新型冠状病毒信息简报

第 10 期（2020 年 3 月 28 日报）

上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台联合编译制作

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1. 2020 年 3 月 27 日疫情

数据来源：WHO
发布时间：2020 年 3 月 27 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 27 日全球累计确诊新型冠状病毒病人超过 50 万，达到 509164 例，当日新增确诊 46484 例，累计死亡 23328 例，当日新增死亡 2501。
中国累计确诊 82078 例，累计死亡 3298 例，当日新增确诊 117 例，新增死亡 5 例。

2. 国家药监局应急批准第 23 个新冠病毒核酸快速检测试剂

来源：国家药品监督管理局
发布时间：2020-03-27
来源链接： http://www.nmpa.gov.cn/WS04/CL2176/376095.html
编译：宋张悦
原文内容：
近日，国家药监局再次应急批准 1 个新冠病毒核酸快速检测产品，进一步服务于疫情防控需要。

上海仁度生物科技有限公司开发的新冠病毒 2019-nCoV 核酸检测试剂， 采用 RNA 特异靶标捕获和转录介导的恒温扩增实时检测技术，在一个反应管中自动化完成核酸提取、扩增步骤，90 分钟可出结果，并可实现连续并行检测，提升检测效率。相关数据显示，检测结果灵敏度、特异性能够达到传统 PCR 方法的水平。

此前，国家药监局已应急批准杭州优思达生物技术有限公司新冠病毒 2019-nCoV 核酸检测试剂盒（恒温扩增-实时荧光法）、安邦（厦门）生物科技有限公司新型冠状病毒 2019-nCoV 核酸检测试剂盒（杂交捕获免疫荧光法）2 个核酸快速检测试剂产品。

上述 3 个核酸快速检测试剂，缩短了核酸检测试剂的检测时间，提高了检测效率，全力服务疫情防控需要。

国家药监局还应急批准了上海复星长征医学科学有限公司新型冠状病毒（2019-nCoV）核酸检测试剂盒（荧光 PCR 法）产品，进一步扩大了疫情防控用检测试剂的供应。

截至目前，国家药监局已经应急批准 23 个新型冠状病毒检测产品，其中新冠病毒核酸检测试剂 15 个，抗体检测试剂 8 个。

已批准新型冠状病毒检测试剂

序号	产品名称	注册人	注册证号
1	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	上海之江生物科技股份有限公司	国械注准 20203400057
2	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	上海捷诺生物科技有限公司	国械注准 20203400058
3	新型冠状病毒 2019-nCoV 核酸检测试剂盒（联合探针锚定聚合测序法）	华大生物科技（武汉）有限公司	国械注准 20203400059
4	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	华大生物科技（武汉）有限公司	国械注准 20203400060
5	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	中山大学达安基因股份有限公司	国械注准 20203400063
6	新型冠状病毒 2019-nCoV 核酸检测试	圣湘生物科技股份有	国械注准

	剂盒（荧光 PCR 法）	限公司	20203400064
7	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	上海伯杰医疗科技有限公司	国械注准 20203400065
8	新型冠状病毒（2019-nCoV）抗体检测试剂盒（胶体金法）	广州万孚生物技术股份有限公司	国械注准 20203400176
9	新型冠状病毒（2019-nCoV）IgM/IgG 抗体检测试剂盒（胶体金法）	英诺特（唐山）生物技术有限公司	国械注准 20203400177
10	六项呼吸道病毒核酸检测试剂盒（恒温扩增芯片法）	成都博奥晶芯生物科技有限公司	国械注准 20203400178
11	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	北京卓诚惠生生物科技股份有限公司	国械注准 20203400179
12	新型冠状病毒（2019-nCoV）IgM 抗体检测试剂盒（磁微粒化学发光法）	博奥赛斯（重庆）生物科技有限公司	国械注准 20203400182
13	新型冠状病毒（2019-nCoV）IgG 抗体检测试剂盒（磁微粒化学发光法）	博奥赛斯（重庆）生物科技有限公司	国械注准 20203400183
14	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	迈克生物科技股份有限公司	国械注准 20203400184
15	新型冠状病毒（2019-nCoV）抗体检测试剂盒（磁微粒化学发光法）	厦门万泰凯瑞生物技术有限公司	国械注准 20203400198
16	新型冠状病毒（2019-nCoV）IgM 抗体检测试剂盒（胶体金法）	广东和信健康科技有限公司	国械注准 20203400199
17	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	武汉明德生物科技股份有限公司	国械注准 20203400212
18	新型冠状病毒（2019-nCoV）IgM/IgG 抗体检测试剂盒（胶体金法）	南京诺唯赞医疗科技有限公司	国械注准 20203400239
19	新型冠状病毒（2019-nCoV）IgM/IgG 抗体检测试剂盒（胶体金法）	珠海丽珠试剂股份有限公司	国械注准 20203400240
20	新型冠状病毒 2019-nCoV 核酸检测试剂盒（恒温扩增-实时荧光法）	杭州优思达生物技术有限公司	国械注准 20203400240
21	新型冠状病毒 2019-nCoV 核酸检测试剂盒（杂交捕获免疫荧光法）	安邦（厦门）生物科技有限公司	国械注准 20203400298
22	新型冠状病毒（2019-nCoV）核酸检测试剂盒（荧光 PCR 法）	上海复星长征医学科学有限公司	国械注准 20203400299
23	新型冠状病毒 2019-nCoV 核酸检测试剂盒（RNA 捕获探针法）	上海仁度生物科技有限公司	国械注准 20203400300

3. SARS-CoV-2 感染自暴露起及症状出现后的血清学特征

Serology characteristics of SARS-CoV-2 infection since the exposure and post symptoms onset

来源：medrxiv

发布时间：2020-03-27

文章链接：https://www.medrxiv.org/content/10.1101/2020.03.23.20041707v1

编译：张怡

摘要：

SARS-CoV-2 感染的及时诊断是治疗和预防的前提。抗体检测对 RNA 检测的血清学特征和补体诊断的价值还有待论证。

浙江大学第一附属医院开展了患者队列研究,收集了 80 名 COVID-19 患者的血浆,检测 SARS-CoV-2 的总抗体(Ab)、IgM 和 IgG 抗体，记录了感染期间抗体的消长变化。

COVID-19 患者体内总抗体、IgM 和 IgG 的血清转化率分别为 98.8%(79/80)、93.8%(75/80)及 93.8%(75/80)。第一个可检测的血清学标志物为总抗体，其次为 IgM 和 IgG，中位血清转换时间分别为暴露后 15、18 或 20 天(d.p.e)或发病后 9、10 和 12 天（d.p.o)。随着发病后 6 天，病毒载量下降，抗体水平迅速升高。在疾病的早期阶段(0-7d.p.o)，患者体内的 Ab 表现出最高灵敏度（64.1%）相较于 IgM 和 IgG(均为 33.3%，p < 0.001)。两周后，抗体、IgM、IgG 的灵敏度分别提高到 100%，96.7%，93.3%。

典型的急性抗体反应是在 SARS-CoV-2 感染期间产生的，血清学检测为 RNA 检测提供了重要的补充，因其可提供病原特异性诊断以及有益的信息来评价患者免疫状况。在临床管理和公共卫生实践中，使用经过充分验证的抗体检测，可以改善 COVID-19 感染的控制。

Abstract

Timely diagnosis of SARS-CoV-2 infection is the prerequisite for treatment and preventive quarantine. The serology characteristics and complement diagnosis value of antibody test to RNA test needs to be demonstrated.

A patient cohort study was conducted at the first affiliated hospital of Zhejiang University, China. Serial plasma of COVID-19 patients and were collected and total antibody (Ab), IgM and IgG antibody against SARS-CoV-2 were detected. The antibody dynamics during the infection were described.

The seroconversion rate for Ab, IgM and IgG in COVID-19 patients was 98.8% (79/80), 93.8% (75/80) and 93.8% (75/80), respectively. The first detectible serology marker is total antibody and followed by IgM and IgG, with a median seroconversion time of 15, 18 and 20 day post exposure (d.p.e) or 9, 10 and 12 days post onset, separately. The antibody levels increased rapidly since 6 d.p.o and accompanied with the decline of viral load. For patients in the early stage of illness (0-7d.p.o),Ab showed the highest sensitivity (64.1%) compared to the IgM and IgG (33.3% for both, $p<0.001$). The sensitivities of Ab, IgM and IgG detection increased to 100%, 96.7% and 93.3% two weeks later, respectively.

Typical acute antibody response is induced during the SARS-CoV-2 infection. The serology testing provides important complementation to RNA test for pathogenic specific diagnosis and helpful information to evaluate the adapted immunity status of patient. It should be strongly recommended to apply well-validated antibody tests in the clinical management and public health practice to improve the control of COVID-19 infection.

4. SARS-CoV-2 蛋白质组芯片的开发及其用于新冠病人血清 IgG/ IgM 的分析

Global profiling of SARS-CoV-2 specific IgG/ IgM responses of convalescents using a proteome microarray

来源：medRxiv

发布时间：2020-03-27

链接：https://www.medrxiv.org/content/10.1101/2020.03.20.20039495v1
编译：孔娟
摘要：
该团队成功地构建了第一款 SARS-CoV-2 蛋白质组芯片。该芯片目前涵盖了 18 个新冠病毒基因组所编码的蛋白质，并且多个蛋白有多个版本，多个来源，如 E.coli 表达、哺乳动物细胞表达以及无细胞体系表达。
应用此芯片分析了 29 例新冠肺炎病人康复期血清中 IgG 和 IgM 抗体的响应，另外纳入了 11 例健康对照和 10 例肺癌对照样本。结果表明，在恢复期 100%的患者对 SARS-CoV-2 有 IgG/IgM 抗体响应，尤其是对 S1 蛋白，而不是 S2 蛋白。除了蛋白质 N 和 S1 外，还鉴定出对 ORF9b 和 NSP5 的显著抗体反应。蛋白 ORF9b，在 29 例病人血清中有 13 例 IgG 呈现阳性，NSP5 在 3 例血清中 IgG 为阳性，NSP10，NSP14，NSP16 等在 1 例病人中 IgG 出现强阳性。这些初步结果说明，除 N 和 S 蛋白外其它新冠病毒蛋白亦可能产生抗体，提示这些蛋白可能具有重要的生理或病理作用。深入分析表明，S1 抗体水平与年龄和乳酸脱氢酶水平呈正相关，与淋巴细胞百分比（Ly%）呈现负相关，女性尤为显著。
基于该芯片的全面血清分析能有助于我们尽快揭示新冠病毒感染后不同人群的免疫反应规律。除此之外，该芯片还可用于但不限于以下方面：血清学分析、疫苗评估及病毒-宿主相互作用研究。
Abstract
COVID-19 is caused by SARS-CoV-2, and has become a global pandemic. There is no highly effective medicine or vaccine, most of the patients were recovered by their own immune response, especially the virus specific IgG and IgM responses. However, the IgG/ IgM responses is barely known. To enable the global understanding of SARS-CoV-2 specific IgG/ IgM responses, a SARS-CoV-2 proteome microarray with 18 out of the 28 predicted proteins was constructed. The microarray was applied to profile the IgG/ IgM responses with 29 convalescent sera. The results suggest that at the convalescent phase 100% of patients had IgG/ IgM responses to SARS-CoV-2, especially to protein N, S1 but not S2. S1 purified from mammalian cell demonstrated the highest performance to differentiate COVID-19 patients from controls. Besides protein N and S1, significant antibody responses to ORF9b and NSP5 were also identified. In-depth analysis showed that the level of S1 IgG positively correlate to age and the level of LDH (lactate dehydrogenase), especially for women, while the level of S1 IgG negatively correlate to Ly% (Lymphocyte percentage). This study presents the first whole picture of the SARS-CoV-2 specific IgG/ IgM responses, and provides insights to develop precise immuno-diagnostics, effective treatment and vaccine.

5. 恢复期病人免疫细胞单细胞测序

Immune Cell Profiling of COVID-19 Patients in the Recovery Stage by Single-Cell Sequencing
来源：medrxiv
发表时间：2020-3-27
链接：https://www.medrxiv.org/content/10.1101/2020.03.23.20039362v1
编译：雷颖

摘要：
目前在 COVID-19 患者中已观察到免疫系统失调，如淋巴细胞减少症和炎性细胞因子风暴，但尚不清楚关键免疫细胞亚群的变化及其在 COVID-19 期间的状态。本文应用单细胞技术全面描述了从 COVID-19 中恢复的 10 例患者外周血单核细胞的转录变化。与健康对照相比，COVID-19 诱导了人体免疫细胞的独特特征，尤其是在早期恢复阶段（ERS）。在 ERS 患者中，T 细胞显著减少，而单核细胞增加。对单核细胞的详细分析表明，具有高度炎症基因表达的经典 CD14 ++单核细胞比例增加，并且 CD14 ++/IL1B +单核细胞的丰度更高。对于自然杀伤（NK）细胞和 T 细胞，CD4 + T 细胞显著减少并表达高水平的炎症标志物，而 NK 细胞则增加。另外，T 细胞是高度扩增的克隆，尤其是在 CD4 + T 记忆细胞和 CD8 + T 细胞中。在 B 细胞中，浆细胞显著增加，幼稚 B 细胞减少。该研究还确定了几种新型 B 细胞受体（BCR）的变化（例如 IGHV1-8 和 IGHV3-7），并确认了以前用于病毒疫苗开发的同型受体（IGKV3-11 和 IGHV3-21）。最强的配对频率 IGHV3-23 + IGHJ4，表示与 SARS-CoV-2 特异性相关的单克隆状态。此外，综合分析表明，IL-1B 和 M-CSF 可能是炎性风暴的新型候选靶基因，而 TNFSF13，IL-18 和 IL-4 可能对 COVID-19 患者的康复有益。该研究提供了恢复初期炎症免疫特征的第一个证据，表明 COVID-19 患者出院后仍然很脆弱。而对新型 BCR 信号转导的鉴定可能可以用于开发治疗 COVID-19 的疫苗和抗体。

Abstract

COVID-19 caused by SARS-CoV-2 has recently affected over 200,000 people and killed more than 8000. Immune system dysregulation such as lymphopenia and inflammatory cytokine storm has been observed in COVID-19 patients, but it remains unclear for the change of key immune cell subsets and their states during COVID-19. Here, we applied single-cell technology to comprehensively characterize transcriptional changes of peripheral blood mononuclear cells in ten patients recovered from COVID-19. Compared with healthy control, COVID-19 induced a unique signature of immune cells in humans, especially in the early recovery stage (ERS). In ERS patients, T cells were decreased remarkably, while monocytes were increased. A detailed analysis of monocytes showed that there was an increased ratio of classical CD14++ monocytes with highly inflammatory genes expression, as well as a greater abundance of CD14++IL1B+ monocytes. For nature killer (NK) cells and T cells, CD4+ T cells were significantly decreased and expressed high level of inflammatory markers, while NK cells were increased. In addition, T cells were highly expanded clone, especially in CD4+ T memory cells and CD8+ T cells. Among B cells, plasma cells were increased remarkably, and naïve B cells were reduced. Our study also identified several novel B cell receptor (BCR) changes (such as IGHV1-8 and IGHV3-7), and confirmed isotypes (IGKV3-11 and IGHV3-21) previously used for virus vaccine development. The strongest pairing frequencies, IGHV3-23+IGHJ4, indicated a monoclonal state associated with SARS-CoV-2 specificity. Furthermore, integrated analysis predicated that IL-1B and M-CSF may be novel candidate target gene for inflammatory storm, and TNFSF13, IL-18 and IL-4 may be benefit for the recovery of COVID-19 patients. Our study provides the first evidence of inflammatory immune signature in early recovery stage, suggesting that the COVID-19 patients are still vulnerable after hospital discharge. Our identification of novel BCR signaling may lead to the development of vaccine and antibodies for the treatment of COVID-19.

6. 欧洲首批 COVID-19 病例的临床和病毒学数据：一个病例系列

Clinical and virological data of the first cases of COVID-19 in Europe: a case series

来源：THE LANCET

发布时间：2020-03-27

来源链接： https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30200-0/fulltext

编译:宋张悦

内容摘要：

背景：2019 年 12 月 31 日，中国报道了一组湖北省武汉市的肺炎病例。致病菌是一种新型冠状病毒，命名为严重急性呼吸综合征冠状病毒 2（SARS-CoV-2）。本文由来自法国巴黎大学、扎克·克劳德·伯纳德大学医院、波尔多大学医院、巴斯德研究所和法国里昂大学等的研究团队报道了欧洲第一批确诊感染 2019 年冠状病毒病（COVID-19）的相关特征，第一例患者于 2020 年 1 月 24 日被确诊感染。

方法：本研究收录的案例是 5 例经法国巴黎 Bichat-Claude-Bernard 大学医院和法国波尔多 Pellegrin 大学医院确诊的 COVID-19 患者，他们通过鼻咽拭子的半定量 RT-PCR 检测确诊。研究团队评估了临床疾病的类型和在不同样本（鼻咽和血液、尿液和粪便样本）中的病毒载量，这些样本在入院前 3 天内每天取一次，以后每 2-3 天取一次，直至出院。所有样本均冷藏运送至国家呼吸道病毒参考中心（National Reference Center，法国巴黎巴斯德研究所和里昂文明医院）的实验室，在那里进行 RNA 提取、实时 RT-PCR、病毒分离和滴定检测等实验。

结果：患者为 3 名男性（31 岁、48 岁和 80 岁）和 2 名女性（30 岁和 46 岁），均为华裔，于 2020 年 1 月中旬从中国前往法国。本研究描述了三种不同的临床进展类型：（1）两例无症状的妇女，她们在出现症状的一天内被诊断，在发病前 24 小时内，在鼻咽样本中能够检测到高滴度的 SARS-CoV-2 病毒（每 1000 个细胞中分别为 5.2 和 7.4 log10 个拷贝），并且在粪便样本中检测到了病毒的 RNA；（2） 两例年轻男子的两步疾病进展类型，在发病后约 10 天，尽管鼻咽样本中的病毒载量减少，但发生了第二次病情恶化；（3）一例 80 岁男性，快速发展为多器官衰竭，上、下呼吸道病毒载量持续增高，病毒传播至全身，在血浆中检测到了病毒。80 岁患者于发病第 14 天（2020 年 2 月 14 日）死亡，其余患者均于 2020 年 2 月 19 日康复出院。

解释：研究团队表示，他们用详细和全面的病毒取样策略描述了 5 例 SARS-CoV-2 感染者的三种不同的临床和生物学进化类型。他们相信，这些发现将有助于更好地了解该疾病的自然史，并将有助于在实施更有效的防控策略方面取得进展。

Background On Dec 31, 2019, China reported a cluster of cases of pneumonia in people at Wuhan, Hubei Province. The responsible pathogen is a novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We report the relevant features of the first cases in Europe of confirmed infection, named coronavirus disease 2019 (COVID-19), with the first patient diagnosed with the disease on Jan 24, 2020.

Methods In this case series, we followed five patients admitted to Bichat-Claude Bernard University Hospital (Paris, France) and Pellegrin University Hospital (Bordeaux, France) and diagnosed with COVID-19 by semi-quantitative RT-PCR on nasopharyngeal swabs. We assessed patterns of clinical disease and viral load

from different samples (nasopharyngeal and blood, urine, and stool samples), which were obtained once daily for 3 days from hospital admission, and once every 2 or 3 days until patient discharge. All samples were refrigerated and shipped to laboratories in the National Reference Center for Respiratory Viruses (The Institut Pasteur, Paris, and Hospices Civils de Lyon, Lyon, France), where RNA extraction, real-time RT-PCR, and virus isolation and titration procedures were done.

Findings The patients were three men (aged 31 years, 48 years, and 80 years) and two women (aged 30 years and 46 years), all of Chinese origin, who had travelled to France from China around mid-January, 2020. Three different clinical evolutions are described: (1) two paucisymptomatic women diagnosed within a day of exhibiting symptoms, with high nasopharyngeal titres of SARS-CoV-2 within the first 24 h of the illness onset (5·2 and 7·4 log10 copies per 1000 cells, respectively) and viral RNA detection in stools; (2) a two-step disease progression in two young men, with a secondary worsening around 10 days after disease onset despite a decreasing viral load in nasopharyngeal samples; and (3) an 80-year-old man with a rapid evolution towards multiple organ failure and a persistent high viral load in lower and upper respiratory tract with systemic virus dissemination and virus detection in plasma. The 80-year-old patient died on day 14 of illness (Feb 14, 2020); all other patients had recovered and been discharged by Feb 19, 2020.

Interpretation We illustrated three different clinical and biological types of evolution in five patients infected with SARS-CoV-2 with detailed and comprehensive viral sampling strategy. We believe that these findings will contribute to a better understanding of the natural history of the disease and will contribute to advances in the implementation of more efficient infection control strategies.

7. 对病毒入侵相关的宿主蛋白进行转录抑制可以作为 SARS-CoV-2 的治疗方案策略

Transcriptional Inhibition of Host Viral Entry Proteins as a Therapeutic Strategy for SARS-CoV-2

来源：preprint

发布时间：2020-03-24

链接:https://www.preprints.org/manuscript/202003.0360/v1

编译：蒋立春

作者对公开的基因表达数据进行了数据挖掘，找到了几个 FDA 批准的药物分子可以下调 TMPRSS2。有 20 个独立的研究提示雌激素和雄激素相关的药物分子可以调控 TMPRSS2 的表达，提示这些药物或者作用在这些通路的药物可能会是有潜力的治疗 COVID-19 的药物。值得注意的是 TMPRSS2 的表达在人群中表达量差异很大跨 2 个数量级，而且在少数人中表达量非常高。在 TMPRSS2 功能缺失可以保护小鼠对抗 SARS 而根据预测抗雌激素治疗增加 TMPRSS2 的表达会恶化 SARS 的症状。根据这些，我们提出 TMPRSS2 的表达和 COVID-19 的严重性呈正相关。

There is an urgent need to identify effective therapies for COVID-19 given that a broadly available and effective vaccine is likely at least one year away.

Here, we identify compounds that transcriptionally inhibit host proteins required for SARS-CoV-2 entry and should be evaluated for efficacy in SARS-CoV-2 viral infection assays. Recognizing the need for immediately available treatment options, we focused particular attention on FDA-approved drugs that could be immediately repurposed to treat COVID-19 patients. By mining publicly available gene expression data, we identify several compounds that down-regulate TMPRSS2, a protein required for SARS-CoV-2 entry that has emerged as a promising therapeutic target. Among these, we find twenty independent studies that implicate estrogen-related and androgen-related compounds as transcriptional modulators of TMPRSS2 expression, suggesting that these drugs and others acting on the pathway may be promising therapeutic candidates for COVID-19 for further testing. It is also noteworthy that TMPRSS2 has highly variable and skewed expression in humans, spanning two orders of magnitude with a small minority of individuals having extremely high expression. Combined with literature showing that TMPRSS2 loss-of-function in mouse is protective against SARS while anti-estrogen treatment predicted to increase TMPRSS2 expression exacerbates SARS, this observation raises the hypothesis that TMPRSS2 expression may positively correlate with severity in COVID-19.

8. 生物信息学分析快速鉴定出可以用于治疗 COVID-19 的老药

Advanced Bioinformatics Rapidly Identifies Existing Therapeutics for Patients with Coronavirus Disease - 2019

来源：chemrxiv

发布时间：2020-03-27

链接：

https://chemrxiv.org/articles/Advanced_Bioinformatics_Rapidly_Identifies_Existing_Therapeutics_for_Patients_with_Coronavirus_Disease_-_2019_COVID-19_/12037416/1

编译：蒋立春

此研究采用两种数据分析方法鉴定了治疗 COVID-19 的可能药物。第一种方法一个基于人工智能的亲和力预测平台对所有 FDA 批准的药物进行筛选，找出能和 ACE2 或者 TMPRSS2 结合的药物。在列表中排名最靠前的是几个 ACE 抑制剂、一个 β-内酰胺类抗生素、两个抗病毒药物 Fosamprenavir 和 Emricasan 以及谷胱甘肽。研究者们也利用这个 AI 筛选平台评估了药物对于 ACE2/ACE1 的特异性。

研究者们采用的第二个方法是一个叫做 DCT（Disease Cancelling Technology）的平台，预测药物分子对冠状病毒诱导的宿主基因表达变化的拮抗作用。我们将这个方法用于 SARS-CoV 动物模型的数据，将药物拮抗疾病相关的相关基因表达信号的能力进行排序。效果最显著的是维生素 E、ruxolitinib 以及谷氨酰胺。谷胱甘肽和它的前体谷氨酰胺在两种独立的方法中都是排名最靠前的药物分子，提示我们值得对它们进行进一步的研究。

The recent global pandemic has placed a high priority on identifying drugs to prevent or lessen clinical infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), caused by Coronavirus disease - 2019 (COVID-19). We applied two computational approaches to identify potential therapeutics. First, we sought to identify existing FDA approved drugs that could block coronaviruses

from entering cells by binding to ACE2 or TMPRSS2 using a high-throughput AI based binding affinity prediction platform. Top results included several ACE inhibitors, a beta-lactam antibiotic, two antiviral agents (Fosamprenavir and Emricasan) and glutathione. The platform also assessed specificity for ACE2 over ACE1, important for avoiding counter regulatory effects. Further studies are needed to weigh the benefit of blocking virus entry against potential counter regulatory effects and possible protective effects of ACE2. However, the data herein suggest readily available drugs that warrant experimental evaluation to assess potential benefit. Second, we sought to identify FDA approved drugs that could attenuate the gene expression patterns induced by coronaviruses, using our Disease Cancelling Technology (DCT) platform. DCT was run on an animal model of SARS-CoV, and ranked compounds by their ability to induce gene expression signals that counteract disease-associated signals. Top hits included Vitamin E, ruxolitinib, and glutamine. Glutathione and its precursor glutamine were highly ranked by two independent methods, suggesting both warrant further investigation for potential benefit against SARS-CoV-2. While these findings are not yet ready for clinical translation, this report highlights the potential use of two bioinformatics technologies to rapidly discover existing therapeutic agents that warrant further investigation for established and emerging disease processes.

9. 从海洋天然产物中筛选 SARS-CoV-2 的主要水解酶的抑制剂

Inhibitors of SARS-CoV-2 Main Protease from a Library of Marine Natural Products: A Virtual Screening and Molecular Modeling Study

来源：preprints

发布时间：2020-03-25

链接：https://www.preprints.org/manuscript/202003.0372/v1

编译：蒋立春

SARS-CoV-2 的主要水解酶是病毒生命周期中必需的酶，是一个优良的抗病毒药物靶点。意大利的研究者们用计算生物学中的分子动力学分析和蛋白质对接等方法对从一个海洋天然产物的库进行了筛选。他们在这个天然产物库中找到了 17 个可能抑制 SARS-CoV-2 主要蛋白酶的抑制剂。

The current emergency due to the worldwide spread of the COVID-19 caused by the new SARS-CoV-2 is a great concern for global public health. Already in the past, the outbreak of severe acute respiratory syndrome (SARS) in 2003 and Middle Eastern respiratory syndrome (MERS) in 2012 demonstrates the potential of coronaviruses to cross-species borders and further underlines the importance of identifying new-targeted drugs. An ideal antiviral agent should target essential proteins involved in the lifecycle of SARS-CoV. Currently, some HIV protease inhibitors (i.e., Lopinavir) are proposed for the treatment of COVID-19, although their effectiveness was not yet assessed. The main protease (Mpro) provides a highly validated pharmacological target for the discovery and design of inhibitors. We identified potent Mpro inhibitors employing computational techniques that entail the screening of a Marine Natural Product (MNP) library. MNP library was screened by hyphenated pharmacophore model, and molecular docking

approaches. Molecular dynamics and re-docking further confirmed the results obtained by structure-based techniques and allowed to highlight some crucial aspects. Seventeen potential SARS-CoV-2 Mpro inhibitors have been identified among the natural substances of marine origin. As these compounds were extensively validated by a consensus approach and by molecular dynamics, the likelihood that at least one of these compounds could be bioactive is excellent.

10. Caspofungin 和 LTX-315 通过抑制 nsp12(RdRP)抑制 SARS-CoV-2 的复制

Caspofungin and LTX-315 inhibit SARS-CoV-2 replication by targeting the nsp12 polymerase

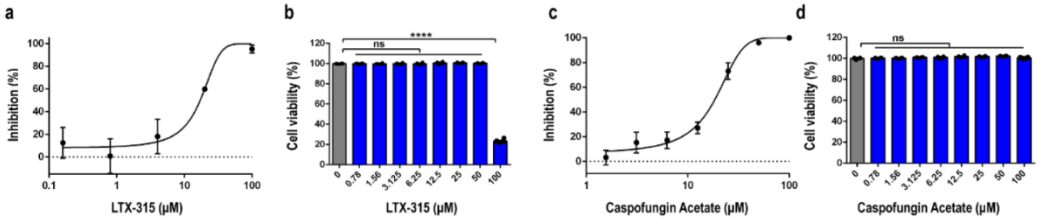
来源：researchsquare

发布时间：2020-03-27

链接：https://www.researchsquare.com/article/rs-19872/v1

编译：蒋立春

中科院微生物研究所根据 SARS-CoV 的 nsp12 也就是 RdRP 的结构（*）通过对 FDA 批准以及正在临床阶段的药物进行了虚拟筛选，得到两个潜在的抗病毒药物分子。分别是临床已经获批的抗真菌药物 Caspofungin Acetate (Cancidas)和处于临床二期的抗肿瘤的多肽 LTX-315。这两个药物在体外实验中都可以和 SARS-CoV-2 的 nsp12 蛋白结合并梯度依赖式抑制其多聚酶活性。活病毒实验也进一步证明这两种药物都可以抑制 SARS-CoV-2 在绿猴肾细胞（vero）中的复制。该研究提示这两个药物具有治疗 COVID-19 的潜力以及作为广谱性的抗冠状病毒的潜力。



LTX-315 和 Caspofungin Acetate 体外抑制病毒复制实验（a,c,病毒抑制曲线，b,d 是细胞毒性实验）

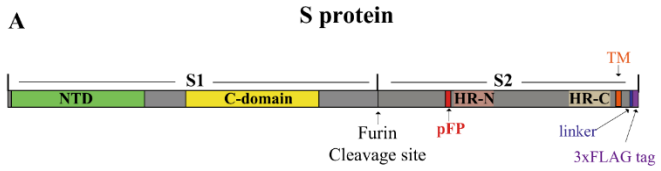
The ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, previously designated as 2019-nCoV) outbreak has caused global concern1. Currently, there are no clinically approved specific drugs or vaccines available for this virus. The viral polymerase is a promising target for developing broad- spectrum antiviral drugs. Here, based on the highly similar structure of SARS- CoV non-structural protein 12 (nsp12) polymerase subunit2, we applied virtual screen for the available compounds, including both the FDA-approved and under- clinic drugs, to identify potential antiviral molecules against SARS-CoV-2. We found two drugs, the clinically approved anti-fungi drug Caspofungin Acetate (Cancidas) and the oncolytic peptide LTX-315, can bind SARS-CoV-2 nsp12 protein to block the polymerase activity in vitro. Further live virus assay revealed that both Caspofungin Acetate and LTX-315 can

effectively inhibit SARS-CoV-2 replication in vero cells. These findings present promising drug candidates for treatment of related diseases and would also stimulate the development of pan- coronavirus antiviral agents.

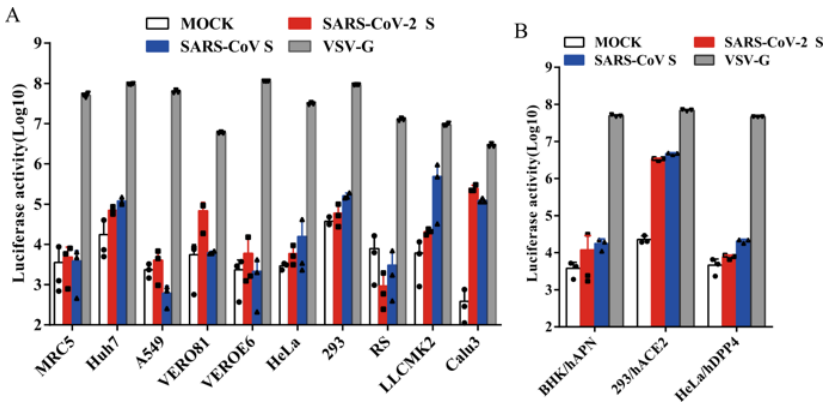
11. SARS-CoV-2 刺突蛋白入侵宿主细胞的特性及其与 SARS-CoV 的免疫交叉反应

来源：Nature Communications
发布时间：2020-03-27
链接：https://www.nature.com/articles/s41467-020-15562-9
编译:王玮
内容摘要：

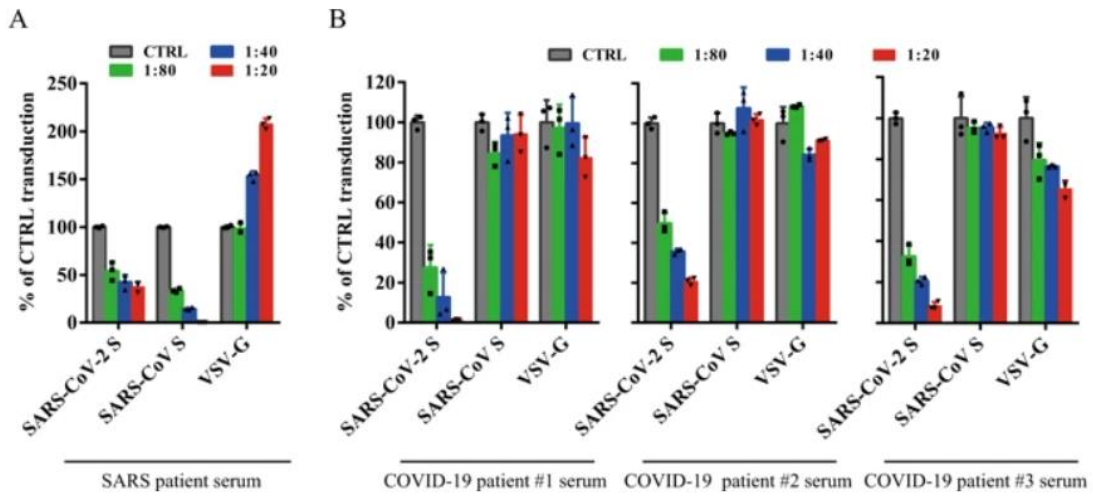
自 2002 年以来，β 冠状病毒（CoV）已导致三次人畜共患传染病的爆发，分别是 2002-2003 年的 SARS CoV，2012 年的 MERS CoV 和 2019 年底新出现的 SARS-CoV-2。但是，目前我们对 SARS-CoV-2 的生物学特性知之甚少。该研究利用含有 SARS-CoV-2 刺突蛋白（图一）的假病毒颗粒，比较了假病毒颗粒侵染不同细胞系（包括人，猴子和蝙蝠细胞系）的效率（图二），证实人类血管紧张素转换酶 2（hACE2）是 SARS-CoV-2 的受体，同时发现 SARS-CoV-2 主要通过内吞作用进入 293/hACE2 细胞，PIKfyve（Phosphatidylinositol 3-phosphate 5-kinase），TPC2（Two pore channel subtype 2）和 cathepsin L 是进入细胞的关键，SARS-CoV-2 刺突蛋白较 SARS-CoV 刺突蛋白不稳定，针对 SARS 刺突蛋白的多克隆抗体 T62 可抑制 SARS-CoV 的进入，但不能抑制含有 SARS-CoV-2 刺突蛋白的假病毒颗粒。利用 SARS 和 COVID-19 治愈患者的血清进行的进一步研究表明，两者之间的交叉中和作用有限（图三），这表明从一种病毒感染中恢复可能无法抵御另一种病毒感染。该研究还发现，即使没有胰蛋白酶，SARS-CoV-2 刺突蛋白也能在 293/hACE2 细胞上触发合胞体的形成，需要进一步研究该现象。该研究结果能够为 SARS-CoV-2 药物和疫苗的开发提供潜在的靶点。



图一 带有 3xFLAG 标签的全长 SARS-CoV-2 刺突蛋白图



图二 假病毒颗粒侵染不同细胞系的效率



图三 有限的 SARS 与 COVID-19 血清交叉中和作用

Abstract

Since 2002, beta coronaviruses (CoV) have caused three zoonotic outbreaks, SARS-CoV in 2002–2003, MERS-CoV in 2012, and the newly emerged SARS-CoV-2 in late 2019. However, little is currently known about the biology of SARS-CoV-2. Here, using SARS-CoV-2 S protein pseudovirus system, we confirm that human angiotensin converting enzyme 2 (hACE2) is the receptor for SARS-CoV-2, find that SARS-CoV-2 enters 293/hACE2 cells mainly through endocytosis, that PIKfyve, TPC2, and cathepsin L are critical for entry, and that SARS-CoV-2 S protein is less stable than SARS-CoV S. Polyclonal anti-SARS S1 antibodies T62 inhibit entry of SARS-CoV S but not SARS-CoV-2 S pseudovirions. Further studies using recovered SARS and COVID-19 patients' sera show limited cross-neutralization, suggesting that recovery from one infection might not protect against the other. Our results present potential targets for development of drugs and vaccines for SARS-CoV-2.

预告：香港科学家用金色叙利亚仓鼠模拟了 COVID-19 感染以及临床病理

其他快讯：

台湾科学家用计算生物学方法预测茶黄素（theaflavin）可以和 SARS-CoV-2 的 S 蛋白 RBD 有很好的结合，氢键在其中发挥重要作用。

The potential SARS-CoV-2 entry inhibitor

链接：https://www.biorxiv.org/content/10.1101/2020.03.26.009803v1

意大利和南非的医疗工作者通过对 59 个住院病人的问卷调查发现有接近 40%的病人有失去味觉和嗅觉中一种的症状。

Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study

链接：

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa330/5811989

德州大学最近的研究表明宿主的拓扑酶 III-beta 是所有正链 RNA 病毒复制所必须的，有可

能是一个潜在的抗病毒药物靶点
Topoisomerase III-beta is required for efficient replication of positive-sense RNA viruses
https://www.biorxiv.org/content/10.1101/2020.03.24.005900v1

武汉中南医院对 6 名 COVID 孕妇病患的新生儿体内的 IgG,IgM 抗体进行了检测
https://jamanetwork.com/journals/jama/fullarticle/2763854

第三军医大学对一个非重症但是带毒时间长达 49 的病人进行了研究，该病人自己无法清除病毒，但是康复病人的血清帮助该病人清除了病毒
A special case of COVID-19 with long duration of viral shedding for 49 days
https://www.medrxiv.org/content/10.1101/2020.03.22.20040071v1

军事医学科研院的医生发现高血压 COVID-19 病人使用 ARB 类高血压药物的获益
Anti-hypertensive Angiotensin II receptor blockers associated to mitigation of disease severity in elderly COVID-19 patients
https://www.medrxiv.org/content/10.1101/2020.03.20.20039586v1

复旦大学中山医院对武汉人民医院 47 位重症患者的数据进行回溯分析，发现乳酸脱氢酶可能是对 COVID-19 病人进行肺损失和发生重症的一个预测性指标
Lactate dehydrogenase, a Risk Factor of Severe COVID-19 Patients
https://www.medrxiv.org/content/10.1101/2020.03.24.20040162v1