



# 新型冠状病毒信息 简报

第 12 期（2020 年 3 月 30 日报）

上海科技大学免疫化学研究所

生物学大数据平台、高通量筛选平台、分析化学平台联合编译制作

联系人：蒋立春 [jianglch@shanghaitech.edu.cn](mailto:jianglch@shanghaitech.edu.cn)

# 内容介绍

分类	标题名称
疫情播报	1. 2020年3月29日疫情播报
流行病学	2. 宁波市新型冠状病毒肺炎密切接触者感染流行病学特征分析：确诊病例、无症状感染者的密切接触者感染率无显著差异 3. 儿童 SARS-CoV-2 感染的特征和持续性粪便病毒脱落的潜在证据 4. 2019 新型冠状病毒病患者对 SARS-CoV-2 的抗体反应
药物研发	5. 以 SARS-CoV-2 主要蛋白酶为靶点的新型抗病毒药物醛基类肽的结构设计、合成及生物学评价 6. 设计针对 SARS-CoV-2（具有高细胞膜融合活性的新型冠状病毒）的强效膜融合抑制剂
疫苗研发	7. SARS-CoV-2 疫苗管线概述
基础研究	8. 用高精度质谱鉴定重组 SARS-CoV-2 刺突蛋白的位点特异性的 N-糖基化 9. 采用蛋白组微阵列对 COVID-19 的抗体进行精确到氨基酸水平的扫描 10. 通过对被 SARS-CoV-2 感染的宿主细胞的蛋白质谱时间序列数据进行重分析，网络分析和通路分析表明炎症可能和病毒感染有关系
快讯	11. 美国 FDA 批准了氯喹用于 COVID-19 治疗 12. 美国 FDA 通过紧急使用授权条例批准了 Battelle 公司为 COVID-19 N95 口罩的消毒方案

免责声明：

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3月29日疫情

数据来源: WHO

发布时间: 2020年3月29日北京时间下午5点

链接: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>

根据 WHO 提供的数据, 2020年3月29日全球累计确诊新型冠状病毒病人 634835 例, 当日新增确诊 63159 例, 累计死亡 29891 例, 当日新增死亡 3398。

中国累计确诊 82356 例, 累计死亡 3306 例, 当日新增确诊 126 例, 新增死亡 5 例。

## 2. 宁波市新型冠状病毒肺炎密切接触者感染流行病学特征分析: 确诊病例、无症状感染者的密切接触者感染率无显著差异

The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city

来源: 中华流行病学杂志

发布时间: 2020-03-04

链接: <http://html.rhhz.net/zhlxbx/028.htm>

通讯作者: 许国章

作者单位: 宁波市疾病预防控制中心传染病防制所, 职业与环境卫生所

整理: 孔娟

内容摘要:

本研究估算了新型冠状病毒肺炎病例密切接触者的感染率, 并对不同暴露状况下新型冠状病毒肺炎的发病风险进行了评估。共追踪调查了 2147 名密切接触者, 总感染率为 6.15%, 确诊病例、无症状感染者的密切接触者感染率分别为 6.30% 和 4.11%, 差异无统计学意义 ( $P>0.05$ )。不同关系的密切接触者中, 以朋友/香客 (22.31%)、家庭成员 (18.01%)、亲戚 (4.73%) 感染较高率, 医务人员密切接触者未发生感染, 各密切接触者人群感染率差异有统计学意义 ( $P<0.005$ )。与病例同住 (13.26%)、乘坐同一个交通工具 (11.91%)、聚餐娱乐 (7.18%) 均是感染高危因素。医院诊疗环境下的交叉感染也不容忽视 (1.94%), 潜伏期中位数为 5 d。另外研究发现, 室外环境中无防护的面对面短暂交谈, 亦能引起疾病传播, 提示该病传染性较强, 需严格按照密切接触者管理方案实施隔离医学观察措施。

Abstract:

Objective To estimate the infection rate of close contacts of COVID-19 cases, and to evaluate the risk of COVID-19 under different exposure conditions.

Methods A prospective study was used to conduct continuous quarantine medical observations of close contacts of people infected with COVID-19, collect epidemiological, clinical manifestations, and laboratory test data to estimate the infection rate of close contacts under different exposures.

Results The epidemiological curve of COVID-19 in Ningbo showed persistent human-to-human characteristics. A total of 2 147 close contacts were tracked and investigated. The total infection rate was 6.15%. The infection rates of confirmed cases and positive contacts were 6.30% and 4.11%, respectively. The difference was not statistically significant ( $P>0.05$ ). Among close contacts of different relationships, friends/pilgrims (22.31%), family members (18.01%), and relatives (4.73%) have a higher infection rate, and close contacts of medical

staff were not infected. Differences in infection rates among the close contacts were statistically significant ( $P < 0.005$ ). Living with the case (13.26%), taking the same transportation (11.91%), and dining together (7.18%) are high risk factors for infection. Cross-infection in the hospital should not be ignored (1.94%). The median of incubation period is 5 days.

Conclusion The infection rate of close contacts of COVID-19 cases is high, and isolation medical observation measures should be implemented in strict accordance with the close contact management plan.

### 3. 儿童 SARS-CoV-2 感染的特征和持续性粪便病毒脱落的潜在证据

Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding

来源: Nature Medicine

发布时间: 2020-03-13

来源链接: <https://www.nature.com/articles/s41591-020-0817-4>

编译: 宋张悦

内容摘要:

来自广州医科大学附属广州市妇女儿童医疗中心、美国宾夕法尼亚州费城儿童医院、广州再生医学与健康实验室和澳门科技大学医学院的研究团队,报道了 10 例儿童 SARS-CoV-2 感染病例的流行病学和临床特征分析。这项研究的通讯作者为夏慧敏、唐金陵、张康和龚四堂教授。

这项研究纳入了截至 2020 年 2 月 20 日在广州指定治疗中心收治入院的全部 10 名儿童,年龄从 2 个月到 15 岁不等,都是因为与相关病例接触史或武汉暴露史,经筛查鼻咽拭子核酸检测结果为阳性而确诊。

临床表现上,这些患儿入院时最常见的症状是发热(7 人),但体温均未超过  $39^{\circ}\text{C}$ ;其次为咳嗽(5 人)、喉咙痛(4 人)、腹泻(3 人)和鼻塞(2 人);有 1 名孩子完全无症状,而在成年人病例中常见的疲劳、恶心呕吐、呼吸困难等症状则没有出现。胸部影像学的结果显示出与成人感染者的明显差别,10 例患儿的 X 光片检查结果均没有肺炎的明确体征,CT 扫描显示 5 例在正常范围,5 例有单发或多发磨玻璃样混浊。实验室检查结果则显示,10 名患儿中有 9 人在血液生化等各项测试上都正常,而成人患者中常见的淋巴细胞减少、白细胞减少、转氨酶升高等也很少在这些儿童患者中出现。在治疗方面,所有患儿都接受了  $\alpha$ -干扰素口腔喷雾剂的抗病毒治疗,只有第 1 例患儿在确诊时还接受了连续多日的阿奇霉素治疗。没有患儿需要呼吸支持或重症监护病房护理。

值得注意的是,即使鼻咽拭子检测结果为阴性,仍有 8 名儿童的直肠拭子检测结果持续呈阳性,这增加了粪便经口传播的可能性。不过作者也指出,粪便样本中的病毒是否具有复制能力还没有证据,因此新冠病毒是否具有粪口传播的能力仍有待进一步确认。

Abstract

We report epidemiological and clinical investigations on ten pediatric SARS-CoV-2 infection cases confirmed by real-time reverse transcription PCR assay of SARS-CoV-2 RNA. Symptoms in these cases were nonspecific and no children required respiratory support or intensive care. Chest X-rays lacked definite signs of pneumonia, a defining feature of the infection in adult cases. Notably, eight children persistently tested positive on rectal swabs even after nasopharyngeal testing was negative, raising the possibility of fecal-oral transmission.

#### 4. 2019 新型冠状病毒病患者对 SARS-CoV-2 的抗体反应

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

来源: Clinical Infectious Diseases

发布时间: 2020. 3. 28

链接: <https://doi.org/10.1093/cid/ciaa344>

通讯作者: 张政, 博士生导师, 现任深圳市第三人民医院肝病研究所副所长, 重点研究 HIV 和 HBV/HCV 感染过程中, 机体天然免疫和特异性免疫特点及其与疾病进展的相关性、机体免疫保护和免疫损伤的分子机制以及新型免疫调节治疗方法的临床应用等

作者单位: 深圳市第三人民医院

编译: 张鹏伟

摘要:

背景: 新型冠状病毒 SARS-CoV-2 是一种新出现的病毒。感染病人的抗体反应仍不清楚, 抗体检测的临床价值尚未充分证明。

方法: 一共纳入 173 例 SARS-CoV-2 感染患者。在住院期间采集的 535 份血浆样本进行抗 SARS-CoV-2 总抗体 (Ab)、IgM 和 IgG 检测。分析了随疾病进展的抗体动力学。

结果: 173 例患者中 Ab、IgM 和 IgG 的血清转化率分别为 93.1%、82.7%和

64.7%。12 例患者抗体阴性的原因可能是在疾病后期缺乏血样。血清转化时间的中位数 Ab、IgM 和 IgG 分别为第 11 天、第 12 天和第 14 天。在患者发病后 1 周内出现抗体 <40%, 到发病后第 15 天迅速增加, 分别为 100.0% (Ab)、94.3% (IgM) 和 79.8% (IgG)。相反, RNA 在第 7 天之前采集的样本中, 可检测性从 66.7% (58/87) 下降到第 15-39 天的 45.5% (25/55)。结合 RNA 和抗体检测可显著提高 COVID-19 的病原学诊断敏感性 ( $p < 0.001$ ), 甚至在 1 周内早期阶段 ( $p = 0.007$ )。此外, 抗体的高滴度与较差临床分型 ( $p = 0.006$ ) 无关。

结论: 抗体检测为 SARS-CoV-2 感染过程提供了重要的临床信息。研究结果为在 COVID-19 患者诊断和治疗中血清学检测的常规应用提供了有力的经验支持。

Abstract:

Background: The novel coronavirus SARS-CoV-2 is a newly emerging virus. The antibody response in infected patient remains largely unknown, and the clinical values of antibody testing have not been fully demonstrated.

Methods: A total of 173 patients with SARS-CoV-2 infection were enrolled. Their serial plasma samples ( $n = 535$ ) collected during the hospitalization were tested for total antibodies (Ab), IgM and IgG against SARS-CoV-2. The dynamics of antibodies with the disease progress was analyzed.

Results: Among 173 patients, the seroconversion rate for Ab, IgM and IgG was 93.1%, 82.7% and 64.7%, respectively. The reason for the negative antibody findings in 12 patients might due to the lack of blood samples at the later stage of illness. The median seroconversion time for Ab, IgM and then IgG were day-11, day-12 and day-14, separately. The presence of antibodies was <40% among patients within 1-week since onset, and rapidly increased to 100.0% (Ab), 94.3% (IgM) and 79.8% (IgG) since day-15 after onset. In contrast, RNA detectability decreased from 66.7% (58/87) in samples collected before day-7 to 45.5% (25/55) during day 15-39. Combining RNA and antibody detections significantly improved the sensitivity of pathogenic diagnosis for COVID-19 ( $p < 0.001$ ), even in early phase of 1-week since onset ( $p = 0.007$ ). Moreover, a higher titer of Ab was independently

associated with a worse clinical classification ( $p=0.006$ ).

Conclusions: The antibody detection offers vital clinical information during the course of SARS-CoV-2 infection. The findings provide strong empirical support for the routine application of serological testing in the diagnosis and management of COVID-19 patients.

## 5. 以 SARS-CoV-2 主要蛋白酶为靶点的新型抗病毒药物醛基类肽的结构设计、合成及生物学评价

Structure-Based Design, Synthesis and Biological Evaluation of Peptidomimetic Aldehydes as a Novel Series of Antiviral Drug Candidates Targeting the SARS-CoV-2 Main Protease

来源: biorxiv

发布时间: 2020-03-28

来源链接: <https://www.biorxiv.org/content/10.1101/2020.03.25.996348v1>

作者单位: 中国科学院上海药物研究所和上海科技大学免疫化学研究所等单位

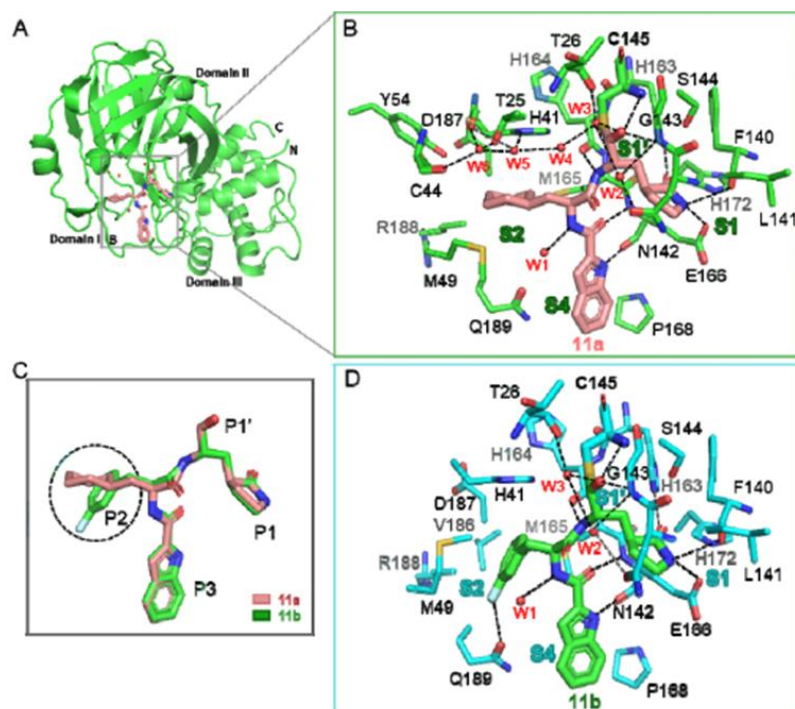
通讯作者: 张磊砢, 许叶春, 杨海涛和柳红

编译: 王玮

内容摘要:

SARS-CoV-2 是武汉市 COVID-19 爆发的病原体。治疗 COVID-19 感染急需特异性抗病毒药物。SARS-CoV-2 的主要蛋白酶 (Mpro) 是一种关键的冠状病毒酶, 在介导病毒复制和转录过程中起着关键作用, 是一种重要的药物靶点。为了快速发现以 Mpro 为靶点的先导化合物, 该研究设计并合成了两种化合物(11a 和 11b, 图一), 这两种化合物均表现出良好的抑制活性, IC<sub>50</sub> 值分别为 0.05  $\mu$ M 和 0.04  $\mu$ M。值得注意的是, 这两种化合物在细胞水平的检测中均显示出较强的抗 SARS-CoV-2 感染的活性, EC<sub>50</sub> 值分别为 0.42  $\mu$ M 和 0.33  $\mu$ M。在 1.5 Å 分辨率下分别测定了 11a 和 11b, 与 SARS-CoV-2 Mpro 结合的 X 射线晶体结构 (图一)。晶体结构表明 11a 和 11b 和主要蛋白酶的的结合是不可逆的, 化合物中的醛基与 Mpro 中的 Cys145 形成共价结合。这两种化合物都是很有前途的先导化合物, 具有临床潜力, 值得进一步研究。

图一 SARS-CoV-2 Mpro 抑制剂结合口袋中的 11a 和 11b



**Figure 2. SARS-CoV-2 M<sup>pro</sup> inhibitor binding pocket for 11a and 11b.**

A. Cartoon representation of the crystal structure of M<sup>pro</sup> in complex with **11a**. The compound **11a** is shown as brown sticks in the substrate-binding pocket located between domain I and II of SARS-CoV-2 M<sup>pro</sup>. Water molecules involve in stabilizing the **11a** shown as spheres colored red.

B. Close-up view of the **11a** binding site. The binding pocket is divided into four subsites (S1', S1, S2 and S4). The residues involving in inhibitor binding are shown as green sticks. **11a** and water molecules are shown as brown sticks and red spheres, respectively. Hydrogen bonds are indicated as dashed lines.

C. Comparison of the binding model of **11a** and **11b** in SARS-CoV-2 M<sup>pro</sup>. The major differences between **11a** and **11b** are marked with dashed circles. The compounds of **11a** and **11b** are shown as brown and green sticks, respectively.

D. Close-up view of the **11b** binding site. Hydrogen bonds are indicated as dashed lines.

#### Abstract

SARS-CoV-2 is the etiological agent responsible for the COVID-19 outbreak in Wuhan. Specific antiviral drug are urgently needed to treat COVID-19 infections. The main protease (M<sup>pro</sup>) of SARS-CoV-2 is a key CoV enzyme that plays a pivotal role in mediating viral replication and transcription, which makes it an attractive drug target. In an effort to rapidly discover lead compounds targeting M<sup>pro</sup>, two compounds (11a and 11b) were designed and synthesized, both of which exhibited excellent inhibitory activity with an IC<sub>50</sub> value of 0.05 μM and 0.04 μM respectively. Significantly, both compounds exhibited potent anti-SARS-CoV-2 infection activity in a cell-based assay with an EC<sub>50</sub> value of 0.42 μM and 0.33 μM, respectively. The X-ray crystal structures of SARS-CoV-2 M<sup>pro</sup> in complex with 11a and 11b were determined at 1.5 Å resolution, respectively. The

crystal structures showed that 11a and 11b are irreversible, the aldehyde groups of which are bound covalently to Cys145 of Mpro. Both compounds are promising drug leads with clinical potential that merits further studies.

## 6. 设计针对 SARS-CoV-2 (具有高细胞膜融合活性的新型冠状病毒) 的强效膜融合抑制剂

Design of potent membrane fusion inhibitors against SARS-CoV-2, an emerging coronavirus with high fusogenic activity

来源: biorxiv

发表时间: 2020-3-26

链接: <https://www.biorxiv.org/content/10.1101/2020.03.26.009233v1>

通讯作者: Yuxian He

作者单位: 中国医学科学院和北京协和医学院

编译: 刘焕珍

摘要:

本文的研究为理解 SARS-CoV-2 的进入途径和靶向膜融合步骤的抗病毒药物设计提供了重要信息。在这项研究中,作者首先验证了人 ACE2 作为 SARS-CoV-2 的细胞受体,其 S 蛋白具有较高的膜融合活性。与 SARS-CoV 的序列相比,SARS-CoV-2 的 S2 融合蛋白中的七肽重复序列 1 (HR1) 具有明显增加的  $\alpha$ -螺旋性和热稳定性,以及对其相应的七肽重复序列 2 (HR2) 具有更高的结合亲和力。然后,作者设计了一种基于 HR2 序列的脂肽融合抑制剂,称为 IPB02,在抑制 SARS-CoV-2 S 蛋白介导的细胞-细胞融合和假病毒感染中表现出强大的活性。IPB02 还有效抑制了 SARS-CoV 假病毒。此外,IPB02 的结构和活性关系 (SAR) 用一组截短的脂肽表征,揭示了对其结合和抗病毒能力至关重要的氨基酸基序。

Abstract

The presented results have provided important information for understanding the entry pathway of SARS-CoV-2 and the design of antivirals that target the membrane fusion step. In this study, we firstly verified that SARS-CoV-2 uses human ACE2 as a cell receptor and its spike (S) protein mediates high membrane fusion activity. Comparing to that of SARS-CoV, the heptad repeat 1 (HR1) sequence in the S2 fusion protein of SARS-CoV-2 possesses markedly increased  $\alpha$ -helicity and thermostability, as well as a higher binding affinity with its corresponding heptad repeat 2 (HR2) site. Then, we designed a HR2 sequence-based lipopeptide fusion inhibitor, termed IPB02, which showed highly potent activities in inhibiting the SARS-CoV-2 S protein mediated cell-cell fusion and pseudovirus infection. IPB02 also inhibited the SARS-CoV pseudovirus efficiently. Moreover, the structure and activity relationship (SAR) of IPB02 were characterized with a panel of truncated lipopeptides, revealing the amino acid motifs critical for its binding and antiviral capacities.

## 7. SARS-CoV-2 疫苗管线概述

The SARS-CoV-2 Vaccine Pipeline: an Overview

来源: Current Tropical Medicine Reports

发表时间: 2020.3.3

链接: <https://link.springer.com/article/10.1007/s40475-020-00201-6>



通讯作者: Maria Elena Bottazzi, 国家热带医学院副院长, 贝勒医学院儿科教授

作者单位: 德克萨斯州儿童医院疫苗发展中心, 美国德克萨斯州休斯顿贝勒医学院国家热带医学院儿科和分子病毒及微生物学系

编译: 雷颖

摘要:

这篇综述的目的是提供为2019年新型冠状病毒 SARS-CoV-2(冠状病毒疾病的病原体(COVID-19)的致病因子)开发疫苗的有关工作的及时概述。作者简要概述了一些主要候选以及实施疫苗策略的挑战。文中主要列了以下三个疫苗策略: 整个病毒疫苗, 减毒或无活性的全病毒疫苗代表了病毒接种的经典策略; 亚单位疫苗, 依赖于引发针对 S-spike 蛋白的免疫反应, 以防止其与宿主 ACE2 受体对接; 核酸疫苗, 几家主要的生物技术公司拥有用于 COVID-19 的先进核酸疫苗平台。同时, 根据先前 SARS-CoV 疫苗的经验, 预计所有 COVID-19 疫苗都需要对免疫增强进行仔细的安全评估, 因为这可能导致感染性或嗜酸性粒细胞浸润增加。除此之外, COVID-19 疫苗目标产品的概况必须针对高危人群, 包括一线医护人员, 60 岁以上的人群以及具有潜在和令人衰弱的慢性病的人群。

Abstract

Purpose of Review

The goal of this review is to provide a timely overview on efforts to develop a vaccine for the 2019 novel coronavirus SARS-CoV-2, the causative agent of coronavirus disease (COVID-19).

Recent Findings

Previous research efforts to develop a severe acute respiratory syndrome coronavirus (SARS-CoV) vaccine in the years following the 2003 pandemic have opened the door for investigators to design vaccine concepts and approaches for the COVID-19 epidemic in China. Both SARS-CoV and SARS-CoV-2 exhibit a high degree of genetic similarity and bind to the same host cell ACE2 receptor. Based on previous experience with SARS-CoV vaccines, it is expected that all COVID-19 vaccines will require careful safety evaluations for immunopotentiality that could lead to increased infectivity or eosinophilic infiltration. Besides this, a COVID-19 vaccine target product profile must address vaccinating at-risk human populations including frontline healthcare workers, individuals over the age of 60, and those with underlying and debilitating chronic conditions. Among the vaccine technologies under evaluation are whole virus vaccines, recombinant protein subunit vaccines, and nucleic acid vaccines.

Summary

Each current vaccine strategy has distinct advantages and disadvantages. Therefore, it is paramount that multiple strategies be advanced quickly and then evaluated for safety and efficacy. Ultimately, the safety studies to minimize undesired immunopotentiality will become the most significant bottleneck in terms of time.

**Table 1** Major COVID-19 vaccine development programs

Consortium	Candidate vaccine	Reference
Whole virus vaccines		
Janssen (Johnson & Johnson)	Adenovirus-vectored vaccine using AdVac® and PER.C6® technology	[10]
Codagenix/Serum Institute of India	Live-attenuated vaccine	[11]
Subunit vaccines		
University of Queensland/CEPI	Protein-based vaccine using Molecular Clamp platform	[12]
Novavax	Recombinant nanoparticle technology	[13]
Clover Bipharmaceuticals	S-trimer recombinant protein using Trimer-Tag technology	[14]
Baylor College of Medicine, Fudan University, New York Blood Center, Univ Texas Medical Branch	Coronavirus RBD protein-based vaccine	[15]
Vaxart	Oral recombinant protein vaccine using VAAST platform	[16]
Nucleic acid vaccines		
Inovio/Beijing Advaccine Biotechnology Co./CEPI	DNA vaccine (INO-4800, based on INO-4700 MERS vaccine)	[17]
Moderna/NIH/CEPI	mRNA vaccine	[18]
CureVac/CEPI	mRNA vaccine	[19]

## 8. 用高精度质谱鉴定重组 SARS-CoV-2 刺突蛋白的位点特异性的 N-糖基化

Site-specific N-glycosylation Characterization of Recombinant SARS-CoV-2 Spike Proteins using High-Resolution Mass Spectrometry

来源: biorxiv

发布日期: 2020-03-29

链接: <https://www.biorxiv.org/content/10.1101/2020.03.28.013276v1>

通讯作者: 四川大学华西医院 Hao Yang

编译: 陈文章

冠状病毒的表面具有高度糖基化的特征, 因此华西医院采用糖蛋白质组的方法鉴定了 SARS-CoV-2 表面的糖基化位点。为了提高鉴定的覆盖度, 作者采用多种酶(trypsin 和 Glu-C)联用的方法。样品采用的是昆虫表达的重组刺突蛋白(S 蛋白), 该蛋白含有 22 可能的 N 糖基化位点。质谱数据表明, 所有的糖基化位点都得到了鉴定, 同冷冻电镜数据吻合。三个非典型的糖基化序列位点(N-X-C)没有糖基化。此外, 作者将 SARS-CoV-2 的序列同 GISAID database 内 753 个 SARS-CoV-2 序列比较, 发现 38 个糖基化位点的变化(Alteration)频率比较低, 22 个 N 糖基化位点几乎都是保守的(除了 N717 glycosite)。同 SARS-CoV S protein 比较, 18 个 N-糖基化位点是保守的, 这表明了糖基化的重要性。新增的 4 个糖基化位点s (N17, N74, N149, and N657)位于 S1 亚基非 RBD 区域。SARS-CoV S 中四个糖基化位点(N29, N73, N109, and N357)在 SARS-CoV-2 中没有被发现, 其中 N357 位于 RBD 区域。

同表达在 human cell 中的相比, 表达在 insect 中的冠状病毒的糖链趋小, 结构趋简单。通常而言, 表达在 insect 的糖蛋白能产生更强的免疫原性。此外, 作者认为, SARS-CoV-2 高度异质化的 N 糖基化可能是产生不同免疫反应性的原因。因此作者提出用 insect 系统表达的 S 蛋白来开发疫苗。

The global pandemic of severe acute pneumonia syndrome (COVID-19) caused by SARS-CoV-2 urgently calls for prevention and intervention strategies. The densely glycosylated spike (S) protein highly exposed on the viral surface is a determinant for virus binding and invasion into host cells as well as elicitation of a protective host immune response. Herein, we characterized the site-specific N-glycosylation of SARS-CoV-2 S protein using stepped collision energy (SCE) mass spectrometry (MS). Following digestion with two complementary proteases to cover all potential N-glycosylation sequons and integrated N-glycoproteomics

analysis, we revealed the N-glycosylation profile of SARS-CoV-2 S proteins at the levels of intact N-glycopeptides and glycosites, along with the glycan composition and site-specific number of glycans. All 22 potential canonical N-glycosites were identified in S protein protomer. Of those, 18 N-glycosites were conserved between SARS-CoV and SARS-CoV-2 S proteins. Nearly all glycosites were preserved among the 753 SARS-CoV-2 genome sequences available in the public influenza database Global Initiative on Sharing All Influenza Data. By comparison, insect cell-expressed SARS-CoV-2 S protein contained 38 N-glycans, which were primarily assigned to the high-mannose type N-glycans, whereas the human cell-produced protein possessed up to 140 N-glycans largely belonging to the complex type. In particular, two N-glycosites located in the structurally exposed receptor-binding domain of S protein exhibited a relatively conserved N-glycan composition in human cells. This N-glycosylation profiling and determination of differences between distinct expression systems could shed light on the infection mechanism and promote development of vaccines and targeted drugs.

## 9. 采用蛋白组微阵列对 COVID-19 的抗体进行精确到氨基酸水平的扫描

SARS-CoV-2 proteome microarray for mapping COVID-19 antibody interactions at amino acid resolution

来源: biorxiv

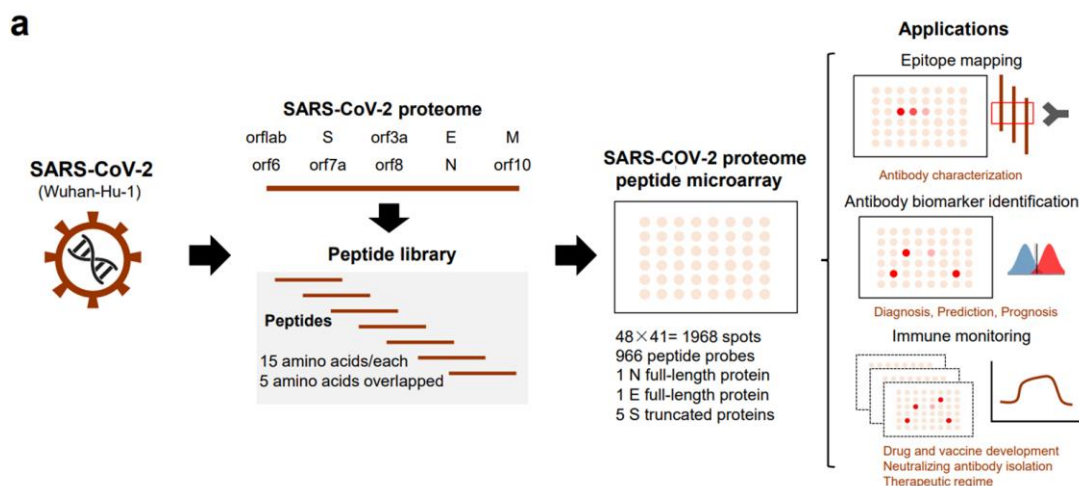
发布时间: 2020-03-28

链接: <https://www.biorxiv.org/content/10.1101/2020.03.26.994756v1>

通讯作者: 国家蛋白质科学中心(北京, 又名凤凰中心) Xiaobo Yu

编译: 蒋立春

国家蛋白质科学中心(北京, 又名凤凰中心)的研究团队利用蛋白质组微阵列的方式对 COVID-19 病人产生的抗体进行了氨基酸精度的扫描(mapping)。研究们针对 SARS-CoV-2 的 10 个蛋白质设计了 966 个 15 个氨基酸长度的多肽(多肽之间按照 5 氨基酸重叠设计)。将这些肽段以及全长 E、N 蛋白以及 5 个截断的 S 蛋白通过生物素-链霉亲和素印到微芯片上。将这个芯片和病人的血清进行孵育对抗体进行扫描。这个芯片的处理时间只有 1.5 小时, 有 100 倍的检测范围, 最低的检测极限是 94 皮克/毫升。研究中发现这个 SARS-CoV-2 的蛋白组芯片发现商品化的 SARS-CoV-1 抗体可以识别 SARS-CoV-2 的蛋白。该研究对 10 个 COVID-19 病人的 IgM 和 IgG 的抗原表位进行了分析。阳性信号的表位可以帮助我们了解 COVID-19 免疫反应的分子标记物, 既可能可以用来做 COVID-19 的诊断, 也可能用于疫苗的开发。通过比较病人中的数据, 该研究鉴定中了一些可能有中和活性的抗体可以抑制病毒通过 ACE2 进入细胞。



文中用到的蛋白组微阵列技术示意图

( ) has quickly become a worldwide pandemic, which has significantly impacted the economy, education, and social interactions. Understanding the humoral antibody response to SARS-CoV-2 proteins may help identify biomarkers that can be used to detect and treat COVID-19 infection. However, no immunoproteomics platform exists that can perform such proteome-wide analysis. To address this need, we created a SARS-CoV-2 proteome microarray to analyze antibody interactions at amino acid resolution by spotting peptides 15 amino acids long with 5-amino acid offsets representing full-length SARS-CoV-2 proteins. Moreover, the array processing time is short (1.5 hours), the dynamic range is  $\sim 2$  orders of magnitude, and the lowest limit of detection is 94 pg/mL.

### 10. 通过对被 SARS-CoV-2 感染的宿主细胞的蛋白质谱时间序列数据进行重分析，网络分析和通路分析表明炎症可能和病毒感染有关系

Re-analysis of SARS-CoV-2 infected host cell proteomics time-course data by impact pathway analysis and network analysis. A potential link with inflammatory response.

<https://www.biorxiv.org/content/10.1101/2020.03.26.009605v1>

来源: biorxiv

发布时间:

通讯作者:

编译: 蒋立春

来自西班牙和丹麦的科学家对已经发表的 SARS-CoV-2 感染细胞蛋白质谱数据 (文献 1, 也是我们 3 月 25 日简报第一条) 进行了重分析, 对受到影响的通路和基因网络进行了分析。他们发现免疫反应通路、以及和有丝分裂中染色体分离相关的信号通路发生了变化。他们认为观察的炎症相关的蛋白上调可能和 COVID-19 的疾病晚期的肺部损失有关系。

编者注:

原数据集感染的是 Caco-2 细胞, 一种结肠癌症, 看到炎症相关的基因变化和引起组织变化的炎症反应似乎有点牵强。

不过该研究中用到的 pathway 分析软件来源于其中一个作者公司的商用软件。

值得重新分析引文中的数据集，理解这篇文章和原引文分析结果的差异。

The disease known as coronavirus disease 19 (COVID-19), potentially caused by an outbreak of the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) in Wuhan, China, has hit the world hard, and has led to an unprecedented health and economic crisis. In order to develop treatment options able to stop or ameliorate SARS-CoV-2 effects, we need to understand the biology of the virus inside cells, but this kind of studies are still scarce. A recent study investigated transcriptome and proteome host cell changes induced in vitro by SARS-CoV-2. In the present study, we use the publicly available proteomics data from this study to re-analyze the mechanisms altered by the virus infection by impact pathways analysis and network analysis. Proteins linked to inflammatory response, but also proteins related to chromosome segregation during mitosis, were found to be regulated. The up-regulation of the inflammatory-related proteins observed could be linked to the propagation of inflammatory reaction and lung injury that is observed in advanced stages of COVID-19 patients.

文献 1: Bojkova, D.; Klann, K.; Koch, B.; Widera, M.; Krause, D.; Ciesek, S.; Cinatl, J.; Münch, C. SARS-CoV-2 infected host cell proteomics reveal potential therapy targets. Preprint available at Research Square 2020 Mar 11. <https://dx.doi.org/10.21203/rs.3.rs-17218/v1>

#### 11. FDA 批准了氯喹用于 COVID-19 治疗。

**FDA approved Chloroquine for COVID-19 on last Sunday.**

尽管缺少对照试验结果支持，美国 FDA 3 月 29 日通过紧急使用授权的方式批准了氯喹和羟氯喹用于治疗 COVID-19。这是美国 FDA 首次批准没有对照试验的药物。

链接: <https://www.biocentury.com/article/304766>

#### 12. 美国 FDA 通过紧急使用授权条例批准了 Battelle 公司为 COVID-19 N95 口罩的消毒方案

FDA approves expansion to Battelle's COVID-19 mask decontamination process  
发布时间: 2020-03-28

链接:

<https://www.battelle.org/newsroom/press-releases/press-releases-detail/battelle-ccds-critical-care-decontamination-system-being-deployed-to-meet-urgent-need-for-personal-protective-equipment-for-nation-s-healthcare-workforce>

根据 Battelle 的报道，该公司的一套 CCDS Critical Care Decontamination System 一天最多可以消毒 80000 个口罩。这个系统可扩展，每天可以消毒的个人防护物品可以更多。Battelle CCDS 系统用将 N95 口罩在高浓度的气相过氧化氢对污染的处理 2.5 小时以达到去除包括 SARS-CoV-2 的生物污染。

Each Battelle CCDS Critical Care Decontamination System™ is capable of decontaminating up to 80,000 masks per day at full capacity. Because it is scalable, the system is capable of processing even more pieces of personal

protective equipment (PPE) each day. Battelle CCDS™ uses concentrated, vapor phase hydrogen peroxide (VPHP) and works by exposing used respirator masks to the validated concentration level for 2.5 hours to decontaminate biological contaminants, including SARS-CoV-2.

