-CoV-2 peptide pools as a functional readout. Frequencies of T cells specific for the different SARS-CoV-2 proteins in the early phases of recovery were similar between asymptomatic and symptomatic individuals. However, we detected an increased IFN-γ and IL-2 production in asymptomatic compared to symptomatic individuals after activation of SARS-CoV-2-specific T cells in blood. This was associated with a proportional secretion of IL-10 and pro-inflammatory cytokines (IL-6, TNF-α and IL-1β) only in asymptomatic infection, while a disproportionate secretion of inflammatory cytokines was triggered by SARS-CoV-2-specific T cell activation in symptomatic individuals. Thus, asymptomatic SARS-CoV-2 infected individuals are not characterized by a weak antiviral immunity; on the contrary, they mount a robust and highly functional virus-specific cellular immune response. Their ability to induce a proportionate production of IL-10 might help to reduce inflammatory events during viral clearance.

9. COVID-19 感染后气道抗体迅速消失，但无论疾病严重程度如何均会产生 B 细胞记忆

Airway antibodies wane rapidly after COVID-19 but B cell memory is generated across disease severity

来源：medrxiv

发布时间：2020-11-29

链接：https://www.medrxiv.org/content/10.1101/2020.11.25.20238592v1

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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.11.25.20238592

编译者：刘焕珍

中文摘要：

了解 SARS-CoV-2 感染后的免疫反应与 COVID-19 严重程度的关系，对于预测长期免疫记忆对病毒传播的影响至关重要。在这里，我们纵向评估了系统和气道对 SARS-CoV-2 的免疫反应，该队列由 147 名感染者组成，代表了 COVID-19 的全部严重程度；从无症状感染到致命疾病。中重度患者全身和气道抗体反应较高，急性病后全身 IgG 水平维持不变，但气道 IgG 和 IgA 明显下降。相反，具有轻度症状的个体显示出明显较低的抗体反应，但其抗原特异性记忆 B 细胞的水平与中度至重度疾病患者中观察到的水平相当。这表明气道中的抗体可能无法维持在防止局部病毒再次接触时进入的水平，因此通过激活记忆 B 细胞池来保护病毒是至关重要的。

Abstract:

Understanding immune responses following SARS-CoV-2 infection in relation to COVID-19 severity is critical to predicting the effects of long-term

immunological memory on viral spread. Here we longitudinally assessed systemic and airway immune responses against SARS-CoV-2 in a well-characterized cohort of 147 infected individuals representing the full spectrum of COVID-19 severity; from asymptomatic infection to fatal disease. High systemic and airway antibody responses were elicited in patients with moderate to severe disease, and while systemic IgG levels were maintained after acute disease, airway IgG and IgA declined significantly. In contrast, individuals with mild symptoms showed significantly lower antibody responses but their levels of antigen-specific memory B cells were comparable with those observed in patients with moderate to severe disease. This suggests that antibodies in the airways may not be maintained at levels that prevent local virus entry upon re-exposure and therefore protection via activation of the memory B cell pool is critical.

10. COVID-19 患者的病毒表位分析显示交叉反应并与严重程度相关

Viral epitope profiling of COVID-19 patients reveals cross-reactivity and correlates of severity

来源：science

发布时间：2020-11-27

链接：https://science.sciencemag.org/content/370/6520/eabd4250

第一作者：Ellen Shrock

通讯作者：Stephen J. Elledge

通讯作者单位：美国哈佛医学院，美国马萨诸塞州病原体研究联合会

DOI 或 PUBMED ID：10.1126/science.abd4250

编译者：刘焕珍

中文摘要：

了解严重急性呼吸综合征冠状病毒 2 型（SARS-CoV-2）的体液反应对提高诊断、治疗和疫苗水平至关重要。使用 VirScan 对 232 名 COVID-19 患者和 190 名 COVID-19 之前时代对照者的血清学分析显示，SARS-CoV-2 蛋白质组中有 800 多个表位，包括 10 个可能通过中和抗体识别的表位。对照组中已有的抗体识别 SARS-CoV-2 ORF1，而只有 COVID-19 患者抗体主要识别刺突蛋白和核蛋白。一个基于 VirScan 数据训练的机器学习模型预测 SARS-CoV-2 暴露史，其敏感性和特异性分别为 99%和 98%；基于 Luminex 的快速诊断是从最具区分性的 SARS-CoV-2 肽发展而来的。严重 COVID-19 的个体表现出更强和更广泛的 SARS-CoV-2 反应，对先前感染的抗体反应较弱，巨细胞病毒和单纯疱疹病毒 1 的发病率更高，可能受人口统计学协变量的影响。在住院病人中，男性比女性产生更强的 SARS-CoV-2 抗体反应。

Abstract:

Understanding humoral responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is critical for improving diagnostics, therapeutics, and vaccines. Deep serological profiling of 232 coronavirus disease 2019 (COVID-19) patients and 190 pre–COVID-19 era controls using VirScan revealed more than 800 epitopes in the SARS-CoV-2 proteome, including 10 epitopes likely recognized by neutralizing antibodies. Preexisting antibodies in controls recognized SARS-CoV-2 ORF1, whereas only COVID-19 patient antibodies primarily recognized spike protein and nucleoprotein. A machine learning model trained on VirScan data predicted SARS-CoV-2 exposure history with 99% sensitivity and 98% specificity;

a rapid Luminex-based diagnostic was developed from the most discriminatory SARSCoV-2 peptides. Individuals with more severe COVID-19 exhibited stronger and broader SARS-CoV-2 responses, weaker antibody responses to prior infections, and higher incidence of cytomegalovirus and herpes simplex virus 1, possibly influenced by demographic covariates. Among hospitalized patients, males produce stronger SARS-CoV-2 antibody responses than females.

11. 新冠病毒 COVID-19 感染的重症患者 T 细胞和特异性抗体之间功能关联

T cell and antibody functional correlates of severe COVID-19

来源：MedRxiv

发布时间：2020-11-23

链接：https://www.medrxiv.org/content/10.1101/2020.11.25.20235150v1

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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.11.25.20235150

编译者：姜连连

中文摘要：

有基础疾病的人群，如肥胖和糖尿病，感染新冠病毒 COVID-19 后住院和死亡风险会更高。而患有基础疾病的人群在感染新冠病毒后的免疫系统做何种调整呢？利用多参数流式技术和系统血清学方法全面展示新冠康复患者体内 T 细胞和病毒 Spike 蛋白，核衣壳蛋白及膜蛋白相关抗体的变化情况。这些患者中有 20 人曾接受过住院治疗，40 人为门诊病例。将这些患者按年龄，性别，种族和症状出现时间进行归类分析。结果发现：住院治疗患者，尤其是慢性疾病患者体内病毒特异性 CD4+T 细胞和抗体反应的高度和功能广泛性始终表现出较高水平。但是，综合分析数据显示门诊治疗患者体内检测出多功能 CD4+T 细胞和 spike 蛋白 S1 特异性抗体的协调性更好，此数据表明基础疾病患者体内 T 细胞和新冠病毒特异性抗体的功能多样性和协调性降低，从而感染新冠后临床症状会更严重。该研究数据也表明在高风险人群中若仅检测 spike 蛋白特异性免疫反应高低可能无法全面评估疫苗免疫保护效果。

Abstract:

Comorbid medical illnesses, such as obesity and diabetes, are associated with more severe COVID-19, hospitalization, and death. However, the role of the immune system in mediating these clinical outcomes has not been determined. We used multi-parameter flow cytometry and systems serology to comprehensively profile the functions of T cells and antibodies targeting spike, nucleocapsid, and envelope proteins in a convalescent cohort of COVID-19 subjects who were either hospitalized (n=20) or not hospitalized (n=40). To avoid confounding, subjects were matched by age, sex, ethnicity, and date of symptom onset. Surprisingly, we found that the magnitude and functional breadth of virus-specific CD4 T cell and antibody responses were consistently higher among hospitalized subjects, particularly those with medical comorbidities. However, an integrated analysis identified more coordination between polyfunctional CD4 T-cells and antibodies targeting the S1 domain of spike among subjects that were not hospitalized. These data reveal a functionally diverse and coordinated response between T cells and antibodies targeting SARS-CoV-2 which is reduced in the presence of comorbid

illnesses that are known risk factors for severe COVID-19. Our data suggest that isolated measurements of the magnitudes of spike-specific immune responses are likely insufficient to anticipate vaccine efficacy in high-risk populations.

12. 冠状病毒和其他病原体共享的 B 细胞记忆在人类各年龄组和组织中有所不同

Shared B cell memory to coronaviruses and other pathogens varies in human age groups and tissues

来源：biorxiv

发布时间：2020.12.02

文章链接：https://www.biorxiv.org/content/10.1101/2020.12.01.407015v1

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doi: https://doi.org/10.1101/2020.12.01.407015

编译者：张怡

摘要

疫苗接种和感染促进编码体液免疫记忆的 B 细胞的形成，组织分布和克隆进化。研究者们评估了在儿童和成人血液以及死亡器官供体组织中共享的相似序列的趋同抗原特异性抗体基因。B 细胞的记忆在不同病原体中不一样。多糖抗原特异性克隆不只存在于脾脏中。成人的趋同克隆通常在血液中表达突变的 IgM 和 IgD，并在淋巴组织中发生类别转换。相比之下，儿童在血液会出现许多类别转换的趋同克隆。跟血清学报告一致，大流行前的儿童对将趋同克隆转变为 SARS-CoV-2，在季节性冠状病毒的交叉反应性克隆中富集，而成人的血液或淋巴组织中很少有这样的克隆。这些结果扩展了我们对关于人类体液特异性病原免疫和年龄以及解剖定位相关的认知。

Vaccination and infection promote the formation, tissue distribution, and clonal evolution of B cells encoding humoral immune memory. We evaluated convergent antigen-specific antibody genes of similar sequences shared between individuals in pediatric and adult blood, and deceased organ donor tissues. B cell memory varied for different pathogens. Polysaccharide antigen-specific clones were not exclusive to the spleen. Convergent clones in adults often express mutated IgM or IgD in blood and are class-switched in lymphoid tissues; in contrast, children have abundant class-switched convergent clones in blood. Consistent with serological reports, pre-pandemic children had class-switched convergent clones to SARS-CoV-2, enriched in cross-reactive clones for seasonal coronaviruses, while adults showed few such clones in blood or lymphoid tissues. These results extend age-related and anatomical mapping of human humoral pathogen-specific immunity.

13. 土耳其宣布本月开始接种中国新冠疫苗 将分四阶段进行

https://feeds.cloud.huawei.com/landingpage/latest?docid=1051054ucms_81uCCkpWSoi&to_app=hwbrowser&dy_scenario=today1&tn=a2ac05aa2ad69ba97ea228fb6af9077899cae24f94f3f11b2fa907f8d5049105&share_to=weixinmoments&channel=HW_TRENDING&ctype=news&appid=hwbrowser&cpid=666

14. 辉瑞/BioNTech 新冠疫苗在英国率先获得紧急使用授权

医药魔方公众号：https://mp.weixin.qq.com/s/xe970yi3KzawLPpRx1GtEA

摘要:12 月 2 日，辉瑞/BioNTech 宣布英国药品和健康产品管理局（MHRA）给予其 mRNA 新冠疫苗 BNT162b2 紧急使用临时授权（temporary authorization），这是全球首个给予 BNT162b2 紧急使用授权的国家。辉瑞/BioNTech 表示未来几天至几周，有望在全球更多国家获得紧急使用授权，双方也已经做好了疫苗供应准备。

PFIZER AND BIONTECH ACHIEVE FIRST AUTHORIZATION IN THE WORLD FOR A VACCINE TO COMBAT COVID-19

Link: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-achieve-first-authorization-world

15. Moderna 今日(2020-11-30 日)将向美国 FDA 申请新冠 mRNA 疫苗紧急使用授权！

来源：即刻药闻

发布时间：2020-11-30

链接：

https://www.wuximediatech.com/content/post/detail.html?sn=08c6bee427f94310bbee67005d95b9ed&from=wechat

作者：药明康德内容团队

作者单位：药明康德

编译者：张丽双

中文摘要：

11 月 30 日，Moderna 公司宣布，其开展的 mRNA-1273 新冠疫苗 3 期临床试验中 196 例出现症状的 COVID-19 病例主要疗效分析表明该疫苗有效率为 94.1%，确证了第一次中期分析时观察到的高疗效。安全性数据得到积累，研究继续由美国国立卫生研究院（NIH）任命的独立数据安全监测委员会（DSMB）监测。公司同时宣布，今日计划向美国 FDA 申请紧急使用授权（EUA），并向欧洲药品管理局（EMA）申请有条件批准。

16. 英国、南非实验数据可能成为美国 Novavax 公司寻求新冠疫苗紧急使用授权的备选方案

U.K., South African data backup plan for Novavax in U.S.

来源：BioCentury

发布时间：2020-12-01

链接：https://www.biocentury.com/article/632317

第一作者：STEVE USDIN 编辑

通讯作者：

通讯作者单位：

DOI 或 PUBMED ID：

编译者：孔娟

中文摘要：

美国对 Novavax 新冠肺炎候选疫苗的第三阶段试验启动推迟，意味着它可能不得不依赖英国和南非试验的数据来寻求在美国的紧急使用授权。目前 Novavax 已完成英国 III 期试验和南非 IIb 期新冠肺炎疫苗招募工作，共有 15000 名参与者参与了英国的 NVX-cov 2373 III 期试验。在南非进行的 4442 人的 IIb 期试验有 245 名 HIV 阳性参与者，该试验可能在下个季度完成。Novavax 周一表示，最初计划于 10 月在美国和墨西哥启动的、由 3 万人的 NVX-cov 2373 III 期试验将在未来数周内启动。如果无法完成美国的 III 期试验，Glenn 说，

Novavax 可以用英国和南非的试验数据“整理出一个非常有说服力的方案”。
编者注：这是一款重组蛋白疫苗
Abstract：
A delay in starting the U.S. Phase III trial for its COVID-19 vaccine candidate means Novavax may have to rely on data from U.K. and South African trials to seek emergency use authorization in the U.S. A total of 15,000 participants have enrolled in the U.K. Phase III trial of NVX-CoV2373. The trial was designed to align with FDA requirements and could support approval in the U.K., by EMA and by other regulators, Gregory Glenn, president for R&D at Novavax Inc. (NASDAQ:NVAX), told BioCentury. Glenn said Novavax has not determined how long it would take after it receives interim data from the U.K. trial to submit a request to FDA for an EUA, but “other companies have been able to pivot quicky from getting data to applying for an EUA .” The 4,442-person Phase IIb trial in South Africa, which includes 245 HIV-positive participants, may be completed next quarter, Glenn said. The 30,000-person Operation Warp Speed-supported Phase III trial of NVX-CoV2373, originally slated to start in the U.S. and Mexico in October, will start in the coming weeks, Novavax said Monday. If it becomes impossible to complete the U.S. Phase III trial, Glenn said Novavax “can put together a very compelling package” with trial data from the U.K. and South Africa.

17. 单剂量减毒黄热病病毒 YF17D 载体 SARS-CoV-2 疫苗候选

A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate
来源：Nature
发布时间：2020-12-1
链接：https://www.nature.com/articles/s41586-020-3035-9
第一作者：Lorena Sanchez-Felipe, Thomas Vercruysse, Sapna Sharma, Ji Ma, Viktor Lemmens, Dominique Van Looveren, Mahadesh Prasad Arkalagud Javarappa, Robbert Boudewijns, Bert Malengier-Devlies, Laurens Liesenborghs
通讯作者：Johan Neyts，Hendrik Jan Thibaut，Kai Dallmeier
通讯作者单位：比利时鲁汶 BE-3000 研究所、美国马里兰州全球病毒网络 GVN
DOI 或 PUBMED ID：https://doi.org/10.1038/s41586-020-3035-9
编译者：张丽双
中文摘要：
研究人员描述了一种以黄热病 17D(YF17D)疫苗为载体，表达 SARS-CoV-2 刺突蛋白抗原的非可清除预灌注形式的 SARS-CoV-2 活疫苗候选物的发现。在几种动物模型中评估疫苗的安全性、免疫原性和有效性。候选疫苗 YF-S0 具有突出的安全性，可在仓鼠、小鼠和恒河猴体内诱导高水平的 SARS-CoV-2 中和抗体，同时对 YFV 产生保护性免疫。体液免疫是由一个有利的 Th1 细胞介导的免疫反应所补充的。在严格的仓鼠模型和非人类灵长类动物模型中，YF-S0 可防止感染 SARS-CoV-2。此外，在仓鼠身上，单次给药可以使大多数接种疫苗的动物在 10 天内免受肺部疾病的侵袭。总的来说，免疫反应的质量和快速的动力学使保护性免疫在单次给药后就可以建立起来，这为进一步开发这种有效的 SARS-CoV-2 疫苗候选人提供了依据。
Abstract:

The explosively expanding COVID-19 pandemic urges the development of safe, efficacious and fast-acting vaccines. Several vaccine platforms are leveraged for a rapid emergency response. We describe the discovery of a live virus-vectored SARS-CoV-2 vaccine candidate using the yellow fever 17D (YF17D) vaccine as vector to express a non-cleavable prefusion form of the SARS-CoV-2 Spike antigen. We assess vaccine safety, immunogenicity and efficacy in several animal models. Vaccine candidate YF-S0 has an outstanding safety profile and induces high levels of SARS-CoV-2 neutralizing antibodies in hamsters, mice and cynomolgus macaques and concomitantly a protective immunity against YFV. Humoral immunity is complemented by a favourable Th1 cell-mediated immune response as profiled in mice. In a stringent hamster model as well as in non-human primates, YF-S0 prevents infection with SARS-CoV-2. Moreover, in hamsters, a single dose confers protection from lung disease in most vaccinated animals within 10 days. Taken together, the quality of immune responses triggered and the rapid kinetics by which protective immunity can be mounted already after a single dose warrant further development this potent SARS-CoV-2 vaccine candidate.

18. 设计的蛋白质将抗体组装成模块化的纳米胶囊

Designed proteins assemble antibodies into modular nanocages

来源：bioRxiv

发布时间：2020-12-01

链接：https://www.biorxiv.org/content/10.1101/2020.12.01.406611v1

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编译者：孔娟

中文摘要：

抗体在生物学和医学中有着广泛的应用，人们对多价抗体形式产生了极大的兴趣，以提高结合亲和力并增强信号通路中的激动作用。然而，目前尚无通用方法来形成具有受控化合价的精确定向的抗体组装体。文中研究者描述了通过结合形式和功能克服了这一限制的两组分纳米胶囊的计算设计。一种结构成分是任何抗体或 Fc 融合体，第二种是设计的 Fc 结合同源低聚物，可驱动纳米胶囊的组装。通过电子显微镜确定的跨越二面体、四面体、八面体和二十面体架构的 8 个抗体纳米胶囊的结构与相应的计算模型匹配，每个纳米胶囊有 2、6、12 和 30 个抗体。与游离抗体或 Fc 融合相比，靶向细胞表面受体的抗体纳米胶囊在 DR5 介导的凋亡，Tie2 介导的血管生成，CD40 活化和 T 细胞增殖中增强了信号传导。纳米胶囊的组装还增加了 α-SARS-CoV-2 单克隆抗体和 Fc-ACE2 融合蛋白对 SARS-CoV-2 假病毒中和。我们预计，在不需要共价修饰的情况下，将任意抗体组装成具有不同几何形状和价态的高度有序组装体的能力将在生物学和医学中产生广泛影响。

Abstract

Antibodies are widely used in biology and medicine, and there has been considerable interest in multivalent antibody formats to increase binding avidity and enhance signaling pathway agonism. However, there are currently no general

approaches for forming precisely oriented antibody assemblies with controlled valency. We describe the computational design of two-component nanocages that overcome this limitation by uniting form and function. One structural component is any antibody or Fc fusion and the second is a designed Fc-binding homo-oligomer that drives nanocage assembly. Structures of 8 antibody nanocages determined by electron microscopy spanning dihedral, tetrahedral, octahedral, and icosahedral architectures with 2, 6, 12, and 30 antibodies per nanocage match the corresponding computational models. Antibody nanocages targeting cell-surface receptors enhance signaling compared to free antibodies or Fc-fusions in DR5-mediated apoptosis, Tie2-mediated angiogenesis, CD40 activation, and T cell proliferation; nanocage assembly also increases SARS-CoV-2 pseudovirus neutralization by α-SARS-CoV-2 monoclonal antibodies and Fc-ACE2 fusion proteins. We anticipate that the ability to assemble arbitrary antibodies without need for covalent modification into highly ordered assemblies with different geometries and valencies will have broad impact in biology and medicine.

19. 中和抗体结合光热纳米颗粒捕获并灭活 SARS-CoV-2

A Neutralizing Antibody-Conjugated Photothermal Nanoparticle Captures and Inactivates SARS-CoV-2

来源： bioRxiv

发布时间：2020-11-30

链接：https://www.biorxiv.org/content/10.1101/2020.11.30.404624v1

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编译者：张鹏伟

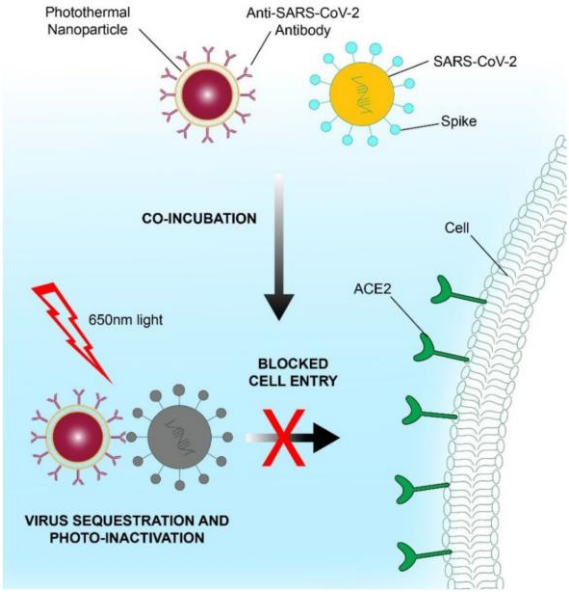
中文摘要：

在这里，我们报告了一种策略，该策略结合了偶联在光热纳米颗粒表面的中和抗体以主动捕获和灭活 SARS-CoV-2。光热纳米粒子由半导体聚合物核和装饰有中和抗体的生物相容性聚乙二醇表面组成。此类纳米粒子显示出有效捕获 SARS-CoV-2 假病毒，出色的光热效应，并通过同时阻断和灭活病毒来完全抑制病毒进入表达 ACE2 的宿主细胞。这种光热纳米粒子是一个灵活的平台，可以轻松适应其他 SARS-CoV-2 抗体，并扩展到新型治疗性蛋白质，从而提供了针对多种 SARS-CoV-2 菌株的广泛保护。

Abstract:

The outbreak of 2019 coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in a global pandemic. Despite intensive research including several clinical trials, currently there are no completely safe or effective therapeutics to cure the disease. Here we report a strategy incorporating neutralizing antibodies conjugated on the surface of a photothermal nanoparticle to actively capture and inactivate SARS-CoV-2. The photothermal nanoparticle is comprised of a semiconducting polymer core and a biocompatible polyethylene glycol surface decorated with neutralizing

antibodies. Such nanoparticles displayed efficient capture of SARS-CoV-2 pseudoviruses, excellent photothermal effect, and complete inhibition of viral entry into ACE2-expressing host cells via simultaneous blocking and inactivating of the virus. This photothermal nanoparticle is a flexible platform that can be readily adapted to other SARS-CoV-2 antibodies and extended to novel therapeutic proteins, thus providing a broad range of protection against multiple strains of SARS-CoV-2.



20. 双抗体混合物 REGN-COV2 可在恒河猴和仓鼠体内有效预防和治疗新冠病毒感染

REGN-COV2 antibodies prevent and treat SARS-CoV-2 infection in rhesus macaques and hamsters

来源：Science

发布时间：2020-11-27

链接：https://science.sciencemag.org/content/370/6520/1110

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DOI 或 PUBMED ID：10.1126/science.abe240

编译者：姜连连

中文摘要：

当前新冠病毒大规模流行，全球都在紧急寻求新型冠状病毒肺炎有效的预防和治疗方案。REGN-COV2 是由两种针对新冠病毒(SARS-CoV-2)Spike 蛋白中和性抗体(REGN10987 and REGN10933)所组成的混合型抗体。这两种抗体可以特异性结合 Spike 蛋白的受体结合区域（RBD）且无交叉性。本研究选择用来研究温和性疾病模式动物恒河猴和用来研究重型疾病模式动物金黄仓鼠，分别评估上述混合型抗体的体内保护效果。研究发现：在预防和保护性试验中，该抗体混合物均可以大大降低恒河猴呼吸道内的病毒载量和缓解病毒造成的病例损伤。同样，金黄仓鼠在注射抗体后，体重出现回升同时肺炎症状得以缓解且肺部病毒滴度降低。该研究结果进一步证明此抗体混合物可作为新冠肺炎的治疗性候选抗体。

Abstract:

An urgent global quest for effective therapies to prevent and treat coronavirus disease 2019 (COVID-19) is ongoing. We previously described REGN-COV2, a cocktail of two potent neutralizing antibodies (REGN10987 and REGN10933) that targets nonoverlapping epitopes on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein. In this report, we evaluate the in vivo efficacy of this antibody cocktail in both rhesus macaques, which may model mild disease, and golden hamsters, which may model more severe disease. We demonstrate that REGN-COV-2 can greatly reduce virus load in the lower and upper airways and decrease virus-induced pathological sequelae when administered prophylactically or therapeutically in rhesus macaques. Similarly, administration in hamsters limits weight loss and decreases lung titers and evidence of pneumonia in the lungs. Our results provide evidence of the therapeutic potential of this antibody cocktail.

21. 拓扑异构酶 1 抑制剂治疗对 SARS-CoV-2 诱导的炎症和死亡的保护作用

Topoisomerase 1 inhibition therapy protects against SARS-CoV-2-induced inflammation and death in animal models

来源：biorxiv

发布时间：2020-12-01

链接：https://www.biorxiv.org/content/10.1101/2020.12.01.404483v1

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DOI 或 PUBMED ID：

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中文摘要：

由 SARS-CoV-2 引起的持续大流行目前正在影响全世界数百万人的生命。大量回顾性研究表明，炎症细胞因子和促炎因子水平的升高与疾病严重程度和死亡率的增加有关。该研究通过多维表观遗传、转录、体外和体内分析发现拓扑异构酶 1（Top1）抑制剂能够抑制 SARS-CoV-2 诱导的致死性炎症。两种剂量的 Topotecan（TPT，是 FDA 批准的 Top1 抑制剂，是一种肿瘤药物），可抑制仓鼠感染性炎症。在转基因小鼠模型中，在感染后 4 天进行 TPT 治疗可降低发病率和挽救死亡率。这些结果支持 Top1 抑制剂作为一种有效的宿主导向治疗 SARS-CoV-2 感染的潜力。TPT 及其衍生物在大多数国家都是廉价的临床级抑制剂。需要进行临床试验来评估将 Top1 抑制剂用于人类 COVID-19 的疗效。

Abstract:

The ongoing pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is currently affecting millions of lives worldwide. Large retrospective studies indicate that an elevated level of inflammatory cytokines and pro-inflammatory factors are associated with both increased disease severity and mortality. Here, using multidimensional epigenetic, transcriptional, in vitro and in vivo analyses, we report that Topoisomerase 1 (Top1) inhibition suppresses

lethal inflammation induced by SARS-CoV-2. Therapeutic treatment with two doses of Topotecan (TPT), a FDA-approved Top1 inhibitor, suppresses infection-induced inflammation in hamsters. TPT treatment as late as four days post-infection reduces morbidity and rescues mortality in a transgenic mouse model. These results support the potential of Top1 inhibition as an effective host-directed therapy against severe SARS-CoV-2 infection. TPT and its derivatives are inexpensive clinical-grade inhibitors available in most countries. Clinical trials are needed to evaluate the efficacy of repurposing Top1 inhibitors for COVID-19 in humans.

22. 处于临床试验阶段的核酸类似物流感药物 MK-4482/EIDD-2801 可阻断雪貂的 SARS-CoV-2 传播

Therapeutically administered ribonucleoside analogue MK-4482/EIDD-2801 blocks SARS-CoV-2 transmission in ferrets

来源：nature microbiology

发布时间：2020-12-03

链接：https://www.nature.com/articles/s41564-020-00835-2

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中文摘要：

流感药物再利用可阻断雪貂的 SARS-CoV-2 传播 |《自然-微生物学》论文

自然科研公众号：https://mp.weixin.qq.com/s/jM9UQ5_CWWI8Z_fL095KYQ

Abstract:

The coronavirus disease 2019 (COVID-19) pandemic is having a catastrophic impact on human health1. Widespread community transmission has triggered stringent distancing measures with severe socio-economic consequences. Gaining control of the pandemic will depend on the interruption of transmission chains until vaccine-induced or naturally acquired protective herd immunity arises. However, approved antiviral treatments such as remdesivir and reconvalescent serum cannot be delivered orally , making them poorly suitable for transmission control. We previously reported the development of an orally efficacious ribonucleoside analogue inhibitor of influenza viruses, MK-4482/EIDD-2801, that was repurposed for use against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is currently in phase II/III clinical trials (NCT04405570 and NCT04405739). Here, we explored the efficacy of therapeutically administered MK-4482/EIDD-2801 to mitigate SARS-CoV-2 infection and block transmission in the ferret model, given that ferrets and related members of the weasel genus transmit the virus efficiently with minimal clinical signs , which resembles the spread in the human young-adult population. We demonstrate high SARS-CoV-2 burden in nasal tissues and secretions, which coincided with efficient transmission through direct contact. Therapeutic treatment of infected animals with MK-4482/EIDD-2801 twice a day significantly reduced the SARS-CoV-2 load in the upper respiratory tract and completely suppressed spread to untreated contact animals. This study

identified oral MK-4482/EIDD-2801 as a promising antiviral countermeasure to break SARS-CoV-2 community transmission chains.

23. 未接触 SARS-CoV-2 的个体和 COVID-19 重症患者 CD4+T 细胞对 SARS-CoV-2 的低亲和力反应

Low avidity CD4+ T cell responses to SARS-CoV-2 in unexposed individuals and humans with severe COVID-19

来源：Immunity

发布时间：2020-11-26

链接：https://www.cell.com/immunity/fulltext/S1074-7613(20)30503-3

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DOI 或 PUBMED ID：

编译者：王玮

DOI 或 PUBMED ID：https://doi.org/10.1016/j.immuni.2020.11.016

中文摘要：

对 SARS-CoV-2 有反应的 CD4+T 细胞存在于未暴露的个体中，这些细胞被认为是对普通感冒冠状病毒（CCCoVs）感染的反应。该研究利用 SARS-CoV-2 反应性 CD4+T 细胞富集来检测这些细胞的抗原亲和力和克隆性，以及 CCCoV 交叉反应的相对贡献。SARS-CoV-2 反应性 CD4+记忆性 T 细胞几乎在所有未暴露的个体中都存在，表现出低功能亲和力和多重、高度可变的交叉反应性，并不局限于 CCCoV。尽管 COVID-19 患者对 CCCoV 有较强记忆性的 T 细胞对 CCCoV 有较强的记忆反应，但 COVID-19 患者的 SARS-CoV-2 反应性 CD4+T 细胞缺乏交叉反应性。在重症 COVID-19 患者中，SARS-CoV-2 特异性 T 细胞表现出较低的功能亲和力和克隆性，尽管频率增加。该研究发现低亲和力 CD4+T 细胞反应是 COVID-19 重症的标志，质疑了 CCCoV 反应性 T 细胞在 SARS-CoV-2 感染中的保护作用。

Abstract:

CD4+ T cells reactive against SARS-CoV-2 can be found in unexposed individuals and these are suggested to arise in response to common cold corona viruses (CCCoVs) infection. Here, we utilized SARS-CoV-2-reactive CD4+ T cell enrichment to examine the antigen-avidity and clonality of these cells, as well as the relative contribution of CCCoV cross-reactivity. SARS-CoV-2-reactive CD4+ memory T-cells were present in virtually all unexposed individuals examined, displaying low functional avidity and multiple, highly variable cross-reactivities that were not restricted to CCCoVs. SARS-CoV-2 reactive CD4+ T cells from COVID-19 patients lacked cross-reactivity to CCCoVs, irrespective of strong memory T-cell responses against CCCoV in all donors analysed. In severe but not mild COVID-19, SARS-CoV-2-specific T-cells displayed low functional avidity and clonality, despite increased frequencies. Our findings identify low avidity CD4+T cell responses as a hallmark of severe COVID-19, and argue against a protective role for CCCoV reactive T cells in SARS-CoV-2 infection.

24. 基因组 RNA 原件驱动了 SARS-CoV-2 核衣壳蛋白的相分离

Genomic RNA elements drive phase separation of the SARS-CoV-2 nucleocapsid
来源：medrxiv
发布时间：2020-11-26
链接:https://www.cell.com/molecular-cell/fulltext/S1097-2765(20)30841-8
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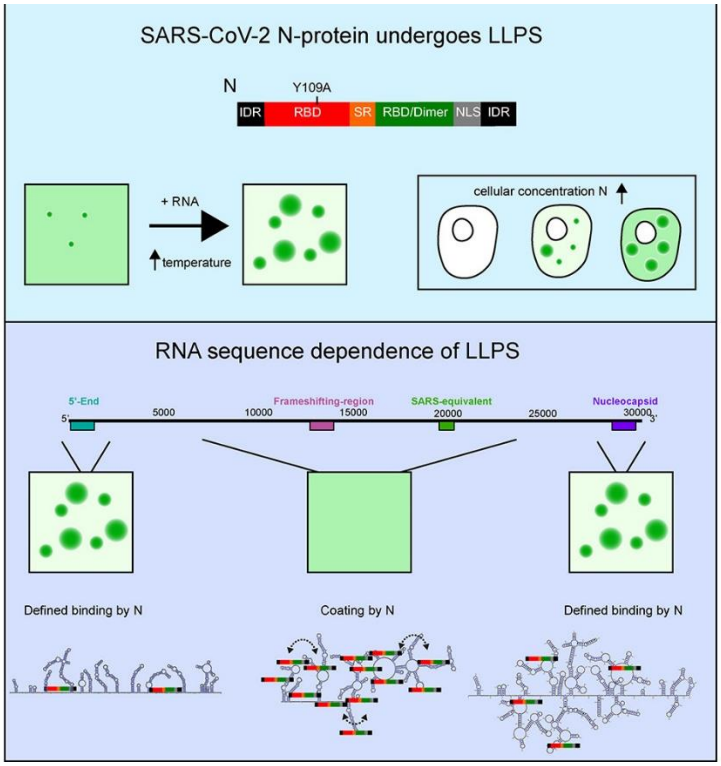
DOI：https://doi.org/10.1016/j.molcel.2020.11.041
编译者：蒋立春



亮点

病毒基因组 RNA 可以在人体体温发生相分离

相分离受特定基因组 RNA 元件驱动

受体结合区域 RBD 突变的 N 蛋白不能进行液-液相分离；和 RNA 的结合发生了改变；N 蛋白在细胞中形成液体样微滴

总结

SARS-CoV-2 的核衣壳 N 蛋白和病毒 RNA 发生液-液相分离。N 蛋白可以和特定的 RNA 基因组元件在生理条件下发生聚集。体温（33° C 和 37° C）聚集比室温（22° C）程度更高。在病毒基因组的特定区域的 RNA 序列和结构调控 N 蛋白的聚集，而基因组其他区域促进聚集的解离可能起到防止基因组发生大范围聚集。低浓度情况下，N 蛋白有选择性地和周边有结构的单链 RNA 发生交联，这些特征决定了和 N 蛋白结合位点的强度，位置以及结合位点的个数。N 蛋白在哺乳动物中形成液体样聚合物，这个过程是浓度依赖的，可以被小分子干预。这个过程可以用来筛选抗 SARS-CoV-2 病毒的药物。

Highlights

Phase separation occurs with the viral genome (gRNA) and at human body temperature.

Phase separation is driven by specific elements in gRNA.

RBD mutant N-protein fails to undergo LLPS; exhibits altered RNA crosslinking. N-protein forms liquid-like droplets in cells.

Summary

We report that the SARS-CoV-2 nucleocapsid protein (N-protein) undergoes liquid-liquid phase separation (LLPS) with viral RNA. N-protein condenses with specific RNA genomic elements under physiological buffer conditions and condensation is enhanced at human body temperatures (33° C and 37° C) and reduced at room temperature (22° C). RNA sequence and structure in specific genomic regions regulate N-protein condensation while other genomic regions promote condensate dissolution, potentially preventing aggregation of the large genome. At low concentrations, N-protein preferentially crosslinks to specific regions with single-stranded RNA flanked by structure and these features specify the location, number, and strength of N-protein binding sites (valency). Liquid-like N-protein condensates form in mammalian cells in a concentration-dependent manner and can be altered by small molecules. Condensation of N-protein is RNA sequence and structure specific, sensitive to human body temperature, and manipulatable with small molecules, and presents a screenable process for identifying antiviral compounds effective against SARS-CoV-2.

25. 对一种先进候选疫苗中的全长 SARS-CoV-2 Spike 蛋白的结构分析

Structural analysis of full-length SARS-CoV-2 spike protein from an advanced vaccine candidate

10月23日第9条报道过该工作的预印本,该工作研究对象是Novavax公司的重组蛋白疫苗。

链接：https://science.sciencemag.org/content/370/6520/1089

26. 从 3 维角度看 COVID-19 疫情流行的前六个月中 SARS-CoV-2 病毒的蛋白质组的进化

Evolution of the SARS-CoV-2 proteome in three dimensions (3D) during the first six months of the COVID-19 pandemic

来源：bioRxiv

发布时间：2020-12-01

链接：https://www.biorxiv.org/content/10.1101/2020.12.01.406637v1

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编译者：宋珂

中文摘要：

利用 PDB 数据库中存储的 SARS-CoV-2 和其他冠状病毒蛋白的三维结构数据，作者分析了 COVID-19 疫情流行的前六个月中病毒蛋白质组的进化情况。通过对超过 48,000 个病毒的蛋白质组序列中发现的氨基酸发生变化的空间位置,化学性质以及对结构和能量的影响进行分析，揭示了在 29 种病毒研究蛋白中，每一种蛋白的氨基酸变化是如何发生的。对每种非冗余的突变序列进行的计算结构建模显示，大多数替换发生在蛋白质的表面和边界层，对

疏水核心的影响很小。与边界层/表面相比，蛋白核心中发现保守变化的频率更高。活性位点和蛋白-蛋白界面发生替换的情况很少。通过能量计算表明，替换对蛋白质热力学稳定性的影响遵循通用的双高斯分布。作者还详细介绍了六个药物发现靶点以及四个构成病毒体的结构蛋白的结果，强调了那些可能影响蛋白质结构，酶活性和功能界面的替换。从三维结构上表征病毒的进化，提供了可供验证的对病毒蛋白功能的理解，并对基于结构的药物发现工作以及对具有耐药可能的氨基酸替换的前瞻性鉴定提供了辅助。

Abstract:
Three-dimensional structures of SARS-CoV-2 and other coronaviral proteins archived in the Protein Data Bank were used to analyze viral proteome evolution during the first six months of the COVID-19 pandemic. Analyses of spatial locations, chemical properties, and structural and energetic impacts of the observed amino acid changes in >48,000 viral proteome sequences showed how each one of the 29 viral study proteins have undergone amino acid changes. Structural models computed for every unique sequence variant revealed that most substitutions map to protein surfaces and boundary layers with a minority affecting hydrophobic cores. Conservative changes were observed more frequently in cores versus boundary layers/surfaces. Active sites and protein-protein interfaces showed modest numbers of substitutions. Energetics calculations showed that the impact of substitutions on the thermodynamic stability of the proteome follows a universal bi-Gaussian distribution. Detailed results are presented for six drug discovery targets and four structural proteins comprising the virion, highlighting substitutions with the potential to impact protein structure, enzyme activity, and functional interfaces. Characterizing the evolution of the virus in three dimensions provides testable insights into viral protein function and should aid in structure-based drug discovery efforts as well as the prospective identification of amino acid substitutions with potential for drug resistance.

27. COVID-19 和结核病之间转录组疾病风险和诊断生物标志物重叠的系统评估：患者水平的荟萃分析

Systematic evaluation of transcriptomic disease risk and diagnostic biomarker overlap between COVID-19 and tuberculosis: a patient-level meta-analysis

来源：medRxiv

发布时间：2020-11-26

链接：https://www.medrxiv.org/content/10.1101/2020.11.25.20236646v1

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DOI 或 PUBMED ID：Preprint

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中文摘要：

背景：新型冠状病毒 SARS-CoV-2 增加了本已因结核病高发而紧张的卫生保健系统的负担，因为共感染和双重表现正在同时发生。我们的目的是通过分析结核病感染者 RNA 测序数据上的 COVID-19 基因表达特征来了解这些疾病之间的相互作用。

方法：通过检索 PubMed 和预印本服务器，我们进行了系统回顾和患者水平的荟萃分析，以从人类全血(WB)、PBMCs 或 BALF 研究中获得符合条件的 COVID-19 基因表达信号。WB 流感数据集作为呼吸道疾病的对照组。我们选择了三个大型的结核病 RNA-seq 数据集来分析这些特征，这些数据集包括来自英国和非洲的多个队列以及不同病谱的结核病患者。使用 TBSignatureProfiler 软件包为结核病数据集中的每个样本生成假定的“COVID-19 风险评分”。在进展期患者与接触肺部和肺外结核病的患者中，风险按诊断时间分层。对结核病和 COVID-19 单细胞 RNA-seq 数据进行整合分析，并进行群体水平荟萃分析，以鉴定疾病之间的共有基因本体及其在 COVID-19 疾病严重程度方面的相对丰富度。

结果：根据来自 853 个个体的 1181 个样本的 TB RNA-seq 数据，从 9 个符合条件的研究，98 个样本中对 35 个 COVID-19 基因标记进行了分析。与潜伏性结核感染相比，在活动性结核病(ATB)中，有 25 个特征有显著的高 COVID-19 风险 ($p < 0·005$)，其中 13 个特征在两个独立数据集中得到验证。在 ATB 期间，在循环中发现表达 FCN1-和 SPP1 的巨噬细胞在严重 COVID-19 期间富集在 BALF 中。共有的扰动本体包括抗原呈递、表观遗传调控、血小板活化和 ROS/RNS 的产生，这些都随着 COVID-19 严重程度的增加而富集。最后，我们证明重叠的转录反应可能会使得开发基于血液的共感染诊断变得复杂。

解释：我们的研究结果表明，COVID-19 和 TB 的共同免疫反应失调是 COVID-19 严重程度和 TB 疾病进展的双重风险。在确诊为 SARS-CoV-2 后的几个月内，应对这些人进行结核病随访。

Abstract

Background The novel coronavirus, SARS-CoV-2, has increased the burden on healthcare systems already strained by a high incidence of tuberculosis (TB) as co-infection and dual presentation are occurring in syndemic settings. We aimed to understand the interaction between these diseases by profiling COVID-19 gene expression signatures on RNA-sequencing data from TB-infected individuals.

Methods We performed a systematic review and patient-level meta-analysis by querying PubMed and pre-print servers to derive eligible COVID-19 gene expression signatures from human whole blood (WB), PBMCs or BALF studies. A WB influenza dataset served as a control respiratory disease signature. Three large TB RNA-seq datasets, comprising multiple cohorts from the UK and Africa and consisting of TB patients across the disease spectrum, were chosen to profile these signatures. Putative “COVID-19 risk scores” were generated for each sample in the TB datasets using the TBSignatureProfiler package. Risk was stratified by time to TB diagnosis in progressors and contacts of pulmonary and extra-pulmonary TB. An integrative analysis between TB and COVID-19 single-cell RNA-seq data was performed and a population-level meta-analysis was conducted to identify shared gene ontologies between the diseases and their relative enrichment in COVID-19 disease severity states.

Results 35 COVID-19 gene signatures from nine eligible studies comprising 98 samples were profiled on TB RNA-seq data from 1181 samples from 853 individuals. 25 signatures had significantly higher COVID-19 risk in active TB (ATB) compared with latent TB infection ($p < 0·005$), 13 of which were validated in two independent datasets. *FCN1*- and *SPP1*-expressing macrophages enriched in BALF

during severe COVID-19 were identified in circulation during ATB. Shared perturbed ontologies included antigen presentation, epigenetic regulation, platelet activation, and ROS/RNS production were enriched with increasing COVID-19 severity. Finally, we demonstrate that the overlapping transcriptional responses may complicate development of blood-based diagnostic signatures of co-infection.

Interpretation Our results identify shared dysregulation of immune responses in COVID-19 and TB as a dual risk posed by co-infection to COVID-19 severity and TB disease progression. These individuals should be followed up for TB in the months subsequent to SARS-CoV-2 diagnosis.