新型冠状病毒信息简报

第 41 期（2020 年 4 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领衔编译制作

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1. 2020 年 4 月 27 日疫情

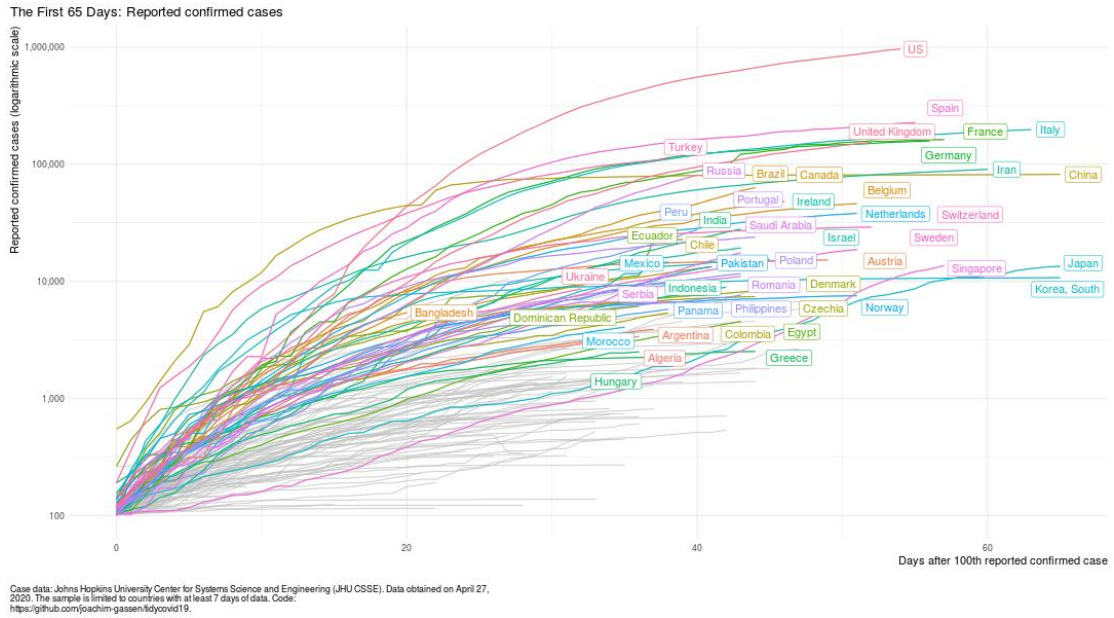
数据来源：WHO

发布时间：2020 年 4 月 27 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 27 日全球累计确诊新型冠状病毒病人 2878196 例，当日新增确诊 85530 例，累计死亡 198668 例，当日新增死亡 4982。

中国累计确诊 84341 例，累计死亡 4643 例，当日新增确诊 3 例，新增死亡 1 例。



重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止 4 月 27 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27日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. SARS-CoV-2 的宿主内变异特征可以提高基因组系统发育图的重新构建，可能可以揭示功能趋同突变

Characterization of intra-host SARS-CoV-2 variants improves phylogenomic reconstruction and may reveal functionally convergent mutations

来源：biorxiv
发布时间：2020-04-26
链接：https://www.biorxiv.org/content/10.1101/2020.04.22.044404v1
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DOI：
编译者：蒋立春
中文摘要：

来自全球不同领域的科学家们都在努力研究 SRAS-CoV-2 病毒突变的特征，并且建立可靠的关于病毒传播的模型。在这方面，受益于公共数据库里猛增的序列数据，基因组学系统发育方法可以通过将积累的基因组突变当作标签追溯病毒的进化史。尽管在单一宿主中时常有发现病毒呈现复杂的亚型结构（一个病人可能有多种序列有差异的病毒），目前做基因组学系统发育方法主要依赖于宿主中占到主要地位的病毒株系。另外，在当前状况下，大多数国家中病毒测序抽样具有很大的局限性，大多数方法由于不考虑突变的累计过程也可能得出不准确的分析结果。

研究者们介绍了一个全新的框架研究 SARS-CoV-2 的病毒亚型进化和传播，借用了癌症进化研究里面的克隆性以及宿主内部次要的变异来解释数据里的突变累积和不确定性（Figure 1）。作者们将该方法运用到 18 个可以拿到原始测序数据的 SARS-CoV-2 样品（编者注：虽然公共数据库里已经有 1 万多条公开的病毒全基因组序列，原始数据却很少），揭示了一个精度高的基因组系统发育模型。该模型证明了最近关于病毒分析的发现，并对该发现进行了进一步改进。这个研究强调存在次要变异的共存模式，该方法可以帮助推测在具有同一个病毒株系的病人间的可能感染路径。作者的研究证明从次要变异来看，SARS-CoV-2 的基因组多样性随着时间明显增加。当数据集的取样非常有限时，不考虑次要变异的标准方法可能会遇到麻烦。

这个框架可以找出的那些在病毒不同亚型里受到正向选择的次要变异以及病毒基因组里受到净化选择的区域，这些可以指导抗病毒治疗和疫苗开发。作者们发现，可以在其他独立数据集中验证一个在多个病毒谱系发现的次要变异 g.29039A>U，该次要变异导致 SARS-CoV-2 失去核衣壳蛋白上的一个主要抗原表位，提示靶向该蛋白 C 端的疫苗有效性可能会出现问题。该研究框架和数据驱动的流行病学模型相结合，可以提供一个高度准确的病毒发现、监测和分析的平台。

该研究中涉及到的代码：https://github.com/BIMIB-DISCo/SARS-CoV-2-IHMV

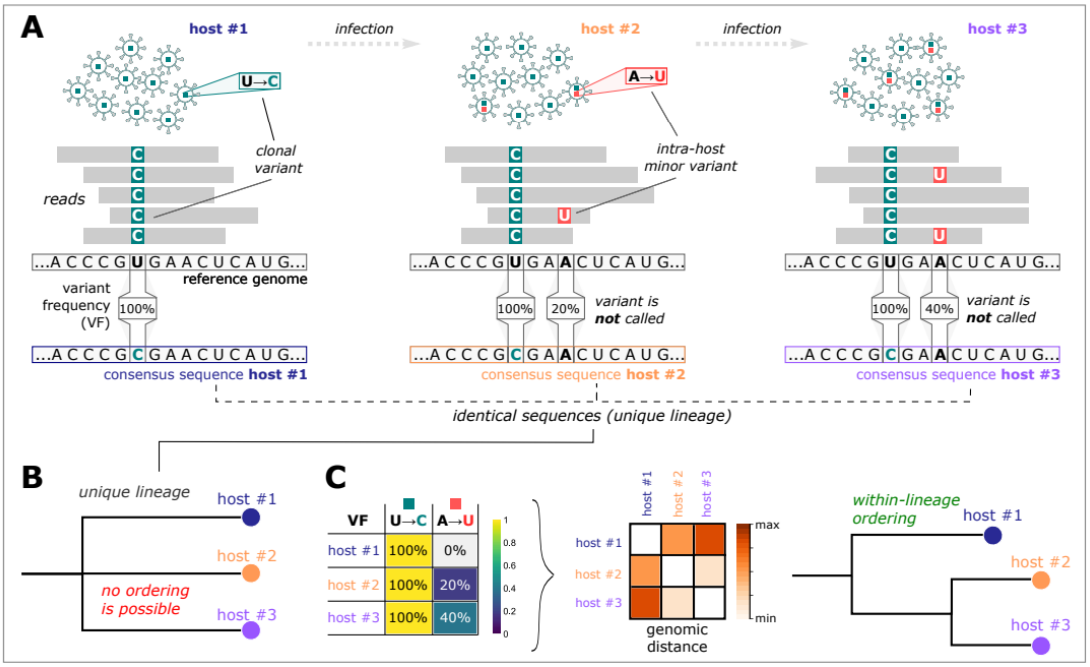
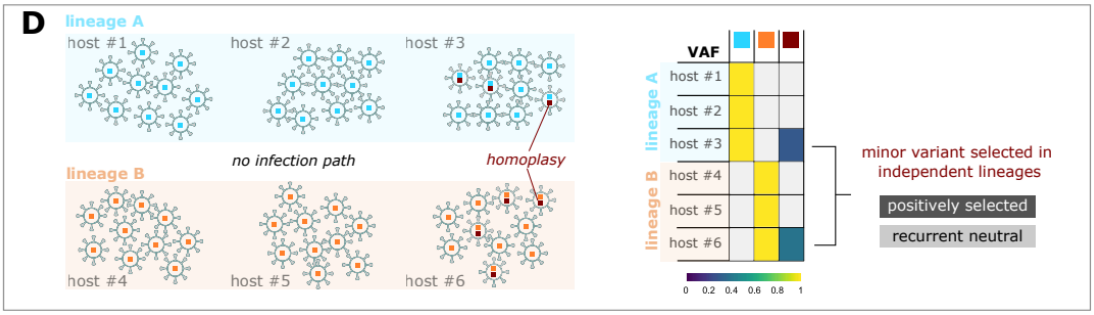
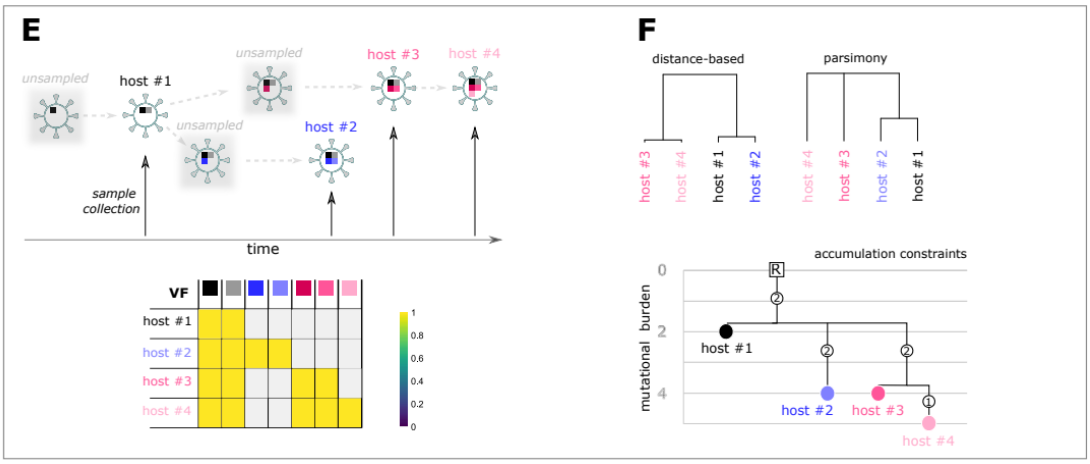


Figure 1: (Sub)lineage evolution and transmission of viral genomes. (A) In this toy example, three hosts infected by the same viral lineage are sequenced. In particular, all hosts share the same clonal mutation (U/C, green), but two of them (#2 and #3) are characterized by a distinct minor mutation (A/U, red), which randomly emerged in host #2 and was transferred to host #3 during the infection. Standard sequencing experiments return an identical consensus RNA sequence for all samples, by employing a threshold on variant frequency (VF) and by selecting mutations characterizing the dominant lineage. (B) By analyzing identical sequences, standard phylogenetic algorithms cannot disentangle any ordering or evolutionary relation among hosts infected by the same viral lineage. (C) By considering the VF distribution, it is possible to compute a refined genomic distance among hosts, as well as to identify a higher-resolution ordering within hosts infected by the same viral lineage, which may indicate possible transmission paths (in the example, we show a distance-based dendrogram).



(D) In this second toy example, 6 infected hosts infected by two independent viral lineages are shown. An individual of each lineage (#3 and #6) display the same minor variant (dark red), which might indicate homoplasy. By analyzing the VF profile of all samples, it is possible to pinpoint such variant, which either is positively selected or recurrent neutral.



(E) In this example, the branched evolution of 7 viral lineages is displayed (for simplicity all shown mutations are clonal and no sublineages are considered). 4 infected hosts harboring distinct clonal variants are tested and sequenced during the epidemics, revealing a typical scenario affected by sampling limitations. (F) From sequencing data of such hosts, distance-based and parsimony phylogenetic methods might return partial or incorrect evolutionary trees. By employing methods that account for mutation accumulation, the correct evolutionary model is inferred. In this representation, each sample is a leaf of the tree, positioned at a level corresponding to its mutational burden, whereas edges starting from the root R are labeled with the number of accumulating mutations. In the example, host #1 is parent of host #2 and #3, and the latter is a parent of host #4.

Abstract:
A global cross-discipline effort is ongoing to characterize the evolution of SARS-CoV-2 virus and generate reliable epidemiological models of its diffusion. To this end, phylogenomic approaches leverage accumulating genomic mutations as barcodes to track the evolutionary history of the virus and can benefit from the surge of sequences deposited in public databases. Yet, such methods typically rely on consensus sequences representing the dominant virus lineage, whereas a complex sublineage architecture is often observed within single hosts.
Furthermore, most approaches do not account for variants accumulation processes and might produce inaccurate results in condition of limited sampling, as witnessed in most countries currently affected by the epidemics. We here introduce a new framework for the characterization of viral (sub)lineage evolution and transmission of SARS-CoV-2, which considers both clonal and intra-host minor variants and exploits the achievements of cancer evolution research to account for mutation accumulation and uncertainty in the data. The application of our approach to 18 SARS-CoV-2 samples for which raw sequencing data are available reveals a high-resolution phylogenomic model, which confirms and improves recent findings on viral types and highlights the existence of patterns of co-occurrence of minor variants, uncovering likely infection paths among hosts harboring the same viral lineage. Our findings confirm a significant increase of genomic diversity of SARS-CoV-2 in time, which is reflected in minor variants, and show that standard methods may struggle when handling datasets with important

sampling limitations. Importantly, our framework allows to pinpoint minor variants that might be positively selected across distinct lineages and regions of the viral genome under purifying selection, thus driving the design of treatments and vaccines. In particular, minor variant g.29039A>U, detected in multiple viral lineages and validated on an independent dataset, shows that SARS-CoV-2 can lose its main Nucleocapsid immunogenic epitopes, raising concerns about the effectiveness of vaccines targeting the C-terminus of this protein. To conclude, we advocate the use of our framework in combination with data-driven epidemiological models, to deliver a high-precision platform for pathogen detection, surveillance and analysis.

3. 英国生物银行队列研究中的 SARS-CoV2 感染的种族和社会经济差异

Ethnic and socioeconomic differences in SARS-CoV2 infection in the UK Biobank cohort study

来源：medrxiv

发布时间：2020-04-27

链接：https://www.medrxiv.org/content/10.1101/2020.04.22.20075663v1

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编译者：王玮

中文摘要：

背景：对种族和社会经济地位在 SARS-CoV-2 感染风险中的作用的了解有限。该研究根据英国生物银行的数据，对此进行了调查研究。

方法：英国生物银行在 2006-2010 年间招募了 40-70 岁的居民，收集关于他们自我定义的种族和社会经济变量（包括汤森剥夺指数（Townsend deprivation index）和教育程度）的信息。将英国公共卫生部的 SARS-CoV-2 检测结果与英国生物库的基线数据相关联。采用 Poisson 回归和稳健的标准误差来评估暴露和二分法变量之间的风险比（RRs）：被测、测试阳性和住院测试阳性。该研究还调查了种族和社会经济地位是否与受试者的测试阳性相关。该研究调整了协变量，包括年龄、性别、社会变量（包括医疗工作和家庭规模）、行为风险因素和基线健康。

调查结果：在 428225 名参与者中，有 1474 人在 2020 年 3 月 16 日至 4 月 13 日期间接受了检测，669 人呈阳性，其中 572 人住院期间接受了测试呈阳性，表明病情更严重。与英国白人相比，黑人、南亚人和爱尔兰白人更容易确诊感染（RR 4.01（95%CI 2.92-5.12）；RR 2.11（95%CI 1.43-3.10）；RR 1.60（95%CI 1.08-2.38），更容易住院。同时发现，检测的更多，更容易检测出阳性。对基础健康和行为风险因素的调整导致的变化很小，仅在考虑社会经济变量时略有减弱。**区域社会经济剥夺和没有学历与确诊感染的高风险相关**（RR 1.91（95%ci1.53-2.38）；RR 2.26（95%ci1.76-2.90）。

解释说明：在英国生物银行的研究中，**一些少数的种族群体（南亚和爱尔兰白人）被证实感染 SARS-CoV-2 的风险更高**，且并不是由社会经济条件、测量的基线健康或行为风险因素的差异造成的。需要紧急应对这些高风险。

Abstract:

Background: Understanding of the role of ethnicity and socioeconomic position in the risk of developing SARS-CoV-2 infection is limited. We investigated this in the UK Biobank study.

Methods: The UK Biobank study recruited 40-70 year olds in 2006-2010 from the general population, collecting information about self-defined ethnicity and socioeconomic variables (including Townsend deprivation index and educational attainment). SARS-CoV-2 test results from Public Health England were linked to baseline UK Biobank data. Poisson regression with robust standard errors was used to assess risk ratios (RRs) between the exposures and dichotomous variables for: being tested, having a positive test and testing positive in hospital. We also investigated whether ethnicity and socioeconomic position were associated with having a positive test amongst those tested. We adjusted for covariates including age, sex, social variables (including healthcare work and household size), behavioural risk factors and baseline health.

Findings: Among 428,225 participants, 1,474 had been tested and 669 had tested positive between 16 March and 13 April 2020. Black, south Asian and white Irish people were more likely to have confirmed infection (RR 4.01 (95%CI 2.92-5.12); RR 2.11 (95%CI 1.43-3.10); and RR 1.60 (95% CI 1.08-2.38) respectively) and were more likely to be hospitalised compared to White British. While they were more likely to be tested, they were also more likely to test positive. Adjustment for baseline health and behavioural risk factors led to little change, with only modest attenuation when accounting for socioeconomic variables. Area socioeconomic deprivation and having no qualifications were consistently associated with a higher risk of confirmed infection (RR 1.91 (95%CI 1.53-2.38); and RR 2.26 (95%CI 1.76-2.90) respectively).

Interpretation: Some minority ethnic groups have a higher risk of confirmed SARS-CoV-2 infection in the UK Biobank study which was not accounted for by differences in socioeconomic conditions, measured baseline health or behavioural risk factors. An urgent response to addressing these elevated risks is required.

4. 武汉两所医院中 SARS-CoV-2 的空气动力学分析

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals

来源：转发“Nature 自然科研（微信公众号）”内容

发布时间：2020-04-28（微信公众号发布时间）

链接：https://www.nature.com/articles/s41586-020-2271-3 （原文）

中文摘要：

今日《自然》发表的一项研究 Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals 证明空气中存在 SARS-CoV-2 RNA。对武汉两家医院和部分公共区域的环境监测揭示了存在空气传播病毒 RNA 的热点区域，但是 SARS-CoV-2 RNA 是否具有感染潜力尚未得到评估。虽然样本量不大（31 个位点，取样样本不到 40 份），但是这一发现印证了之前的观点，即仔细保持卫生清洁、保持良好的通风、避免聚集可以降低空气传播病毒暴露的风险。

已报道的 SARS-CoV-2 RNA 传人模式包括：与感染者密切接触；接触被污染的表面；吸入感染者呼吸系统释放的飞沫。SARS-CoV-2 是否有可能经由空气进一步传播，则不甚明确。

2020 年 2 月至 3 月，中国武汉大学的蓝柯及同事在两家新冠肺炎定点治疗医院的内部和周围设置了气溶胶捕捉装置，一个是接收重症患者的三甲医院，另一个是接收轻症患者的方仓医院（由体育场改造而成）。在通风的病区，空气传播的病毒 RNA 浓度总体非常低，作者将此归因于有效的隔离和空气交换效率高；病人用的厕所没有通风，病毒 RNA 浓度则较高。作者发现在医护人员脱解防护装置的地方，病毒 RNA 浓度尤其高，这意味着在防护装置去除之后，含病毒的气溶胶可以再次悬浮在空气中。但是，在增加清洁消毒的强度和频率之后，在医护人员区域并未发现可检测到的空气传播 SARS-CoV-2 RNA 的证据。

在医院之外的公共区域，如居民住宅和超市，SARS-CoV-2 RNA 的浓度整体不高。但是，在两个有大规模人群通过的地方，包括靠近上述其中一座医院的室外空地，SARS-CoV-2 RNA 的浓度依然较高。作者认为这些拥挤区域内感染了 SARS-CoV-2 的个体可能促成了病毒气溶胶的产生。

这项研究没有调查 SARS-CoV-2 RNA 是否可能具有传染性，而且疫情高峰时期医院进出受限，限制了可取的样本数量。尽管如此，这项研究支持通过彻底消杀潜在的含病毒气溶胶热点区域、保持医院通风良好、避免聚集以降低感染风险的做法。

5. COVID-19 的影像学特征：中国专家的共识声明

Imaging of coronavirus disease 2019: A Chinese expert consensus statement

来源：European Journal of Radiology
发布时间：2020-04-18
链接：
https://www.sciencedirect.com/science/article/pii/S0720048X20301972?via%3Dihub
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DOI 或 PUBMED ID：10.1016/j.ejrad.2020.109008
编译者：宋珂
文章亮点：

- 在声明中，作者综述了 COVID-19 肺炎的病状，临床诊断和典型的影像学特征。
- 作为 RT-PCR 测试的补充，胸部 CT 在诊断中起到了重要作用。
- COVID-19 肺炎的不同病程具有不同的影像学特征。

中文摘要：

COVID-19 具有高度的传染性，主要造成肺部炎症性病变，同时还可能对肠道和肝脏造成损伤。导致 COVID-19 肺炎的冠状病毒的快速传播，给全球的公共卫生带来了复杂的挑战。及早发现，隔离，诊断和治疗是当前预防和控制疫情的最有效手段。目前，中国国内的新型冠状病毒感染的流行趋势已得到控制。然而，在世界许多地区，疫情的发展仍处于快速上升时期。目前对 COVID-19 诊断的金标准是冠状病毒核酸检测。但是，影像诊断在检测肺部病变，分级，评估治疗方案以及区分混合感染方面具有重要作用。这份中国专家的共识性声明总结

了 COVID-19 肺炎的影像学特征，可能会有助于世界各地的放射科医生更好地了解这种疾病。

Abstract:
Coronavirus disease 2019 (COVID-19) is highly contagious, mainly causing inflammatory lesions in the lungs, and can also cause damage to the intestine and liver. The rapid spread of the virus that causes coronavirus disease 2019 (COVID-19) pneumonia has posed complex challenges to global public health. Early detection, isolation, diagnosis, and treatment are the most effective means of prevention and control. At present, the epidemic situation of new coronavirus infection has tended to be controlled in China, and it is still in a period of rapid rise in much of the world. The current gold standard for the diagnosis of COVID-19 is the detection of coronavirus nucleic acids, but imaging has an important role in the detection of lung lesions, stratification, evaluation of treatment strategies, and differentiation of mixed infections. This Chinese expert consensus statement summarizes the imaging features of COVID-19 pneumonia and may help radiologists across the world to understand this disease better.

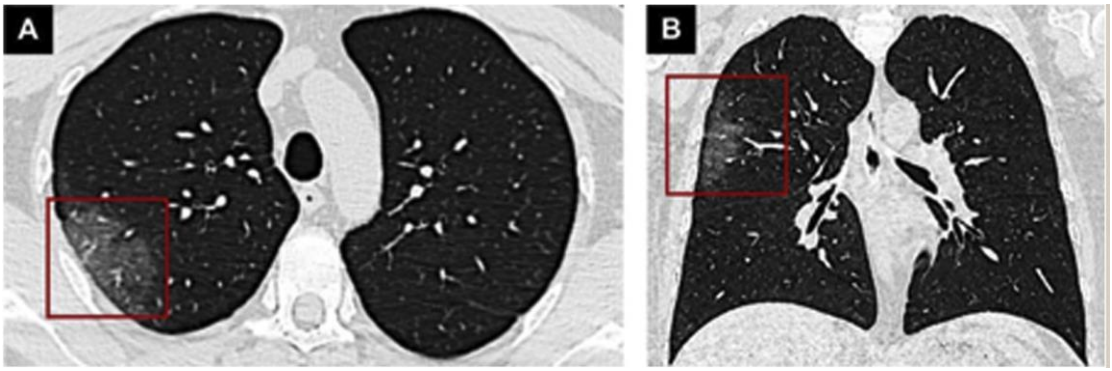

Fig. 1. CT findings of early-stage COVID-19. A 36-year-old male with a history of close contact with comfirmed cases. Fever had been present for six days. Chest CT shows a unilateral pure GGO (ground glass opacity) lesion (red rectangles) in the posterior segment of the right upper lobe on axial (A) and coronal view (B).

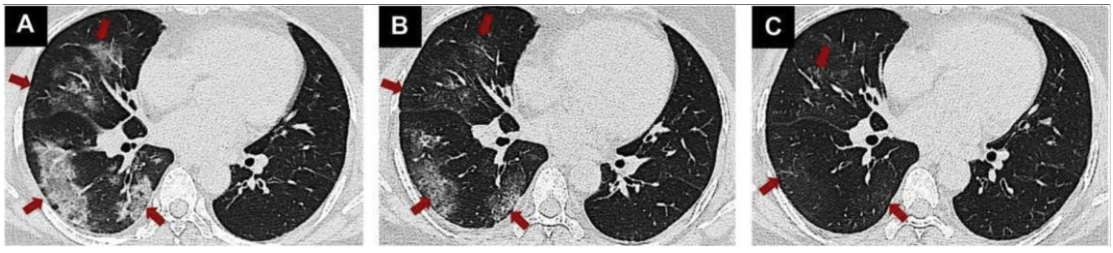

Fig. 6. Temporal lung changes of a 56-year-old female with COVID-19. After three days of fever, lung findings on coronal non-contrast chest CT were multiple consolidations and patchy GGOs located in the subpleural area in the middle and lower lobes of the right lung (A, red arrows). Follow-up chest CT images obtained after one (B) and two (C) weeks show absorption of lesions (red arrows) with a gradual decrease in extent and density.

6. SARS-CoV-2 体外检测的市售方法和实验室开发方法在临床实验室中的比较

Comparison of Commercially Available and Laboratory Developed Assays for in vitro Detection of SARS-CoV-2 in Clinical Laboratories

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第一作者：Joshua A. Lieberman
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DOI：https://doi.org/10.1101/2020.04.24.20074559
编译者：张怡

中文摘要：
为了满足 SARS-CoV-2 大流行的诊断需求，出现了多种实验室开发的测试和商业检测方法。迄今为止，这些不同测试平台的比较数据有限。文中针对 169 支鼻咽拭子样本，比较了在我们临床实验室中开发的基于 CDC 引物集的实验室检测方法（LDT，laboratory developed test）和四种市售的获 FDA 紧急使用授权的 SARS-CoV-2 检测（Cepheid,DiaSorin,Hologic Panther,Roche Cobas）的性能。LDT 和 Cepheid Xpert Xpress 的 SARS-CoV-2 检测是对 SARS-CoV-2 的最灵敏检测，样本之间的一致性为 100%。Hologic Panther Fusion,DiaSorin Simplexa 和 Roche Cobas 6800 只是在基于 CDC 的 LDT 分析检测极限附近检测不到阳性样本。通过使用我们的基于 CDC 的 LDT 作为金标准，所有检测均具有 100%特异性。我们的结果表明了 SARS-CoV-2 RT-PCR 的初始检测的性能特征，并突出了在公共卫生紧急情况下拥有多个病毒检测测试平台的重要性。

Table 4. Same-sample comparison of five testing platforms for SARS-CoV-2

	UW LDT		UW DiaSorin		UW Cobas 6800		LabCorp Seattle Xpert Xpress Sars-CoV2		LabCorp Seattle Panther Fusion SARS-CoV-2
Panel ID	N1 Ct	N2 Ct	S-gene	ORF1ab	ORF1ab	E-gene	E-gene	N2 Ct	Orf1ab/2ab
Neg 01	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 02	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 03	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 04	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 05	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 06	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 07	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 08	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 09	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 10	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 11	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 12	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Neg 13	NDET	NDET	N.D.	N.D.	NDET	NDET	NDET	NDET	N.D.
Pos 01	30.7	30.2	29.2	30	30.5	31.1	31.7	33.8	31
Pos 02	28.5	28.7	27.2	28	29.6	30.5	29.2	31.6	29.7
Pos 03	28.6	28.8	27.3	28.4	30.4	32.2	28.7	31.4	31.2
Pos 04	25.2	24.4	22.4	23.8	26.1	26.2	25.4	25.9	25.2
Pos 05*	35.4	35.6	NDET/NDET	NDET/34.5	33.6	36.2	37.6	37.5	35
Pos 06	27.2	26.7	25	26.9	26.4	27.3	26.8	29.5	26.3
Pos 07	26.3	25.5	22.2	23.3	25.9	26.1	26	28.1	24.7
Pos 08	35.8	34.4	33.6	33	31.7	34.1	35.9	38.5	36.3
Pos 09	18	17.6	15.3	16.4	19.4	19.5	18	19.3	18.6
Pos 10	31.9	32.1	31.1	31.1	31.9	33.6	31.7	34.2	32.2
Pos 11	31.3	31.3	28.1	29.2	30.5	32	31.2	34.6	N.D.
Pos 12*	37.4	NDET	NDET	NDET	NDET	NDET	NDET/42.6	42.7/NDET	NDET
Pos 13	32.6	33.9	32.5	32.5	NDET	35.7	38.1	40	37.1

*Known positive patients in process of clearing virus
NDET, Not Detected
N.D., Not Done

Abstract
Multiple laboratory developed tests and commercially available assays have emerged to meet diagnostic needs related to the SARS-CoV-2 pandemic. To date, there is limited comparison data for these different testing platforms. We compared the analytical performance of a laboratory developed test (LDT) developed in our clinical laboratory based on CDC primer sets and four commercially available, FDA emergency use authorized assays for SARS-CoV-2 (Cepheid, DiaSorin, Hologic Panther, and Roche Cobas) on a total of 169 nasopharyngeal swabs. The LDT and Cepheid Xpert Xpress SARS-CoV-2 assays were the most sensitive assays for SARS-CoV-2 with 100% agreement across specimens. The Hologic Panther Fusion, DiaSorin Simplexa, and Roche Cobas 6800 only failed to detect positive specimens near the limit of detection of our CDC-based LDT assay. All assays were 100% specific, using our CDC-based LDT as the gold standard. Our results provide initial test performance characteristics for SARS-CoV-2 RT-PCR and highlight the importance of having multiple viral detection testing platforms available in a public health emergency.

7. SARS-CoV-2 病毒载量和抗体的长期动态观察性队列研究

Long period dynamics of viral load and antibodies for SARS-CoV-2 infection: an observational cohort study

来源：medRxiv
发布时间：2020-04-22
链接：https://www.medrxiv.org/content/10.1101/2020.04.22.20071258v1
第一作者：Jianping Huang, Tingting Mao
通讯作者：Shaohua Tang
通讯作者单位：温州医科大学
DOI 或 PUBMED ID：Preprint
编译者：张鹏伟
中文摘要：
目的：探讨 SARS-CoV-2 肺炎患者 8 周内病毒 RNA、IgM、IgG 的动态变化及其相互关系。
设计：回顾性观察病例系列。
单位：温州市第六人民医院
对象：33 例实验室确诊的入院 SARS-CoV-2 肺炎患者。数据收集时间为 2020 年 1 月 27 日至 4 月 10 日。
主要措施：采集咽拭子、痰、便、血标本，逆转录聚合酶链反应（RT-PCR）检测病毒载量。分析了抗刺突蛋白(S)、刺突蛋白受体结合域(RBD)和核衣壳蛋白(N)的特异性 IgM 和 IgG。
结果：SARS-CoV-2 病毒在发病初期，喉部拭子和痰中的病毒载量较高，而大便中的病毒载量较低。咽拭子，痰液和粪便中未检出病毒 RNA 的中值（IQR）时间分别为 18.5（13.25-22）天，22（18.5-27.5）天和 17（11.5-32）天。在痰液中，有 17 名患者（51.5％）在 22 天内（短持续性）检测不到病毒 RNA，而 16 名患者（48.5％）在 22 天以上（长持续性）检测出病毒 RNA。3 例（9.1％）患者出院后两周内痰中病毒 RNA 有明显的复发。一名患者的病毒 RNA 阳性持续存在 59 天或更长时间。抗 S IgM，抗 RBD IgM 和抗 N IgM 的中值（IQR）血清转化时间分别为 10.5（7.75-15.5）天，14（9-24）天和 10（7-14）天 。抗 S IgG，抗 RBD IgG

和抗 N IgG 的中位（IQR）血清转化时间分别为 10（7.25-16.5）天，13（9-17）天和 10（7-14）天。在症状出现后的第 8 周，许多先前呈阳性的患者 IgM 呈阴性，20%以上的患者 IgG 水平仍低于峰值水平的 50%。在大约 40％的患者中，恢复期的抗 RBD IgG 水平比急性期高 4 倍。SARS-CoV-2 RNA 与抗体共存 50 天以上。抗 RBD-IgM 和 IgG 水平，包括出现时和高峰时的抗 RBD-IgM 水平，在病毒 RNA 短持续患者中明显高于长持续患者。
结论：本研究为 SARS-CoV-2 病毒载量特征和抗体动态提供了新的重要信息。从这些结果可以明显看出，病毒 RNA 在痰和粪便标本中持续存在的时间相对较长。由于病毒的持久性似乎与抗 RBD 水平有关，因此抗 RBD 还可作为抗 SARS-CoV-2 感染的潜在保护性抗体。早期治疗干预似乎也是病毒持久性的一个因素。

Abstract:

OBJECTIVE: To investigate the dynamics of viral RNA, IgM, and IgG and their relationships in patients with SARS-CoV-2 pneumonia over an 8-week period.

DESIGN: Retrospective, observational case series.

SETTING: Wenzhou Sixth People’s Hospital

PARTICIPANTS: Thirty-three patients with laboratory confirmed SARS-CoV-2 pneumonia admitted to hospital. Data were collected from January 27 to April 10, 2020.

MAIN OUTCOME MEASURES: Throat swabs, sputum, stool, and blood samples were collected, and viral load was measured by reverse transcription PCR (RT-PCR). Specific IgM and IgG against spike protein (S), spike protein receptor binding domain (RBD), and nucleocapsid (N) were analyzed.

RESULTS： At the early stages of symptom onset, SARS-CoV-2 viral load is higher in throat swabs and sputum, but lower in stool. The median (IQR) time of undetectable viral RNA in throat swab, sputum, and stool was 18.5 (13.25-22) days, 22 (18.5-27.5) days, and 17 (11.5-32) days, respectively. In sputum, 17 patients (51.5%) had undetectable viral RNA within 22 days (short persistence), and 16 (48.5%) had persistent viral RNA more than 22 days (long persistence). Three patients (9.1%) had a detectable relapse of viral RNA in sputum within two weeks of their discharge from the hospital. One patient had persistent viral RNA for 59 days or longer. The median (IQR) seroconversion time of anti-S IgM, anti-RBD IgM, and anti-N IgM was 10.5 (7.75-15.5) days, 14 (9-24) days, and 10 (7-14) days, respectively. The median (IQR) seroconversion time of anti-S IgG, anti-RBD IgG, and anti-N IgG was 10 (7.25-16.5) days, 13 (9-17) days, and 10 (7-14) days, respectively. By week 8 after symptom onset, IgM were negative in many of the previously positive patients, and IgG levels remained less than 50% of the peak levels in more than 20% of the patients. In about 40% of the patients, anti-RBD IgG levels were 4-times higher in convalescence than in acute phase. SARS-CoV-2 RNA coexisted with antibodies for more than 50 days. Anti-RBD IgM and IgG levels, including anti-RBD IgM levels at presentation and peak time, were significantly higher in viral RNA short persistence patients than in long persistence patients.

CONCLUSION: This study adds important new information about the features of viral load and antibody dynamics of SARS-CoV-2. It is clear from these results that the viral RNA persists in sputum and stool specimens for a relatively long

time in many patients. Anti-RBD may also serve as a potential protective antibody against SARS-CoV-2 infection, as viral persistence appears to be related to anti-RBD levels. Earlier treatment intervention also appears to be a factor in viral persistence.

8. 儿童中新型多系统炎性疾病病例增加

Increased number of reported cases of novel presentation of multisystem inflammatory disease

来源：https://picsociety.uk/wp-content/uploads/2020/04/PICS-statement-re-novel-KD-C19-presentation-v2-27042020.pdf
发布时间：2020-04-27
编译：蒋立春

近日欧美媒体报道儿童中川崎病(是一种以急性发热、出疹为主要症状的小儿疾病)增加，可能和 COVID-19 有关。

英国儿科重症监护协会于 27 日发布了一份关于儿童中全新多系统炎性疾病病例增加的通知。该通知中讲到他们收到英国 NHS（英国公立医疗系统）强调近日儿童中出现不寻常症状的重症儿童病例出现小幅增加。这些儿童中很多是 COVID-19 阳性。这封警示信讲到这些不寻常病例的症状和中毒性休克综合征以及表现重症儿童 COVID-19 的血相参数(参考文献 1，包括 C 反应蛋白水平高，红细胞沉降率水平高以及铁蛋白水平高）的非典型川崎病一致。这些儿童还常常有肚子痛等肠道系统症状，以及心肌炎。虽然只有为数不多的儿童需要重症监护，这类病例在英国以外的国家也有发现。该通知还提到最近一份发表的关于 COVID-19 表现为川崎病得儿童病例（参考文献 2。编者注：该文章报道在 1000 多例确诊 COVID-19 的儿童中有一例川崎病）。

1. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020 Mar 28;395(10229): 1033-1034. DOI: 10.1016/S0140-6736(20)30628-0.
2. Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki disease: novel virus and novel case. Hosp Pediatr. 2020; doi: 10.1542/hpeds.2020-0123

9. 中国深圳 COVID-19 患者的临床进展特征—症状不同严重程度所需的住院时间

Characterization of clinical progression of COVID-19 patients in Shenzhen, China

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DOI 或 PUBMED ID：
编译者：宋张悦
中文摘要：
COVID-19 大流行对全世界的卫生保健系统造成了压力。了解病例的临床进展是一项重要的公共卫生优先事项，可在紧急情况下提供最佳资源分配。中国深圳的所有病例均在医院进行监测，从临床病程的早期阶段就可获得症状概况、临床及实验室结果，研究人员通过中国深圳的数据描述了 COVID-19 病例的临床进展，并确定了从更快的临床进展到关键临床事件和更长的医疗资源使用的重要预测因素。这项单中心观察性研究是在深圳第三人民医院进行的，该医院是深圳所有 COVID-19 患者的指定收治医院。研究人员收集了 2020 年 1 月 11 日到 3 月 10 日 420 例确诊并住院的 COVID-19 患者的数据，从电子病历中提取流行病学、人口统计学、实验室、临床和结局的数据。在初始临床评估中，23 名患者(5.5%)临床症状轻微，中度占绝大多数(93.8%，n=394)，仅有 3 例为重症或危重。研究发现，那些进展到重症阶段的患者、发展为急性呼吸窘迫综合征、或被转至重症监护病房(ICU)的患者，在症状出现后平均进展时间分别为 9.5 天(95%CI 8.7,10.3)、11.0 天(95%CI 9.7,12.3)和 10.5 天(95%CI 8.2,13.3)。研究人员估计转入 ICUs 的患者平均停留 34.4 天(95%CI 24.1,43.2)，需要机械通气的患者平均使用呼吸机的时间为 28.5 天(95%CI 20.0,39.1)。轻、中度没有进展至重度的患者的中位住院时间为 21.3 天(95%CI, 20.5, 22.2)，但需要入住 ICU 的患者的中位住院时间延长至 52.1 天(95%CI, 43.3, 59.5)。明确的临床进展特征有助于规划 COVID-19 爆发期间的医疗资源分配，并为评估新治疗和疗法的有效性提供依据。

Abstract:
The COVID-19 pandemic has stressed healthcare care systems throughout the world. Understanding clinical progression of cases is a key public health priority that informs optimal resource allocation during an emergency. Using data from Shenzhen, China, where all cases were monitored in hospital and symptom profiles and clinical and lab results were available starting from early stages of clinical course, we characterized clinical progression of COVID-19 cases and determined important predictors for faster clinical progression to key clinical events and longer use of medical resources. Epidemiological, demographic, laboratory, clinical, and outcome data were extracted from electronic medical records. We found that those who progressed to the severe stage, developed acute respiratory distress syndrome, and were admitted to the intensive care unit (ICU) progressed on average 9.5 days (95%CI 8.7,10.3), 11.0 days (95%CI 9.7,12.3), and 10.5 days (95%CI 8.2,13.3) after symptom onset, respectively. We estimated that patients who were admitted to ICUs remained there for an average of 34.4 days (95%CI 24.1,43.2) and the average time on a ventilator was 28.5 days (95%CI 20.0,39.1) among those requiring mechanical ventilation. The median length of hospital stay was 21.3 days (95%CI, 20.5, 22.2) for the mild or moderate cases who did not progress to the severe stage, but increased to 52.1 days (95%CI, 43.3, 59.5) for those who required ICU admission. Clear characterization of clinical progression informs planning for healthcare resource allocation during COVID-19 outbreaks

and provides a basis that helps assess the effectiveness of new treatment and therapeutics.

10. 一项在纽约进行的保密性临床试验测试了胃灼热药物法莫替丁对 COVID-19 的治疗作用

New York clinical trial quietly tests heartburn remedy against coronavirus

来源：*Science*
发布时间：2020-04-26
链接：https://www.sciencemag.org/news/2020/04/new-york-clinical-trial-quietly-tests-heartburn-remedy-against-coronavirus
第一作者：Brendan Borrell
通讯作者：Brendan Borrell
通讯作者单位：洛杉矶一名自由记者
DOI 或 PUBMED ID：10.1126/science.abc4739
编译者：张丽双
中文摘要：
纽约研究人员正在开展一项试验，测试胃灼热药物法莫替丁（Famotidine）对新冠肺炎的治疗作用。这个灵感来自于在武汉亲历一线的美国医生 Michael Callahan。在回顾 6212 例 COVID-19 患者的病历时，医生们注意到许多幸存者患有慢性胃灼热，服用的是法莫替丁，而不是更昂贵的奥美拉唑（Prilosec），这是美国和中国富人的首选药物。住院的服用法莫替丁的 COVID-19 患者的死亡率约为 14%，而未服用法莫替丁的患者的死亡率为 27%，尽管分析结果很粗糙，且无统计学意义。从武汉返回美国后，他向有关部门做了汇报，并通过与计算机模拟方面专家 Malone 进行合作，发现了法莫替丁可能对 SARS-Cov-2 复制的关键病毒酶木瓜蛋白酶有抑制作用。为了避免消息过早泄露导致药物供应不足，他们秘密推进了这个法莫替丁临床试验。同时鉴于总统力推的氯喹药物在美国的广泛临床应用，研究者只好退而求其次，测试法莫替丁和羟氯喹的联合使用效果。
目前纽约州最大的医疗保健服务提供商 Northwell Health 正在 187 名重症新冠肺炎患者身上进行法莫替丁和羟氯喹的联合使用临床试验。研究人员说，几周后将有一些关于安全性的数据公布，但没有说什么时候有数据显示这一药物组合是否有效。
Abstract:
As of Saturday, 187 COVID-19 patients in critical status, including many on ventilators, have been enrolled in the trial, which aims for a total of 1174 people. Reports from China and molecular modeling results suggest the drug, which seems to bind to a key enzyme in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), could make a difference. But the hype surrounding hydroxychloroquine and chloroquine—the unproven antimalarial drugs touted by President Donald Trump and some physicians and scientists—has made Tracey wary of sparking premature enthusiasm. He is tight-lipped about famotidine's prospects, at least until interim results from the first 391 patients are in. "If it does work, we'll know in a few weeks," he says.

11. 新冠肺炎临床试验的实时仪表板

A real-time dashboard of clinical trials for COVID-19

来源：Lancet Digital Health
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编译者：刘焕珍
中文摘要：

为了应对 2019 年全球新冠肺炎的紧急情况，评估临床候选干预措施治疗新冠肺炎的疗效和安全性的临床试验研究正在以空前的速度出现。截至 2020 年 4 月 21 日，已经在国际和国家不同的临床试验注册中心注册了 500 多个临床试验。鉴于出现试验信息和结果的速度越来越快，迫切需要跟踪临床试验，避免不必要的重复工作，并了解正在进行的试验以及此试验在何处进行。因此我们开发了新冠肺炎临床试验注册中心以整理所有试验，数据来自国际临床试验注册平台（https://www.covid-trials.org/）。自动搜索和手动搜索都可以确保最大程度地减少重复条目，并确保对研究问题的适当性。由两个独立的审阅者对确定的研究进行手动审阅，然后再输入注册表。同时，我们已经开发了基于人工智能（AI）的数据搜索方法，以识别未在试验注册表中存在的潜在临床研究。和手动查看所有条目需要的时间相比，使用基于 AI 的方法可节省 50－80%的时间，准确性与手动查看保持一致。最后，我们将使用内容整合服务，以确保我们的数据获取策略是完整的。通过此三步过程，丢失重要出版物的可能性大大降低，因此所得数据代表了全球新冠肺炎的研究工作。

当这些数据可用时，可以根据地理、试验、患者和干预特征来划分新冠肺炎的试验。这些数据安全地存储在后端数据库中，并且在前端功能上进行可视化输出。在传达试验结果时，必须对这些数据进行集中化和实时荟萃分析。迫切需要对这些试验进行整合，来协助临床医生、研究人员和政策制定者做出循证决策，以最大程度地降低新冠肺炎导致的发病率和死亡率。

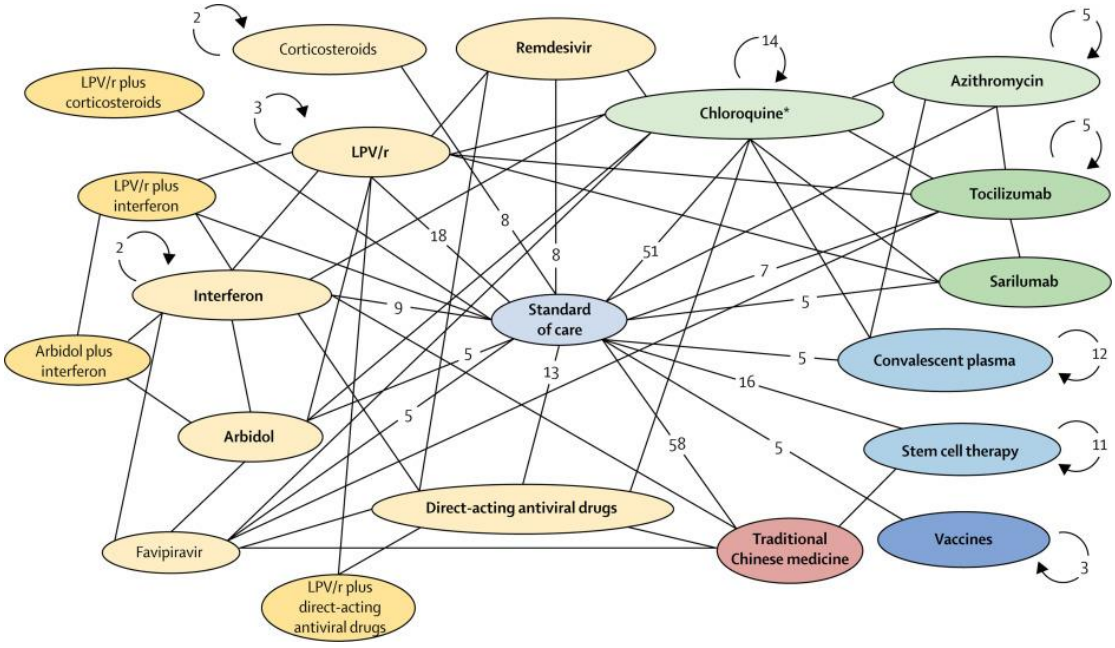

Figure. Evidence network of COVID-19 clinical trials of top 15 interventions
Circles (node) represent interventions or intervention groups (categories). Lines

between two circles indicate comparisons in clinical trials. The numbers on the lines are the number of clinical trials making the specific comparison. Circular arrows and numbers indicate the number of non-comparative clinical trials in which that intervention is included. A few trials examining combination therapies are excluded from the figure due to space limitations. COVID-19=coronavirus disease 2019.
LPV/r (lopinivir‐ritonavir). *Includes trials on hydroxychloroquine and chloroquine.

Abstract:
In response to the global coronavirus disease 2019 (COVID-19) emergency, clinical trial research assessing the efficacy and safety of clinical candidate interventions to treat COVID-19 are emerging at an unprecedented rate. As of April 21, 2020, well over 500 clinical trials have been registered at the various international and national clinical trial registry sites. Given the accelerated rate at which trial information and findings are emerging, an urgent need exists to track clinical trials, avoid unnecessary duplication of efforts, and understand what trials are being done and where. In response, we have developed a COVID-19 clinical trials registry to collate all trials. Data are pulled from the International Clinical Trials Registry Platform. Both automated and manual searches are done to ensure minimization of duplicated entries and for appropriateness to the research questions. Identified studies are then manually reviewed by two separate reviewers before being entered into the registry. Concurrently, we have developed artificial intelligence (AI)- based methods for data searches to identify potential clinical studies not captured in trial registries. Use of AI-based methods saves 50‐80% of the time required to manually review all entries without loss of accuracy. Finally, we will use content aggregator services to ensure our data acquisition strategy is complete. With this three-step process, the probability of missing important publications is greatly diminished and so the resulting data are representative of global COVID-19 research efforts.
Trials for COVID-19 are then mapped according to geographical, trial, patient, and intervention characteristics, when these data are available. These data are stored securely in a backend database and outputs are visualised on a frontend feature. As trial findings are communicated, these data must be centralised and meta-analysed in real-time. Syntheses of these trials are urgently needed to assist clinicians, researchers, and policy makers to make evidence-informed decisions to minimise the morbidity and mortality due to COVID-19.

12.默克和系统生物学研究所启动大规模COVID-19研究

Merck and Institute for Systems Biology Initiate Large-Scale COVID-19 Study

来源：Biospace
发布时间：2020.04.27

链 接 ： https://www.biospace.com/article/merck-partners-with-institute-for-systems-biology-on-covid-19/

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中文摘要：

为更高效地开发针对 COVID-19 相关药物和疫苗，默克公司正在与总部位于西雅图的系统生物学研究所(ISB)签订合作协议，即将启动大规模 COVID-19 研究。生物医学高级研究和发展管理局(BARDA)将提供部分资金支持 ISB 的研究工作。该试验由 ISB 和瑞典医学中心共同领导，两者都是普罗维登斯圣约瑟夫健康网络的一部分。相关研究联盟将分析瑞典医疗中心 COVID-19 患者在不同时间采集的血液和鼻腔样本，包括首次就诊、急性疾病和恢复期。这些小组将使用多种蛋白质组学、代谢组学、转录组学和遗传学技术研究样本，以确定可能用于预测严重疾病风险的生物标志物。这项研究还将致力于开发免疫反应的概况，如感染后患者免疫细胞的数量变化，以及康复期患者中和抗体的特征。这项研究将从 200 名患者的样本开始，并可扩展至 300 名。合作有助于我们为了更好地理解为什么一些病人会变得严重，而另一些病人病情较轻或没有疾病。ISB 所长吉姆·希思说:“每个 COVID-19 患者都有一个独特的机制，告诉我们医学和科学界如何才能最有效地应对这一流行病。”因此，这实际上是一个双管齐下的方法:确定标记物以确定哪些患者最有可能受到严重疾病的影响，以及更好地理解感染的分子机制以创造有效的治疗。他们打算让这些数据“迅速、免费地提供给参与相关研究的全球科学和生物医学界。”

Abstract

Merck is entering a collaboration agreement with the Seattle-based Institute for Systems Biology (ISB) to investigate and define the molecular activity of SARS-CoV-2 infection and COVID-19, the resulting disease. The intention is to identify targets for drugs and vaccines. ISB researchers, health care staff from the Swedish Medical Center, and a consortium of research groups and biopharma companies will analyze blood and nasal samples from Swedish Medical Center COVID-19 patients collected at different times—initial presentation, acute disease and convalescence. The groups will study the samples using a variety of proteomic, metabolomic, transcriptomics and genetic techniques to identify possible biomarkers that could be used to predict the risk of severe disease. It will start with samples from 200 patients with the option to expand to 300. The rationale behind the collaboration is to better understand why some patients become seriously ill while others have milder or no disease. “Each of the COVID-19 patients has a unique lesson to teach us about how the medical and scientific community can respond most effectively to this pandemic,” Heath said.