新型冠状病毒信息简报

第 28 期（2020 年 4 月 15 日报）

上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

联系人：蒋立春 jianglch@shanghaitech.edu.cn

内容介绍

分类	标题名称
疫情播报	1. 2020 年 4 月 14 日疫情
疾病检测	2. 唾液检测 3. 在产妇中进行 SARS-CoV-2 的广泛筛查 4. 国家药监局审批试剂盒 5. 美国通过紧急使用授权批准的体外检测
流行病学	6. 新型冠状病毒在潮湿、干燥以及酸性条件下的稳定性
疾病病理	7. 中性粒细胞胞外陷阱（NETs）作为 COVID-19 疾病严重程度的标志
基础研究	8. SARS-CoV-2 里面极低的 CpG 和逃避宿主抗病毒防御可能的联系 9. 单核多组学分析揭示 SARS-CoV-2 感染相关宿主基因的年龄动态调控
药物研发	10. 获批药物治疗流感和 COVID19 相关研究的一种方法 --- 器官芯片 11. 在体外黄芩苷和黄芩素作为 SARS-CoV-2 3CL 蛋白酶新型天然产物抑制剂的发现 12. 没有证据表明羟氯喹在感染 COVID-19 需氧患者中的临床疗效：使用常规收集的数据模拟目标试验的研究结果 13. 羟氯喹在 COVID-19 患者中的应用：一项开放标签、随机、对照试验
疫苗研发	14. 转载：如果新冠疫苗真的上市了，人手一支可能吗？

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 4 月 14 日疫情

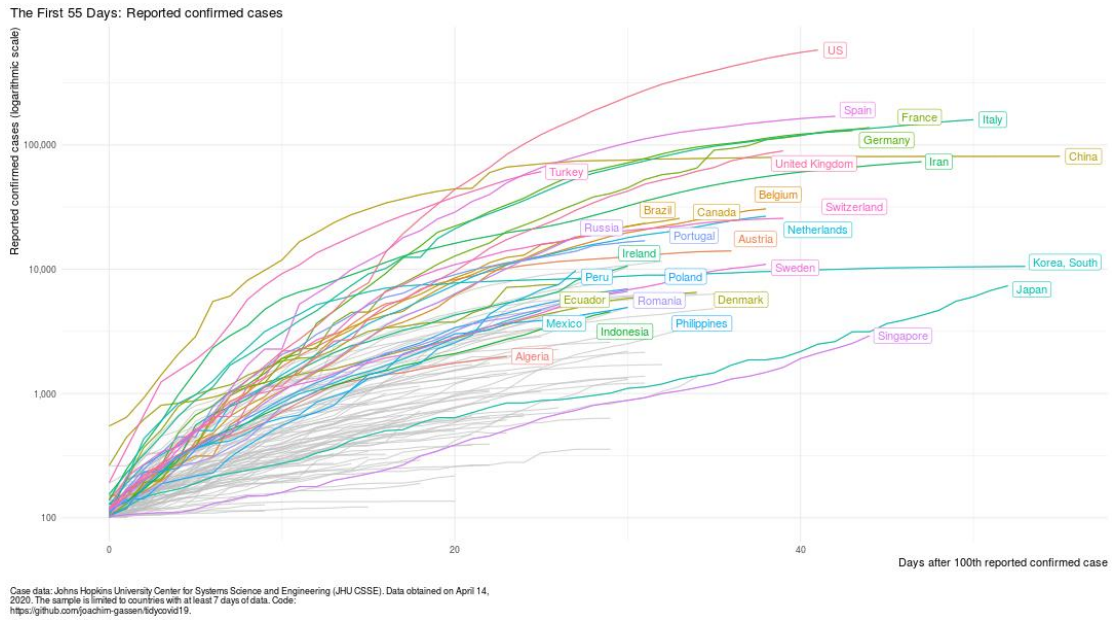
数据来源：WHO

发布时间：2020 年 4 月 14 日北京时间下午 4 点

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

根据 WHO 提供的数据，2020 年 4 月 14 日全球累计确诊新型冠状病毒病人 1844863 例，当日新增确诊 71779 例，累计死亡 117021 例，当日新增死亡 5369。

中国累计确诊 83696 例，累计死亡 3351 例，当日新增确诊 99 例，新增死亡 0 例。



重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止 4 月 14 日北京时间下午 4 点）

全国新型冠状病毒肺炎新增确诊病例分布图（4 月 14 日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 罗格斯大学的首个新冠病毒“唾液检测”获 FDA 紧急使用授权

A new Rutgers coronavirus test based on a simple spit into a tube will come to a N.J. testing site this week

来源：Rutgers University
发布时间：2020-04-14
链接：https://www.nj.com/coronavirus/2020/04/a-new-rutgers-coronavirus-test-based-on-a-simple-spit-into-a-tube-will-come-to-a-nj-testing-site-this-week.html
第一作者：Ted Sherman
通讯作者：
通讯作者单位：
DOI 或 PUBMED ID：
编译者：宋张悦
中文摘要：

美国罗格斯大学(Rutgers University)开发了一种新的 COVID-19 检测方法已经获得美国食品和药物管理局(Food and Drug Administration，简称 FDA)的紧急使用授权，预计最早将于本周三投入使用。该方法使用唾液样本，而不是鼻腔和咽喉拭子。该方法由 RUCDR 与 Spectrum Solutions 和 Accurate Diagnostic Labs 合作开发，极大地增加了可检测人数，它将比目前的鼻咽拭子和口咽拭子方法更能广泛地用于人群筛查。该方法于上周五获得了 FDA 的紧急使用授权。

这项检测意味着人们只需要把唾液吐到收集管里，而不是用棉签在鼻腔深处采集样本——目前的传统检测方法可能会让人感到不舒服，常常很痛，而且在全国范围内检测的范围有限。在此之前，RUCDR 推出了新冠病毒基因检测服务，每天可以检测数千个样本。随着新唾液检测方法的应用，这一数字可能会增加到每天数以万计的样本，为大规模 COVID-19 筛查提供了一条途径。

这些唾液样本将在罗格斯大学的实验室进行分析，该实验室也获得了美国食品和药物管理局(FDA)的审批。通过使用自动化实验室设备从采集的样本中进行“核提取”，该实验室将能够每天分析多达 1 万个样本。无论是通过拭子还是唾液，检测 COVID-19 的方法通常都是相同的，使用的是“标准 QPCR 方法”。

Abstract:

A new COVID-19 test developed at Rutgers University that uses saliva samples instead of nasal and throat swabs has gotten emergency approval by the Food and Drug Administration, and is expected to be put out into the field as early as Wednesday. The test will mean people will need only spit into a tube, rather than submit to swabbing deep into their nasal passages to obtain samples — the current conventional testing method that can be uncomfortable, often painful, and has limited testing nationwide. Officials said the saliva tests, coupled with a genetic testing service for the coronavirus also developed at Rutgers that can process thousands of samples daily, offering a route to large-scale testing that will be able to greatly increase the numbers of people screened for COVID-19.

RUCDR developed the collection method and a new lab method to greatly increase the number of tests that can be done, in partnership with Spectrum Solutions and Accurate Diagnostic Labs. The FDA granted emergency use authorization to RUCDR

and its partners for the saliva collection approach on Friday, which officials said was the first such approval granted by the federal agency. The saliva samples will be analyzed at a Rutgers lab, which also received FDA approval, and will be able to analyze as many as 10,000 samples daily, by using automated lab equipment to perform "nuclear extractions" from collected specimens. Whether by swab or saliva, the science for detecting COVID-19 is typically the same, utilizing what is known as "standard QPCR approaches."

Figure1. A saliva collection kit used to test for the coronavirus, which will allow people to spit into a tube, rather than submit to swabbing deep into their nasal passages to obtain samples for the detection of viral material. Photo courtesy of Spectrum Solutions

3. 在产妇中进行 SARS-CoV-2 的广泛筛查

Universal Screening for SARS-CoV-2 in Women Admitted for Delivery

来源：NEJM (to Editor)

发布时间：2020-04-13

链接：https://www.nejm.org/doi/full/10.1056/NEJMc2009316?query=featured_home

第一作者：Desmond Sutton, M.D.

通讯作者：Dena Goffman, M.D.

通讯作者单位：Columbia University Irving Medical Center, New York, NY

DOI 或 PUBMED ID：10.1056/NEJMc2009316

编译者：宋珂

中文摘要：

Covid-19 疫情在纽约市的迅速传播为产科的医护人员制造了特殊的挑战。由于产妇会大量接触卫生保健系统，大多数最终也会被送往医院分娩。作者于 2020 年 3 月 13 日首次在产妇中诊断出 Covid-19 病例，其中包括两名初期无症状的产妇。此后，便开始使用鼻咽拭子和 PCR 检测对待产孕妇进行广泛筛查。

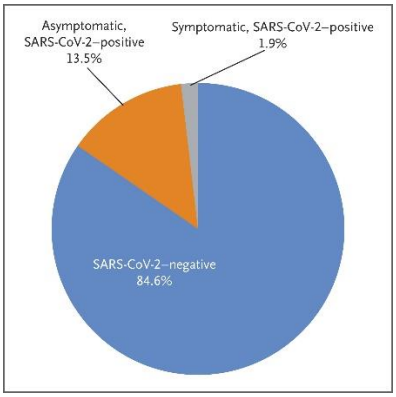
在 2020 年 3 月 22 日至 4 月 4 日间，共有 215 名孕妇在 New York-Presbyterian Allen

Hospital 和 Columbia University Irving Medical Center 分娩，这些产妇都进行了 Covid-19 筛查。入院时，四名孕妇（1.9%）出现发烧或其他 Covid-19 临床症状，其 SARS-CoV-2 检测均为阳性。211 名无症状（未发热）孕妇中，提取了 210 名（99.5%）的鼻咽拭子，其中 29 名（13.7%）的 SARS-CoV-2 检测呈阳性。因此，入院时有 87.9%（29/33）的孕妇表现为无症状的 Covid-19 感染者。

这 29 名无症状但 SARS-CoV-2 检测为阳性的孕妇中，有 3 例（10%）在产后出院前（中位住院时间为 2 天）出现发烧。其中 2 人因怀疑子宫内膜炎而接受了抗生素治疗（尽管 1 名患者没有局部症状）。另一人由于怀疑感染 Covid-19 而发烧，因而接受了支持治疗。一名入院时检测为阴性的孕妇在生产后出现了 COVID-19 症状，3 天后重复检测，结果转阳。

在当前纽约市 Covid-19 疫情严重的情况下，大多数无症状孕妇的 SARS-CoV-2 检测呈阳性。进入分娩部门时，超过 1/8 的产妇感染 SARS-CoV-2，却没有临床症状。尽管这只是纽约的数据，但也表现出产妇中存在无症状感染者的风险。另外，于检测假阴性的干扰，实际的感染率可能并不知晓。

通用对产妇进行 Covid-19 广泛筛查，确定医院隔离措施和床位分配，对新生儿护理和个人防护设备的使用进行指导，在此特殊时期，对婴儿、产妇和医护人员都非常重要。



Symptom Status and SARS-CoV-2 Test Results among 215 Obstetrical Patients Presenting for Delivery.

4. 国家药监局应急批准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：2020-04-14

来源链接：http://www.nmpa.gov.cn/WS04/CL2042/

编译：宋张悦

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	中山大学达安基因	国械注准

	（荧光 PCR 法）	股份有限公司	20203400063
6	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	圣湘生物科技股份有限公司	国械注准 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 20203400241
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
24	新型冠状病毒 2019-nCoV 核酸检测试剂盒（RNA 恒温扩增-金探针层析法）	武汉中帜生物科技股份有限公司	国械注准 20203400301
25	新型冠状病毒 2019-nCoV 核酸检测试剂盒（双扩增法）	武汉中帜生物科技股份有限公司	国械注准 20203400302
26	新型冠状病毒 2019-nCoV 核酸检测试剂盒（荧光 PCR 法）	北京金豪制药股份有限公司	国械注准 20203400322

27	新型冠状病毒（2019-nCoV）IgG 抗体检测试剂盒（磁微粒化学发光法）	丹娜（天津）生物科技有限公司	国械注准20203400365
28	新型冠状病毒（2019-nCoV）IgM 抗体检测试剂盒（磁微粒化学发光法）	丹娜（天津）生物科技有限公司	国械注准20203400366
29	新型冠状病毒(2019-nCoV)抗体检测试剂盒（胶体金法）	上海芯超生物科技有限公司	国械注准20203400367

5. 美国通过紧急使用授权批准的体外检测

https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

截止 2020 年 4 月 15 日美国 FDA 通过紧急使用授权的商业试剂盒一共有 33 个

Test Kit Manufacturers and Commercial Laboratories Table:

Search: Show 100 entries

Date EUA Issued	Manufacturer	Diagnostic (Letter of Authorization)	Technology	Authorized Setting(s)[1]	Authorization Documents[2]	Other Documents
04/10/2020	Atila BioSystems, Inc.	iAMP COVID-19 Detection Kit	Molecular	H	HCP, Patients, IFU	None
04/08/2020	DiaCarta, Inc	QuantiVirus SARS-CoV-2 Test kit	Molecular	H	HCP, Patients, IFU	None
04/08/2020	Becton, Dickinson & Company	BD SARS-CoV-2Reagents for BD MAX System	Molecular	H, M	HCP, Patients, IFU	None
04/07/2020	InBios International, Inc	Smart Detect SARS-CoV-2 rRT-PCR Kit	Molecular	H	HCP, Patients, IFU	None
04/06/2020	Gnomegen LLC	Gnomegen COVID-19 RT-Digital PCR Detection Kit	Molecular	H	HCP, Patients, IFU	None
04/03/2020	Co-Diagnostics, Inc.	Logix Smart Coronavirus Disease 2019 (COVID-19) Kit	Molecular	H	HCP, Patients, IFU	None
04/03/2020	ScienCell Research Laboratories	ScienCell SARS-CoV-2 Coronavirus Real-time RT-PCR (RT-qPCR) Detection Kit	Molecular	H	HCP, Patients, IFU	None
04/03/2020	Luminex Corporation	ARIES SARS-CoV-2 Assay	Molecular	H, M	HCP, Patients, IFU	None
04/02/2020	Becton, Dickinson & Company (BD)	BioGX SARS-CoV-2 Reagents for BD MAX System	Molecular	H, M	HCP, Patients, IFU	None
04/01/2020	Ipsum Diagnostics, LLC	COV-19 IDx assay	Molecular	H	HCP, Patients, EUA Summary	None
04/01/2020	Cellex Inc.	qSARS-CoV-2 IgG/IgM Rapid Test	Serology IgM and IgG	H, M	HCP, Patients, IFU	None
03/30/2020	QIAGEN GmbH	QIAstat-Dx Respiratory SARS-CoV-2 Panel	Molecular	H, M	HCP, Patients, IFU	None

03/30/2020	NeuMoDx Molecular, Inc.	NeuMoDx SARS-CoV-2 Assay	Molecular	H, M	HCP, Patients, IFU	None
03/27/2020	Luminex Molecular Diagnostics, Inc.	NxTAG CoV Extended Panel Assay	Molecular	H	HCP, Patients, IFU	None
03/27/2020	Abbott Diagnostics Scarborough, Inc.	ID NOW COVID-19	Molecular	H, M, W	HCP, Patients, IFU	None
03/26/2020	BGI Genomics Co. Ltd	Real-Time Fluorescent RT-PCR Kit for Detecting SARS-2019-nCoV	Molecular	H	HCP, Patients, IFU	None
03/25/2020	Avellino Lab USA, Inc.	AvellinoCoV2 test	Molecular	H	HCP, Patients, EUA Summary	None
03/24/2020	PerkinElmer, Inc.	PerkinElmer New Coronavirus Nucleic Acid Detection Kit	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (April 1, 2020)
03/23/2020	Mesa Biotech Inc.	Accula SARS-Cov-2 Test	Molecular	H, M, W	HCP, Patients, IFU	None
03/23/2020	BioFire Defense, LLC	BioFire COVID-19 Test	Molecular	H, M	HCP, Patients, IFU	None
03/20/2020	Cepheid	Xpert Xpress SARS-CoV-2 test	Molecular	H, M, W	HCP, Patients, IFU for Labs, IFU for Point-of-Care	Letter Granting EUA Amendment(s) (April 10, 2020)
03/20/2020	Primerdesign Ltd.	Primerdesign Ltd COVID-19 genesig Real-Time PCR assay	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (April 8, 2020)
03/19/2020	GenMark Diagnostics, Inc.	ePlex SARS-CoV-2 Test	Molecular	H, M	HCP, Patients, IFU	None
03/19/2020	DiaSorin Molecular LLC	Simplexa COVID-19 Direct assay	Molecular	H, M	HCP, Patients, IFU	• Letter Granting EUA Amendment(s) (March 26, 2020) • Letter Granting EUA Amendment(s) (April 13, 2020)
03/18/2020	Abbott Molecular	Abbott RealTime SARS-CoV-2 assay	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (April 1, 2020)
03/17/2020	Quest Diagnostics Infectious Disease, Inc.	Quest SARS-CoV-2 rRT-PCR	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (March 26, 2020)
03/17/2020	Quidel Corporation	Lyra SARS-CoV-2 Assay	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (April 8, 2020)
03/16/2020	Laboratory Corporation of America (LabCorp)	COVID-19 RT-PCR Test	Molecular	H	HCP, Patients, EUA Summary	None
03/16/2020	Hologic, Inc.	Panther Fusion SARS-CoV-2	Molecular	H	HCP, Patients, IFU	None
03/13/2020	Thermo Fisher Scientific, Inc.	TaqPath COVID-19 Combo Kit	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (March 24, 2020)
03/12/2020	Roche Molecular Systems, Inc. (RMS)	cobas SARS-CoV-2	Molecular	H, M	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (March 31, 2020)
02/29/2020	Wadsworth Center, New York State Department of Public Health's (CDC)	New York SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Panel	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (March 15, 2020)

02/04/2020	Centers for Disease Control and Prevention's (CDC)	CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel (CDC)	Molecular	H	HCP, Patients, IFU	Letter Granting EUA Amendment(s) (March 30, 2020)

值得注意的批准的场景（authorized setting）分为H,M以及W三类。

H - authorized for use in Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests.

M - authorized for use in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity and moderate complexity tests.

W - authorized for use in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity and moderate complexity tests, and deemed to be CLIA waived for use in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance.

另外美国FDA批准了12个CLIA实验室可以用实验室开发的方法开展新冠的特定检测项目。其中包括我们上一条简报里罗格斯大学开发的针对唾液的检测方法。

Date EUA Issued	Laboratory	Letter Granting Inclusion under EUA	EUA Summary	Other Documents
04/13/2020	Integrity Laboratories	SARS-CoV-2 Assay	EUA Summary	None
04/13/2020	Pathology/Laboratory Medicine Lab of Baptist Hospital Miami	COVID-19 RT-PCR Test	EUA Summary	None
04/10/2020	Orig3n, Inc.	Orig3n 2019 Novel Coronavirus (COVID-19) Test	EUA Summary	None
04/10/2020	Rutgers Clinical Genomics Laboratory-Rutgers University	ThermoFisher - Applied Biosystems TaqPath COVID-19 Combo Kit	EUA Summary	None
04/10/2020	Specialty Diagnostic (SDI) Laboratories	SDI SARS-CoV-2 Assay	EUA Summary	None
04/10/2020	University of North Carolina Medical Center	UNC Health SARS-CoV-2 real-time RT-PCR test	EUA Summary	None
04/08/2020	Stanford Health Care Clinical Virology Laboratory	Stanford SARS-CoV-2 assay	EUA Summary	None
04/06/2020	Viracor Eurofins Clinical Diagnostics	Viracor SARS-CoV-2 assay	EUA Summary	None
04/03/2020	Massachusetts General Hospital	MGH COVID-19 qPCR assay	EUA Summary	None
04/02/2020	Diagnostic Molecular Laboratory – Northwestern Medicine	SARS-Cov-2 Assay	EUA Summary	None
04/02/2020	Infectious Disease Diagnostics Laboratory - Children's Hospital of Philadelphia	SARS-CoV-2 RT-PCR test	EUA Summary	None
03/31/2020	Yale New Haven Hospital, Clinical Virology Laboratory	SARS-CoV-2 PCR test	EUA Summary	None

Showing 1 to 12 of 12 entries

Previous 1 Next

[1] The tests listed in this table are all molecular-based tests for COVID-19 and the authorized setting is for use in the identified laboratory that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high

另外，美国FDA网站也会持续更新获批产品、市场上假冒伪劣产品的相关消息。

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-

daily-roundup-april-14-2020

6. 新型冠状病毒在潮湿、干燥以及酸性条件下的稳定性

Stability of the COVID-19 virus under wet, dry and acidic conditions

来源：medrxiv

发布时间：2020-04-14

链接：https://www.medrxiv.org/content/10.1101/2020.04.09.20058875v1

第一作者：Zhi-ping Sun, Xia Cai

通讯作者：Di Qu, Youhua Xie, Zheng-hong Yuan

通讯作者单位：Chan Zuckerberg Initiative

DOI（预印本不需要，会变）：

编译者：蒋立春

中文摘要：

复旦大学的研究者发现新型冠状病毒感染性很高，一个空斑形成单位（PFU）就可以在体外系统感染 Vero-E6 细胞，只是发生感染需要的时间更长—72 小时，更高滴度的病毒只需要 24 小时就可以造成感染。研究者们还通过将病毒放入培养基里和滤纸上，检测病毒在室温条件下 经过 1 到 7 天后的感染性。两种条件下的病毒在 3 天之后都还保持着感染能力，只是在干燥条件下保存的病毒造成的致细胞病变效应（CPE）更弱。4 天之后两种条件保存的病毒不能导致细胞病变效应。研究还考察了病毒对酸性条件的容忍度，发现高滴度的病毒在模拟胃部环境的 ph2.2 的酸性条件下还可以存活至少一个小时。

PFU: plaque forming unit，空斑形成单位。感染性滴度的单位一般表示为 PFU/ml

CPE：致细胞病变效应（cytopathic effect，CPE）：指病毒在宿主细胞内大量增殖，导致细胞病变甚至死亡的现象。致细胞病变效应（cytopathic effect,CPE）:大多数动物病毒感染敏感细胞培养都能引起其显微表现改变

Using the strain nCoV-SH01 and these criteria, we first investigated the infectivity of the COVID-19 virus. We found that as the virus titer decreases (2000, 1000, 500, 250, 100, 50, 10, 5, and 1 PFU), the time for CPE to appear is delayed. One PFU is able to cause infection of Vero-E6 cells, resulting in obvious CPE at 72 hours, whereas higher titer of the virus induced CPE at 24 hours post inoculation (Table 1). It indicates that the COVID-19 virus is highly infectious, and underscores the challenge to control the spread of the COVID-19 virus.

We then studied the stability of the COVID-19 virus in the wet (in 100 uL culture medium) and dry (10 uL supernatant on filter paper) environments at room temperature (22℃) for 1, 2, 3, 4, 5, 6, 7 days respectively. Our results show that the COVID-19 virus can survive for 3 days in the wet or dry environment investigated in this study. Although the virus maintained its infectivity within 3 days in the dry condition, CPE appeared later than that kept in the wet environment, indicating that the dry environment may be less favorable for the survival of the COVID-19 virus (Table 2 & Table 3). However, when the virus had been kept in the wet or dry condition for more than 4 days, no CPE was observed (Table 2 & Table 3), which was confirmed by immune florescence staining (data

not shown) with the antibody against viral N protein as well as qRT-PCR. We further investigated the stability of the COVID-19 virus at pH2.2 condition. It shows that the COVID-19 virus has a certain degree of tolerance to acidic environment. In the present study, when 1.2 x 103 PFU of the COVID-19 virus were treated with acidic saline of pH2.2 for 30 or 60 minutes, it still resulted in CPE in the cells, whereas 1.0 x 103 PFU of the COVID-19 virus treated with pH2.2 saline for 30 or 60 minute, no CPE were observed (Table 4). It suggests under the acidic condition the COVID-19 virus at a relatively high titer can survive under acidic condition for at least 1 hour.

7. 中性粒细胞胞外陷阱（NETs）作为 COVID-19 疾病严重程度的标志

Neutrophil extracellular traps (NETs) as markers of disease severity in COVID-19

来源：medRxiv
发布时间：2020-04-15
链接：https://www.medrxiv.org/content/10.1101/2020.04.09.20059626v1
第一作者：Yu Zuo
通讯作者：Yogendra Kanthi 和 Jason S. Knight
通讯作者单位：密歇根大学
DOI 或 PUBMED ID：Preprint
编译者：张丽双
中文摘要：

在 2019 年冠状病毒病（COVID-19）的严重病例中，病毒性肺炎进展为呼吸衰竭。中性粒细胞胞外陷阱（NETs）是由染色质、杀菌蛋白和氧化酶组成的胞外网状结构，由中性粒细胞死亡后释放以控制感染。然而，如果调节不当，NETs 有可能促进炎症和微血管血栓，包括在急性呼吸窘迫综合征患者的肺部。虽然血中性粒细胞水平升高预示 COVID-19 的预后较差，但 NETs 的作用尚未被研究。作者发现 COVID-19 患者（患者数 n=50，样本数 n=84）血清中无细胞 DNA、髓过氧化物酶（MPO）DNA 和瓜氨酸化组蛋白 H3（Cit-H3）水平升高，后两个是 NETs 的高度特异性标记。这里强调了这些指标的临床相关性：无细胞 DNA 与急性期反应物（包括 C-反应蛋白、D-二聚体、乳酸脱氢酶）以及中性粒细胞绝对计数密切相关；MPO-DNA 与无细胞 DNA 和中性粒细胞绝对计数相关；而 Cit-H3 与血小板水平相关。重要的是，接受机械通气的住院患者的无细胞 DNA 和 MPO-DNA 均高于呼吸室内空气的住院患者。最后，COVID-19 患者的血清在体外引起了对照中性粒细胞的 NET 释放。总之，这些数据揭示了许多 COVID-19 患者体内高水平的 NETs，它们可能导致细胞因子释放和呼吸衰竭。今后的研究应探讨纵向人群中循环系统 NETs 的预测能力，并确定 NETs 在多大程度上可能作为严重 COVID-19 中新的治疗靶点。

Abstract:

In severe cases of coronavirus disease 2019 (COVID-19), viral pneumonia progresses to respiratory failure. Neutrophil extracellular traps (NETs) are extracellular webs of chromatin, microbicidal proteins, and oxidant enzymes that are released by neutrophils to contain infections. However, when not properly regulated, NETs have potential to propagate inflammation and microvascular thrombosis, including in the lungs of patients with acute respiratory distress

syndrome. While elevated levels of blood neutrophils predict worse outcomes in COVID-19, the role of NETs has not been investigated. We now report that sera from patients with COVID-19 (n=50 patients, n=84 samples) have elevated levels of cell-free DNA, myeloperoxidase(MPO)-DNA, and citrullinated histone H3 (Cit-H3); the latter two are highly specific markers of NETs. Highlighting the potential clinical relevance of these findings, cell-free DNA strongly correlated with acute phase reactants including C-reactive protein, D-dimer, and lactate dehydrogenase, as well as absolute neutrophil count. MPO-DNA associated with both cell-free DNA and absolute neutrophil count, while Cit-H3 correlated with platelet levels. Importantly, both cell-free DNA and MPO-DNA were higher in hospitalized patients receiving mechanical ventilation as compared with hospitalized patients breathing room air. Finally, sera from individuals with COVID-19 triggered NET release from control neutrophils in vitro. In summary, these data reveal high levels of NETs in many patients with COVID-19, where they may contribute to cytokine release and respiratory failure. Future studies should investigate the predictive power of circulating NETs in longitudinal cohorts, and determine the extent to which NETs may be novel therapeutic targets in severe COVID-19.

8. SARS-CoV-2 里面极低的 CpG 和逃避宿主抗病毒防御可能的联系

Extreme genomic CpG deficiency in SARS-CoV-2 and evasion of host antiviral defense

来源：Molecular Biology and Evolution

发布时间：2020-04-14

链接：https://academic.oup.com/mbe/article/doi/10.1093/molbev/msaa094/5819559

第一作者：Xuhua Xia

通讯作者：University of Ottawa

通讯作者单位：University of Ottawa

DOI（预印本不需要，会变）：https://doi.org/10.1093/molbev/msaa094

编译者：蒋立春

中文摘要：

包括蝙蝠在内的野生动物，是 SARS、MERS、SARS-CoV2 等 beta 冠状病毒的天然宿主。不同的宿主或者宿主组织提供不同的细胞环境，宿主不同的抗病毒活性以及 RNA 修饰活性会引起病毒 RNA 基因组的改变。抗病毒锌指蛋白（ZAP）可以特异性结合到病毒 RNA 基因组上 CpG 双核苷酸并且招募其他的蛋白来降解病毒的 RNA 基因组。很多哺乳动物里的 RNA 病毒都进化出 CpG 缺失的特征。在病毒锌指蛋白存在的条件下提高这些低 CpG 双核苷酸的病毒 RNA 基因组里的 CpG 会导致病毒复制减慢，毒力下降。因为抗病毒锌指蛋白的表达呈现组织特异性，研究者预期感染不同组织的病毒会呈现不同的 CpG 特征，这提示可以根据这个一点来判断病毒感染的组织是否发生了切换事件。研究者发现 SARS-CoV-2 在所有 beta 冠状病毒属里面 CpG 的缺失是最严重的。这提示 SARS-CoV-2 可能在一个 ZAP 表达量高的宿主里发生过进化。对病毒基因组的 CpG 缺失进行研究后，研究者发现一个有毒性的犬的冠状病毒（Alphacoronavirus）和 SARS-CoV-2 想比，有同样严重的 CpG 缺失。这提示犬的组织在被犬的冠状病毒感染后可以产生很强的对抗 CpG 的选择压力。着眼于病毒里 CpG 的降低，可以为我们研究病毒在原宿主中进化时遭遇的环境选择和抗病毒防御机制提供线索。

Abstract:
Wild mammalian species, including bats, constitute the natural reservoir of Betacoronavirus (including SARS, MERS, and the deadly SARS-CoV-2). Different hosts or host tissues provide different cellular environments, especially different antiviral and RNA modification activities that can alter RNA modification signatures observed in the viral RNA genome. The zinc finger antiviral protein (ZAP) binds specifically to CpG dinucleotides and recruits other proteins to degrade a variety of viral RNA genomes. Many mammalian RNA viruses have evolved CpG deficiency. Increasing CpG dinucleotides in these low-CpG viral genomes in the presence of ZAP consistently leads to decreased viral replication and virulence. Because ZAP exhibits tissue-specific expression, viruses infecting different tissues are expected to have different CpG signatures, suggesting a means to identify viral tissue-switching events. I show that SARS-CoV-2 has the most extreme CpG deficiency in all known Betacoronavirus genomes. This suggests that SARS-CoV-2 may have evolved in a new host (or new host tissue) with high ZAP expression. A survey of CpG deficiency in viral genomes identified a virulent canine coronavirus (Alphacoronavirus) as possessing the most extreme CpG deficiency, comparable to that observed in SARS-CoV-2. This suggests that the canine tissue infected by the canine coronavirus may provide a cellular environment strongly selecting against CpG. Thus, viral surveys focused on decreasing CpG in viral RNA genomes may provide important clues about the selective environments and viral defenses in the original hosts.
编者注：
作者为研究 SARS-CoV-2 的中间天然宿主的溯源提供了新的线索。但是文章中和犬的相关性，需要进一步的研究以确认犬是否以及如何在 SARS-CoV-2 的进化、传播中扮演角色。

9. 单核多组学分析揭示 SARS-CoV-2 感染相关宿主基因的年龄动态调控

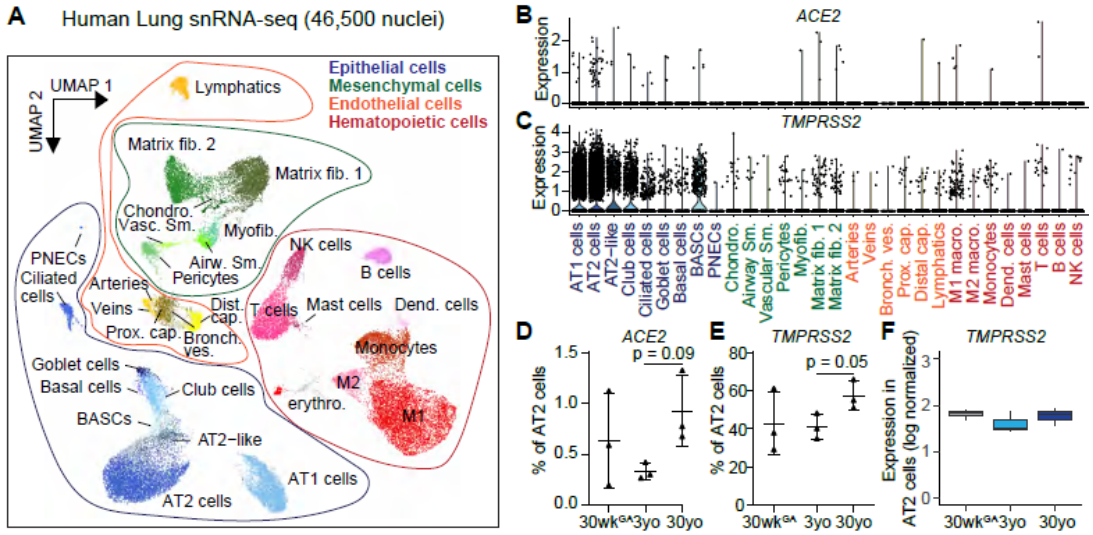
Single Nucleus Multiomic Profiling Reveals Age-Dynamic Regulation of Host Genes Associated with SARS-CoV-2 Infection
来源：biorxiv
发布时间：2020-04-14
链接：https://www.biorxiv.org/content/10.1101/2020.04.12.037580v1
第一作者： Allen Wang, Joshua Chiou, Olivier B Poirion, Justin Buchanan
通讯作者： Xin Sun，Sebastian Preissl，Kyle J Gaulton，Allen Wang
通讯作者单位： 加州大学圣迭戈分校
DOI 或 PUBMED ID：
编译者：王玮

中文摘要：
呼吸衰竭是 COVID-19 患者死亡的主要原因，对成人的影响比儿童更大。该文章展示了一组人类肺的大规模单核测序数据集，包括 snATAC-seq 数据集（90980 个核）和 snRNA-seq 数据集（46500 个核），该测序数据集来自 9 个健康捐赠者，可分成三组年龄组：30 周，~3 岁和~30 岁，每组各包含三个捐赠者，包含男性和女性。关注 SARS-CoV-2 进入宿主细胞相关

基因，该研究发现成人肺泡上皮细胞表达 ACE2（p value = 0.09）和 TMPRSS2（p value =0.05）的比例较幼年肺有所增加（图一）。与表达动力学一致，10 个与 TMPRSS2 相关的染色质峰随着年龄的增加活性显著增加，包含 IRF 和 STAT 结合位点。此外，该研究在随着年龄增长的染色质峰中发现了 14 个可能具有调节功能的常见序列变异，调节作用包括呼吸相关特性和 TMPRSS2 表达。该研究发现揭示了为什么儿童对 COVID-19 不易感的一个可能的原因，并为将这种不易感性转移到更加年长的人群提供了表观遗传学基础。

编者注

该文章的 snRNA-seq 数据集中仅有极少数细胞核（共 80 个细胞核）检测到了 ACE2 转录本。



图一 snRNA-seq of human lungs reveals expression of SARS-CoV-2 cell entry genes in the epithelial cell lineage. A UMAP embedding and clustering result of 46,500 snRNA-seq data from 9 donors (Premature born (30 weekGA of pregnancy), 3 yo, 30 yo; n = 3 per time point) identifies 31 clusters. Each dot represents a nucleus. Spread-out grey dots correspond to nuclei of unclassified cluster. B, C Cluster specific violin blots of gene expression of B ACE2 and C TMPRSS2. D, E Fraction of AT2 cells with expression of ACE2 and TMPRSS2 at each time point. All data are represented as mean ± SD. p values derived from t-tests; One-way ANOVA did not reach significance. F Box plot of log normalized expression of TMPRSS2 in AT2 cells at each time point. Displayed are the median expression values for AT2 nuclei in individual samples with at least 1 UMI.

Abstract

Respiratory failure is the leading cause of COVID-19 death and disproportionately impacts adults more than children. Here, we present a large-scale snATAC-seq dataset (90,980 nuclei) of the human lung, generated in parallel with snRNA-seq (46,500 nuclei), from healthy donors of ~30 weeks, ~3 years and ~30 years of age. Focusing on genes implicated in SARS-CoV-2 cell entry, we observed an increase in the proportion of alveolar epithelial cells expressing ACE2 and TMPRSS2 in adult compared to young lungs. Consistent with expression dynamics, 10 chromatin

peaks linked to TMPRSS2 exhibited significantly increased activity with age and harbored IRF and STAT binding sites. Furthermore, we identified 14 common sequence variants in age-increasing peaks with predicted regulatory function, including several associated with respiratory traits and TMPRSS2 expression. Our findings reveal a plausible contributor to why children are more resistant to COVID-19 and provide an epigenomic basis for transferring this resistance to older populations.

10. 获批药物治疗流感和 COVID19 相关研究的一种方法 --- 器官芯片

Human organs-on-chips as tools for repurposing approved drugs as potential influenza and COVID19 therapeutics in viral pandemics

来源：bioRxiv
发布时间：2020.04.13
链接：https://www.biorxiv.org/content/10.1101/2020.04.13.039917v1
第一作者：Long long Si
通讯作者：Donald E. Ingber,
通讯作者单位：Wyss Institute for Biologically Inspired Engineering at Harvard University
DOI 或 PUBMED ID：Preprint
编译者：孔娟
中文摘要：
文中研究者首次利用器官芯片—人气道芯片微流体培养装置，研究了 7 种临床获批的广谱抗病毒药物(氯喹、阿比朵尔、托瑞米芬、氯米芬、阿莫地喹、维拉帕米和胺碘酮)对 SARS-CoV-2 病毒侵入细胞的抑制作用。该芯片包含两个平行的微通道，由细胞外基质包被的多孔膜隔开。原代人肺气道基底干细胞在“气道通道”中的膜一侧的气液界面(ALI)下生长，与相对侧的原代人肺内皮细胞接触，并暴露于平行“血管通道”内的连续液体流中，通过连续灌注的方法进行培养。此外，研究发现气道细胞在 ALI 芯片上的分化伴随着 SARS-CoV-2 受体、ACE2、TMPRSS2 及 TMPRSS4 蛋白酶表达水平的显著上升。鉴于这些特征，人气道芯片更能有效地模拟人体内病毒入侵及对抗流感的免疫应答环境。
首先研究者在人 Huh-7 细胞模型中验证了假病毒颗粒 SARS-CoV-2pp 对细胞感染的有效性，同时在该细胞模型中对 7 种药物的抗病毒效果进行了评价，结果显示 7 种药物在人 Huh-7 细胞水平均呈现剂量依赖性的抑制假病毒颗粒 SARS-CoV-2pp 对细胞的感染。然而，在人体气道芯片模型中，在人体血液中的最大浓度 Cmax 连续灌注 48h 这些更具临床相关性的给药条件下，只有阿莫地喹和托瑞米芬显示出对病毒感染具有显著抑制作用。当以临床相关剂量给药时，发现阿比朵尔没有显著抑制 SARS-CoV-2pp 进入人气道芯片，而在静态条件下，阿比朵尔在 Huh-7 细胞中抑制作用较为明显。同时氯喹在人体气道芯片中以其最大剂量给药时，并没有产生统计学上显著的抑制作用。
这项研究表明，人体器官芯片技术可以与现有的基于细胞的快速筛选试验联合使用，以助力于抗 COVID19 药物的快速研发。
Abstract:
Rapidly spreading viral pandemics, such as those caused by influenza and SAR-CoV-2 (COVID19), require rapid action and the fastest way to combat this challenge is by repurposing existing drugs as anti-viral therapeutics. Here we first show

that human organ-on-a-chip (Organ Chip) microfluidic culture devices lined by a highly differentiated, primary, human lung airway epithelium cultured under an air-liquid interface and fed by continuous medium flow can be used to model virus entry, replication, strain-dependent virulence, host cytokine production, and recruitment of circulating immune cells in response to infection by influenza, as well as effects of existing and novel therapeutics. These Airway Chips, which contain human lung epithelial cells that express high levels of ACE2 and TMPRSS2, were then used to assess the inhibitory activities of 7 clinically approved drugs (chloroquine, arbidol, toremifene, clomiphene, amodiaquine, verapamil, and amiodarone) that we found inhibit infection by viral pseudoparticles expressing SARS-CoV-2 spike protein in human Huh-7 cells, and others recently showed suppress infection by native SARS-CoV-2 in Vero cells. However, when these drugs were administered under flow at the maximal concentration in blood reported in clinical studies in human Airway Chips, only two of these drugs amodiaquine and toremifene significantly inhibited entry of the pseudotyped SARS-CoV-2 virus. This work suggests that human Organ Chip technology may be used in conjunction with existing rapid cell-based screening assays to study human disease pathogenesis and expedite drug repurposing in biothreat crises caused by pandemic viruses.

11. 在体外黄芩苷和黄芩素作为 SARS-CoV-2 3CL 蛋白酶新型天然产物抑制剂的发现

Discovery of baicalin and baicalein as novel, natural product inhibitors of SARS-CoV-2 3CL protease in vitro

来源：bioRxiv

发布时间：2020-04-13

链接：https://www.biorxiv.org/content/10.1101/2020.04.13.038687v1

第一作者：Haixia Su

通讯作者：许叶春，叶阳，Yan Wu, 白芳

通讯作者单位：上海药物所，上海药物所，中国科学院武汉病毒学研究所，上海科技大学免疫化学研究所

DOI 或 PUBMED ID：Preprint

编译者：张鹏伟

中文摘要：

类 3C 蛋白酶（3CLpro）是冠状病毒复制所必需的一种高度保守的蛋白酶，是广谱抗病毒药物开发的重要靶点。为了加快药物的发现和开发速度，作者研究了中药天然产物对 SARS-CoV-23clpro 的抑制作用。黄芩苷和黄芩素是 SARS-CoV-2 3CLpro 的第一个非共价、非拟肽抑制剂，在细胞系统中具有很强的抗病毒活性。X 射线蛋白晶体学测定黄芩素与 SARS-CoV-2 3CLpro 的结合方式与已知抑制剂的结合方式明显不同。黄芩素通过与两个催化残基（关键的 S1/S2 亚基和氧阴离子环）相互作用，完美地包裹在底物结合袋的核心，在催化二元体前起到“屏蔽”作用，防止肽底物接近活性位点。黄芩素化学结构简单，作用方式独特，体外抗病毒活性强，加上临床试验的良好安全性数据，为开发急需的抗冠状病毒药物提供了巨大的机遇。

Abstract:

Human infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-

2) cause coronavirus disease 19 (COVID-19) and there is currently no cure. The 3C-like protease (3CLpro), a highly conserved protease indispensable for replication of coronaviruses, is a promising target for development of broad-spectrum antiviral drugs. To advance the speed of drug discovery and development, we investigated the inhibition of SARS-CoV-2 3CLpro by natural products derived from Chinese traditional medicines. Baicalin and baicalein were identified as the first non-covalent, non-peptidomimetic inhibitors of SARS-CoV-2 3CLpro and exhibited potent antiviral activities in a cell-based system. Remarkably, the binding mode of baicalein with SARS-CoV-2 3CLpro determined by X-ray protein crystallography is distinctly different from those of known inhibitors. Baicalein is perfectly ensconced in the core of the substrate-binding pocket by interacting with two catalytic residues, the crucial S1/S2 subsites and the oxyanion loop, acting as a “shield” in front of the catalytic dyad to prevent the peptide substrate approaching the active site. The simple chemical structure, unique mode of action, and potent antiviral activities in vitro, coupled with the favorable safety data from clinical trials, emphasize that baicalein provides a great opportunity for the development of critically needed anti-coronaviral drugs.

12. 没有证据表明羟氯喹在感染 COVID-19 需氧患者中的临床疗效：使用常规收集的数据模拟目标试验的研究结果

No evidence of clinical efficacy of hydroxychloroquine in patients hospitalized for COVID-19 infection with oxygen requirement: results of a study using routinely collected data to emulate a target trial

来源：medRxiv
发布时间：2020-04-14
链接：https://www.medrxiv.org/content/10.1101/2020.04.10.20060699v1
第一作者：Matthieu Mahévas
通讯作者：Nathalie Costedoat-Chalumeau
通讯作者单位：法国巴黎大学流行病学和统计研究中心
DOI 或 PUBMED ID：Preprint
编译者：雷颖
中文摘要：
背景：迫切需要恰当的治疗来预防 COVID-19 引起的呼吸衰竭和死亡。近期羟氯喹（HCQ）由于在小型研究中的正面结果而受到了世界各地的关注。
方法：作者从 4 家法国医院中收集了所有患 SARS-CoV-2 肺炎并需要输氧≥2 升/min 的成人的常规护理数据，来模拟一项旨在评估 600 毫克/天 HCQ 的有效性的试验。主要终点是 7 天内转移到重症监护病房（ICU）和/或任何原因死亡。根据治疗加权的逆概率对混杂因素进行了调整。
结果：本研究共有 181 例 SARS-CoV-2 肺炎患者，84 例在入院 48 小时内接受 HCQ（HCQ 组），97 例未接受 HCQ（NO-HCQ 组）。最初的严重程度在两组之间得到了很好的平衡。在加权分析中，20.2%的 HCQ 组患者在 7 天内被转移到 ICU 或死亡，无 HCQ 组为 22.1%（16 例对 21 例，相对风险[R R]为 0.91，95% CI 为 0.47-1.80）。HCQ 组有 2.8%的患者在 7 天内死亡，无 HCQ 组为 4.6%（3 例对 4 例，RR 为 0.61，95% CI 为 0.13-2.89），27.4%和 24.1%的患者在 7 天

内出现急性呼吸窘迫综合征（24 例对 23 例，RR 为 1.14，95% CI 为 0.65-2.00）。接受 HCQ 的 8 例患者（9.5%）发生了心电图改变，需要停止 HCQ。
解释：这些结果不支持在被确诊为 SARS-CoV-2 阳性的低氧性肺炎的患者中使用 HCQ。
Abstract
Background: Treatments are urgently needed to prevent respiratory failure and deaths from coronavirus disease 2019 (COVID-19). Hydroxychloroquine (HCQ) has received worldwide attention because of positive results from small studies.
Methods: We used data collected from routine care of all adults in 4 French hospitals with documented SARS-CoV-2 pneumonia and requiring oxygen ≥ 2 L/min to emulate a target trial aimed at assessing the effectiveness of HCQ at 600 mg/day. The composite primary endpoint was transfer to intensive care unit (ICU) within 7 days from inclusion and/or death from any cause. Analyses were adjusted for confounding factors by inverse probability of treatment weighting.
Results: This study included 181 patients with SARS-CoV-2 pneumonia; 84 received HCQ within 48 hours of admission (HCQ group) and 97 did not (no-HCQ group). Initial severity was well balanced between the groups. In the weighted analysis, 20.2% patients in the HCQ group were transferred to the ICU or died within 7 days vs 22.1% in the no-HCQ group (16 vs 21 events, relative risk [RR] 0.91, 95% CI 0.47-1.80). In the HCQ group, 2.8% of the patients died within 7 days vs 4.6% in the no-HCQ group (3 vs 4 events, RR 0.61, 95% CI 0.13-2.89), and 27.4% and 24.1%, respectively, developed acute respiratory distress syndrome within 7 days (24 vs 23 events, RR 1.14, 95% CI 0.65-2.00). Eight patients receiving HCQ (9.5%) experienced electrocardiogram modifications requiring HCQ discontinuation.
Interpretation: These results do not support the use of HCQ in patients hospitalised for documented SARS-CoV-2-positive hypoxic pneumonia.

13. 羟氯喹在 COVID-19 患者中的应用：一项开放标签、随机、对照试验

Hydroxychloroquine in patients with COVID-19: an open-label, randomized, controlled trial
来源：medRxiv
发布时间：2020-04-
链接：https://www.medrxiv.org/content/10.1101/2020.04.10.20060558v1
第一作者：Wei Tang, Zhujun Cao, Mingfeng Han, Zhengyan Wang
通讯作者：瞿介明，宁光，时国朝，谢青
通讯作者单位：瑞金医院
DOI 或 PUBMED ID：Preprint
编译者：雷颖
中文摘要：
目的：评价羟氯喹（HCQ）加上标准护理（SOC）与单纯 SOC 相比对成人 COVID-19 患者的疗效和安全性。
设计：多中心，开放标签，随机对照试验。在 2020 年 2 月 11 至 29 日在中国设立 16 个政府指定的 COVID-19 治疗中心。参与者为 150 名 COVID-19 住院患者。将 75 例患者分配给 HCQ 加 SOC，75 例单独分配给 SOC（对照组）。HCQ 干预的剂量为每日 1,200 毫克，持续三天，然后接下来的剂量为每日 800 毫克（总治疗时间：轻度/中度或重度患者分别为 2 或 3 周）。

主要结果指标：主要终点为 SARS-CoV-2 的 28 天阴性转化率。评估的次要终点为第 4 天、第 7 天、第 10 天、第 14 天或第 21 天的阴性转化率、28 天内临床症状改善率、C 反应蛋白正常化和血淋巴细胞计数正常。主要和次要分析旨在治疗。不良事件用来评估人群安全。
结果：SOC 加 HCQ 和 SOC 组 28 天的阴性转化率差异不大（Kaplan-Meier 估计为 85.4%对 81.3%，P=0.341）。 第 4、7、10、14 或 21 天的阴性转化率在两组之间也是相似的。两组 28 天症状缓解率无差异。在 HOC 后分析中，当去除抗病毒药物的混杂效应时，HCQ 对缓解症状有显著的疗效（危险比为 8.83，95% CI 为 1.09~71.3）。CRP 的大量减少进一步支持这一点（6.986 在 SOC 加上 HCQ，而 2.723 在 SOC，毫克/升，P=0.045），这也导致了更快的淋巴细胞减少的恢复，尽管没有统计意义。不良事件发生在 8.8%的 SOC 和 30%的 HCQ 接受者中，有两个严重的不良事件。最常见的不良事件是腹泻（10%）。
结论：在未接受抗病毒治疗的 COVID-19 住院患者中，HCQ 的给药不会导致较高的阴性转换率，但比 SOC 更能缓解临床症状，可能是通过抗炎作用。不良事件在 HCQ 接受者中显著增加，但严重不良事件没有明显增加。临床试验注册号 ChiCTR2000029868。

Abstract

Objectives: To assess the efficacy and safety of hydroxychloroquine (HCQ) plus standard-of-care (SOC) compared with SOC alone in adult patients with COVID-19.
Design: Multicenter, open-label, randomized controlled trial. Setting 16 government-designated COVID-19 treatment centers in China through 11 to 29 in February 2020. Participants 150 patients hospitalized with COVID-19. 75 patients were assigned to HCQ plus SOC and 75 were assigned to SOC alone (control group).
Interventions HCQ was administrated with a loading dose of 1, 200 mg daily for three days followed by a maintained dose of 800 mg daily for the remaining days (total treatment duration: 2 or 3 weeks for mild/moderate or severe patients, respectively).
Main outcome measures: The primary endpoint was the 28-day negative conversion rate of SARS-CoV-2. The assessed secondary endpoints were negative conversion rate at day 4, 7, 10, 14 or 21, the improvement rate of clinical symptoms within 28-day, normalization of C-reactive protein and blood lymphocyte count within 28-day. Primary and secondary analysis was by intention to treat. Adverse events were assessed in the safety population.
Results: The overall 28-day negative conversion rate was not different between SOC plus HCQ and SOC group (Kaplan-Meier estimates 85.4% versus 81.3%, P=0.341). Negative conversion rate at day 4, 7, 10, 14 or 21 was also similar between the two groups. No different 28-day symptoms alleviation rate was observed between the two groups. A significant efficacy of HCQ on alleviating symptoms was observed when the confounding effects of anti-viral agents were removed in the post-hoc analysis (Hazard ratio, 8.83, 95%CI, 1.09 to 71.3). This was further supported by a significantly greater reduction of CRP (6.986 in SOC plus HCQ versus 2.723 in SOC, milligram/liter, P=0.045) conferred by the addition of HCQ, which also led to more rapid recovery of lymphopenia, albeit no statistical significance. Adverse events were found in 8.8% of SOC and 30% of HCQ recipients with two serious adverse events. The most common adverse event in the HCQ recipients was diarrhea (10%).
Conclusions: The administration of HCQ did not result in a higher negative

conversion rate but more alleviation of clinical symptoms than SOC alone in patients hospitalized with COVID-19 without receiving antiviral treatment, possibly through anti-inflammatory effects. Adverse events were significantly increased in HCQ recipients but no apparently increase of serious adverse events. Trial registration ChiCTR2000029868.

14. 转载：如果新冠疫苗真的上市了，人手一支可能吗？

来源：Nature 自然科研 微信公众号

原文作者：Roxanne Khamsi

内容概述：

该评论讲到产能制约和囤积行为可能会限制 SARS-CoV-2 疫苗的全球供应，面临的各种问题以及可能的解决方案。

翻译链接：https://mp.weixin.qq.com/s?__biz=MzAwNTAyMDY0MQ==&mid=2652568880&idx=1&sn=cf8e3eb86ac55c8e8ca566cb18749402&chksm=80cd53beb7badaa88094716fbcda6b7df5f03de54c965de8f560c9129869a327c91b85f4e37f&scene=126&sessionid=1586924476&key=b88f41026479d4a2ecdd9fd584b76b652ebda0765058a8ee4135d5817e0235a5898b2ddc49d95fc74e056ac1a3fc77d4ec98e2c077de7268118c74941a0757ed0d07eb879eea988b339ef01b35c906ef&ascene=1&uin=MjgxMjY4NjgxNQ%3D%3D&devicetype=Windows+10&version=62080085&lang=zh_CN&exportkey=A1vr2wAhcmq9q%2FUy4u6LIO8%3D&pass_ticket=uB7YCjHSuUuvcLTjVuH%2BlChwYc8d7bFauOnAxJcTZXFuGwKIO1Sl%2BIXBd3TTl%2F2Nhttps://www.nature.com/articles/d41586-020-01063-8

Original article：https://www.nature.com/articles/d41586-020-01063-8