新型冠状病毒信息简报

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上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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1. 2020 年 4 月 30 日疫情

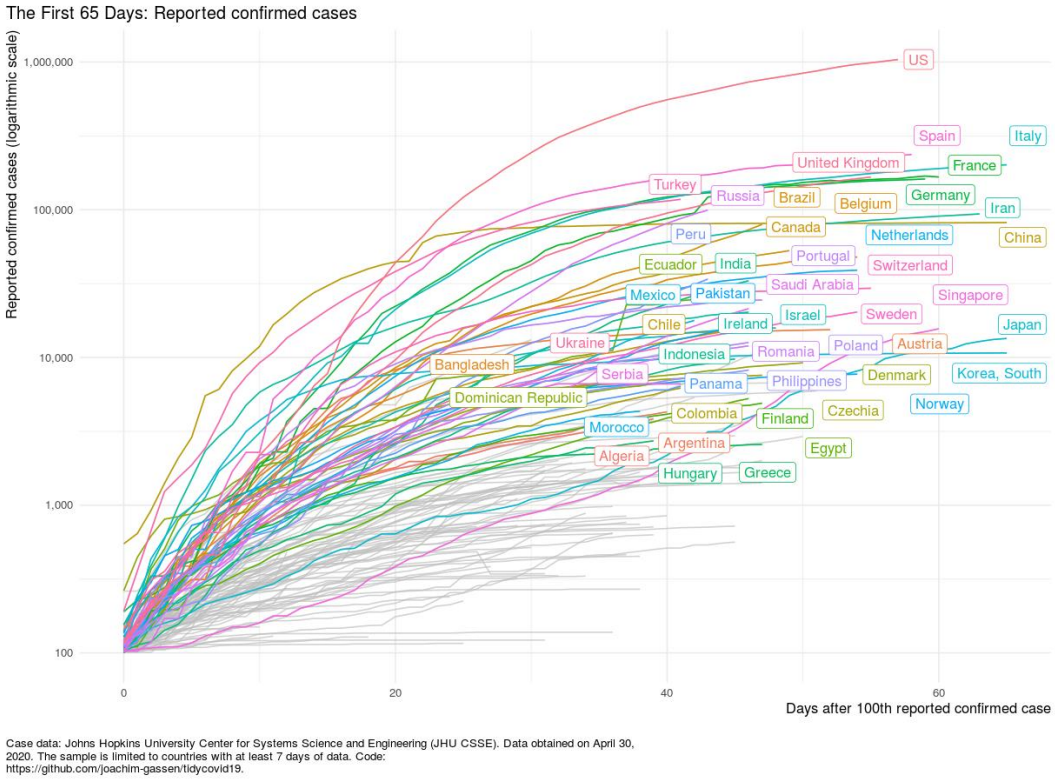
数据来源：WHO

发布时间：2020 年 4 月 30 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 30 日全球累计确诊新型冠状病毒病人 3090445 例，当日新增确诊 71839 例，累计死亡 217769 例，当日新增死亡 9797。

中国累计确诊 84373 例，累计死亡 4643 例，当日新增确诊 4 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 30 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30日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

2. 采用 ISARIC WHO 临床特征描述方案对 16749 例英国 COVID-19 住院患者的特征分析

Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol

来源：medrxiv

发布时间：2020-04-28

链接：https://www.medrxiv.org/content/10.1101/2020.04.23.20076042v1

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DOI 或 PUBMED ID：

编译者：王玮

中文摘要：

目的：探讨英国 COVID-19 重症患者的临床特点。

设计：采用 WHO 预先批准的调查表，快速收集数据并进行接近实时的前瞻性观察队列研究分析。

场景：2020 年 2 月 6 日至 4 月 18 日，英国 166 家医院。

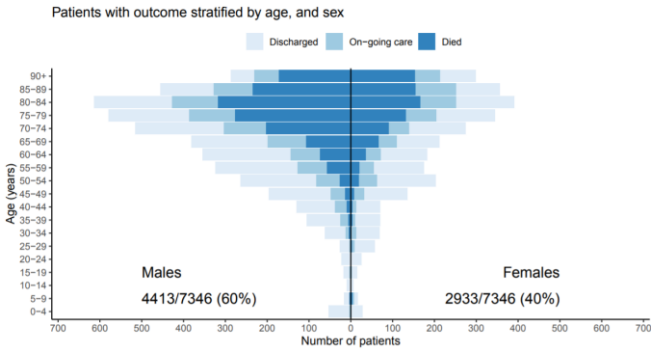
参与者：16749 名 COVID-19 住院患者。

干预措施：未进行干预，但出于研究目的采集了经同意的样本。许多参与者参与了其他的介入研究和临床试验。

结果：中位年龄为 72 岁[IQR（Inter-Quartile Range）57，82；范围 0，104]，入院前症状的中位持续时间为 4 天[IQR1，8]，住院时间的中位持续时间为 7 天[IQR4，12]。最常见的合并症是慢性心脏病（29%）、单纯性糖尿病（19%）、非哮喘性慢性肺病（19%）和哮喘（14%）；47%的患者没有记录到合并症。年龄增加和包括肥胖在内的共病与较高的死亡率相关。该研究发现明显的症状种类：1,呼吸系统（咳嗽、痰、喉咙痛、流鼻涕、耳痛、气喘和胸痛）。2,全身性（肌痛、关节痛和疲劳）。3,肠道（腹痛、呕吐和腹泻）。总的来说，49%的病人出院，33%病人死亡，17%在报告之日继续接受治疗。17%病人需要进入高依赖或重症监护病房；截止报告日，其中有 31%病人出院，45%病人死亡，24%病人继续接受治疗。在接受机械通气的患者中，20%病人出院，53%病人死亡，27%病人留院。

结论：该研究对欧洲 COVID-19 患者进行了最详细的描述，表明了防备大流行的重要性，以及在应对疫情时开展研究的必要性。

预文档：请访问 https://isaric4c.net/protocols。伦理认证：英格兰和威尔士（13/SC/0149）和苏格兰（20/SS/0028）。ISRCTN（待定）。



图一: Patients with outcome (n=7,346) stratified by age, and sex. Bar fills are outcome(discharge/ongoing care/death) at the time of report (18/04/2020, n=16,749).

Abstract:

Objective: To characterize the clinical features of patients with severe COVID-19 in the UK.

Design: Prospective observational cohort study with rapid data gathering and near real-time analysis, using a pre-approved questionnaire adopted by the WHO.

Setting: 166 UK hospitals between 6th February and 18th April 2020.

Participants: 16,749 people with COVID-19.

Interventions: No interventions were performed, but with consent samples were taken for research purposes. Many participants were co-enrolled in other interventional studies and clinical trials.

Results: The median age was 72 years [IQR 57, 82; range 0, 104], the median duration of symptoms before admission was 4 days [IQR 1,8] and the median duration of hospital stay was 7 days [IQR 4,12]. The commonest comorbidities were chronic cardiac disease (29%), uncomplicated diabetes (19%), non-asthmatic chronic pulmonary disease (19%) and asthma (14%); 47% had no documented reported comorbidity. Increased age and comorbidities including obesity were associated with a higher probability of mortality. Distinct clusters of symptoms were found: 1. respiratory (cough, sputum, sore throat, runny nose, ear pain, wheeze, and chest pain); 2. systemic (myalgia, joint pain and fatigue); 3. enteric (abdominal pain, vomiting and diarrhoea). Overall, 49% of patients were discharged alive, 33% have died and 17% continued to receive care at date of reporting. 17% required admission to High Dependency or Intensive Care Units; of these, 31% were discharged alive, 45% died and 24% continued to receive care at the reporting date. Of those receiving mechanical ventilation, 20% were discharged alive, 53% died and 27% remained in hospital.

Conclusions: We present the largest detailed description of COVID-19 in Europe, demonstrating the importance of pandemic preparedness and the need to maintain readiness to launch research studies in response to outbreaks.

Trial documentation: Available at https://isaric4c.net/protocols. Ethical approval in England and Wales (13/SC/0149), and Scotland (20/SS/0028). ISRCTN (pending).

3. COVID19 住院的关键预测因素:来自对 2,618,948 名 COVID 症状追踪应用程序用户的一项调查研究

Key predictors of attending hospital with COVID19: An association study from the COVID Symptom Tracker App in 2,618,948 individuals

来源：medRxiv

发布时间：2020-04-24

链接：https://www.medrxiv.org/content/10.1101/2020.04.25.20079251v1

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DOI 或 PUBMED ID：Preprint
编译者：孔娟
中文摘要：

背景：随着 COVID-19 大流行的升级，各国医疗保健系统正面临越来越大的压力， 为了解决这一问题，**研究者使用在 COVID 症状追踪应用程序上收集的 2,618,948 份自我报告数据来确定住院治疗的关键人口统计学风险因素和 COVID-19 呼吸支持的需求。**

材料和方法：COVID 症状跟踪器由伦敦国王学院、马萨诸塞州总医院和佐伊全球有限公司共同开发的智能手机应用程序于于 2020 年 3 月 29 日在美国上市。鼓励没有症状的个人使用该应用程序。它捕获了与 COVID-19 症状相关的自我报告信息。首次使用时，该应用会记录用户自我报告的位置、年龄和核心健康风险因素。后续参与者每天提供关于症状的最新信息包括医疗保健访视、COVID-19 测试结果，以及他们是否寻求医疗保健，包括干预水平和相关结果。主要观察指标:到医院就诊和住院的患者，分为三个亚组(I)自我报告的具有典型症状的 COVID-19 感染(SR-COVID-19)，(ii)自我报告阳性 COVID-19 检测结果(T-COVID-19)，和(iii)根据症状学估算/预测的 COVID-19 感染(I-COVID-19)。对每个结果和每个亚组的多变量逻辑回归进行了年龄和性别调整，对共病进行了敏感性分析。典型症状被定义为高烧和持续几天的咳嗽。

结果：总的研究样本包括 2，618，948 名通过 COVID 症状追踪应用程序提供自我评估的个人，共有 171，899 人(10.5%)对这个问题做出了肯定的回答:“你已经有 COVID-19 了吗？”84260 人(3.2%)对关于 COVID-19 经典症状的问题作出了肯定的回答。75163 人(2.9%)报告了糖尿病，55196 人(2.1%)报告了心脏病，316845 人(12.1%)报告了肺病，16177 人(0.6%)报告了肾病。16.3%的样本报告了至少一种以下共病: 糖尿病、肺病、心脏病或肾病。**结果发现年龄较大和所有共病测试与 COVID-19 需要住院治疗的几率增加相关**。在所有模型中，肥胖(体重指数> 30)预示着住院治疗，比值比(OR)从 1.20[1.11;1.31]至 1.40[1.23;1.60]。既往肺部疾病和糖尿病一直被认为与医院就诊相关，最大 OR 值为 1.79 [1.64，1.95]和 1.72[1.27; 2.31])。在评估呼吸支持需求时，年龄和男性扮演了重要的角色。

结论:由于年龄较大、肥胖、糖尿病或患有预先存在的肺、心脏或肾脏疾病，参与者 COVID-19 就诊的风险增加。各国政府以及科学界和医学界需要共同努力，找到循证手段，保护那些被认为患病风险较高的人群。

Abstract

Objectives: We aimed to identify key demographic risk factors for hospital attendance with COVID-19 infection.

Design: Community survey Setting: The COVID Symptom Tracker mobile application co-developed by physicians and scientists at Kings College London, Massachusetts General Hospital, Boston and Zoe Global Limited was launched in the UK and US on 24th and 29th March 2020 respectively. It captured self-reported information related to COVID-19 symptoms and testing. Participants: 2,618,948 users of the COVID Symptom Tracker App. UK (95.7%) and US (4.3%) population. Data cut-off for this analysis was 21st April 2020. Main outcome measures: Visit to hospital and for those who attended hospital, the need for respiratory support in three subgroups (i) self-reported COVID-19 infection with classical symptoms (SR-COVID-19), (ii) self-reported positive COVID-19 test results (T-COVID-19), and (iii) imputed/predicted COVID-19 infection based on symptomatology (I-COVID-19).

Multivariate logistic regressions for each outcome and each subgroup were adjusted for age and gender, with sensitivity analyses adjusted for comorbidities. Classical symptoms were defined as high fever and persistent cough for several days.
Results: Older age and all comorbidities tested were found to be associated with increased odds of requiring hospital care for COVID-19. Obesity (BMI >30) predicted hospital care in all models, with odds ratios (OR) varying from 1.20 [1.11; 1.31] to 1.40 [1.23; 1.60] across population groups. Pre-existing lung disease and diabetes were consistently found to be associated with hospital visit with a maximum OR of 1.79 [1.64,1.95] and 1.72 [1.27; 2.31]) respectively. Findings were similar when assessing the need for respiratory support, for which age and male gender played an additional role.
Conclusions: Being older, obese, diabetic or suffering from pre-existing lung, heart or renal disease placed participants at increased risk of visiting hospital with COVID-19. It is of utmost importance for governments and the scientific and medical communities to work together to find evidence-based means of protecting those deemed most vulnerable from COVID-19.

4. 用于细胞移植治疗的临床级 SARS-CoV-2 特异性 T 细胞的成功制备

SUCCESSFUL MANUFACTURING OF CLINICAL-GRADE SARS-CoV-2 SPECIFIC T CELLS FOR ADOPTIVE CELL THERAPY
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发布时间：2020-04-24
链接：https://www.medrxiv.org/content/10.1101/2020.04.24.20077487v1
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DOI 或 PUBMED ID：Preprint
编译者：张鹏伟
中文摘要：
背景：SARS-CoV-2 特异性 T 细胞移植治疗 COVID-19 尚未报道。无论是现在还是以前的大流行病，都尚未证明这种从恢复期供体中快速制造临床级病毒特异性 T 细胞的可行性。
方法：按照标准血库惯例，从每个恢复期献血者中采集一单位全血。血浆分离后，用覆盖 S 蛋白的免疫显性序列结构域以及 N 和 M 蛋白的全序列的 SARS-CoV-2 重叠肽刺激白细胞。此后，使用捕获 IFNγ 分泌细胞的自动装置将功能性反应性细胞富集过夜。
结果：前两位供体的 $1x10^9$ 白细胞分别产生 0.56-$1.16x10^6$ IFNγ+T 细胞。多数 T 细胞（64%～71%）为 IFNγ＋，CD56＋T 细胞、效应记忆 T 细胞和效应记忆 RA＋T 细胞优先富集。TCRVβ谱型显示寡克隆分布，包括 Vβ3，Vβ16 和 Vβ17 的亚家族过度表征。在只有两个供体的情况下，同一种族中的接受者共享至少一个供体 HLA 等位基因或一种单倍型的可能性分别高达> 90％和> 30％。
解释：本研究受到捐助者数量少和缺乏接受者数据的限制；但是，提供了重要的首个概念性验证数据，证明了临床级生产 SARS-CoV-2 特异性 T 细胞用于紧急临床用途（与血浆疗法同时进行）的可行性。我们的数据表明，用 SARS-CoV-2 特异性肽短暂刺激后，病毒特异性 T 细胞可以很容易地被检测出来，这表明可以开发一种和血清学检测的平行诊断方法。

Abstract:
Background: Adoptive therapy with SARS-CoV-2 specific T cells for COVID-19 has not been reported. The feasibility of rapid clinical-grade manufacturing of virus-specific T cells from convalescent donors has not been demonstrated for this or prior pandemics.
Methods: One unit of whole blood was collected from each convalescent donor following standard blood bank practices. After the plasma was separated and stored separately, the leukocytes were stimulated using overlapping peptides of SARS-CoV-2, covering the immunodominant sequence domains of the S protein and the complete sequence of the N and M proteins. Thereafter, functionally reactive cells were enriched overnight using an automated device capturing IFNγ-secreting cells.
Findings: From $1x10^9$ leukocytes, 0.56 to $1.16x10^6$ IFNγ+ T cells were produced from each of the first two donors. Most of the T cells (64% to 71%) were IFNγ+, with preferential enrichment of CD56+ T cells, effector memory T cells, and effector memory RA+ T cells. TCRVβ spectratyping revealed oligoclonal distribution, with over-representation of subfamilies including Vβ3, Vβ16 and Vβ17. With just two donors, the probability that a recipient in the same ethnic group would share at least one donor HLA allele or one haplotype could be as high as >90% and >30%, respectively.
Interpretations: This study is limited by small number of donors and absence of recipient data; however, crucial first proof-of-principle data are provided demonstrating the feasibility of clinical-grade production of SARS-CoV-2 specific T cells for urgent clinical use, conceivably with plasma therapy concurrently. Our data showing that virus-specific T cells can be detected easily after brief stimulation with SARS-CoV-2 specific peptides suggest that a parallel diagnostic assay can be developed alongside serology testing.

5. 一种可干扰 SARS-Cov-2 刺突蛋白进入宿主细胞的工程稳定微蛋白

An engineered stable mini-protein to plug SARS-Cov-2 Spikes
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发布时间：2020-04-29
链接：https://www.biorxiv.org/content/10.1101/2020.04.29.067728v1
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DOI 或 PUBMED ID：https://doi.org/10.1101/2020.04.29.067728
编译者：刘焕珍
中文摘要：
新型β-冠状病毒 SARS-CoV-2 是当前大流行 COVID-19 的病原体。像其他冠状病毒一样，这种新型病毒依靠表面刺突糖蛋白进入宿主细胞，主要是通过病毒受体结合域（RBD）与人血管紧张素转化酶 2（ACE2）的相互作用来实现的。因此，能够干扰 SARS-CoV-2 刺突蛋白与 ACE2 结合的分子药物具有抑制病毒进入的巨大潜力。从现有的 SARS-CoV-2 刺突蛋白与宿主 ACE2 受体相互作用的结构数据出发，作者设计了一种微蛋白，目的是建立一种可溶的稳定

的刺突蛋白相互作用分子药物。这种高产量的重组微蛋白，具有稳定的α螺旋构象，能够与SARS-CoV-2 糖基化的刺突蛋白的 RBD 相互作用，并具有纳摩尔级别的分子亲和力。通过干扰刺突蛋白，这种微蛋白将成为开发针对不同类型冠状病毒的疗法的有效工具。

Abstract:

The novel betacoronavirus SARS-CoV-2 is the etiological agent of the current pandemic COVID-19. Like other coronaviruses, this novel virus relies on the surface Spike glycoprotein to access the host cells, mainly through the interaction of its Receptor Binding Domain (RBD) with the human angiotensin-converting enzyme 2 (ACE2). Therefore, molecular entities able to interfere with binding of the SARS-CoV-2 Spike protein to ACE2 have a great potential to inhibit viral entry. Starting from the available structural data on the interaction between SARS-CoV-2 Spike protein and the host ACE2 receptor, we here engineered a mini-protein with the aim of creating a soluble and stable Spike interactor. This mini-protein, which was recombinantly produced in high yields, possesses a stable α helical conformation and is able to interact with the RBD of glycosylated Spike protein from SARS-CoV-2 with nanomolar affinity. By plugging the Spike protein, our mini-protein constitutes a valid tool for the development of treatments against different types of coronavirus.

6. 印度成为主要的 COVID-19 疫苗生产国

India emerging as major COVID-19 vaccine manufacturer

来源：Biocentury

发布时间：2020-04-30

链接：https://www.biocentury.com/article/305047?editionId=ck9m4xb8exjw00957xtq8efyk&editionType=daily

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通讯作者：Steve Usdin

通讯作者单位：Washington Editor

DOI 或 PUBMED ID：新闻

编译者：雷颖

中文摘要：

目前至少有六家印度公司正在开发或共同开发 COVID-19 疫苗，但印度在对抗大流行中的最大贡献很可能来自其制造能力。印度血清研究所是全球销量最大的疫苗制造商，它正在合作制造由牛津大学詹纳研究所开发的 ChAdOx1 nCoV-19 腺病毒候选疫苗，以及由 Codagenix 公司正在研发的减毒活疫苗。印度血清研究所（SII）宣布了今年计划生产 6000 万剂 ChAdOx1 的计划。该公司计划在 5 月或 6 月开始在印度进行该候选疫苗的临床试验。牛津小组得到了流行病防范创新联盟（CEPI）的支持。除 SII 之外，牛津还签署了默克公司（Xetra：MRK），Halix BV，Advent srl 和 Cobra Biologics AB 来生产其疫苗。牛津大学已启动其 ChAdOx1 nCoV-19 疫苗的 1,112 人一期试验，并表示今年可能已准备好紧急使用剂量。该大学已经表示，不会为该疫苗寻求专利或其他知识产权保护。SII 的制造设施已通过 WHO 认证，但尚未获得 FDA 或 EMA 的许可。该公司宣称不打算为其 COVID-19 疫苗寻求 FDA 或 EMA 许可，而只会在发展中国家销售产品。虽然由 SII 生产的疫苗将在印度出售，但印度能否以可承受的价格不受限制地获得在美国或欧洲生产的 COVID-19 疫苗的可能性并不确定。

Abstract

At least six Indian companies are developing or co-developing COVID-19 vaccines,

but India’s biggest contribution to fighting the pandemic is likely to come from its manufacturing might.
The Serum Institute of India, the world’s largest vaccine manufacturer by volume, is partnering to manufacture the ChAdOx1 nCoV-19 adenovirus vaccine candidate that is being developed by the University of Oxford’s Jenner Institute, as well as a live-attenuated vaccine that Codagenix Inc. is developing. The Serum Institute of India Pvt. Ltd. (SII) has announced plans to produce 60 million doses of ChAdOx1 this year. The company plans to run clinical trials of the vaccine candidate in India with enrollment starting in May or June. The Oxford group is backed by the Coalition for Epidemic Preparedness Innovations (CEPI). In addition to SII, Oxford has signed up Merck KGaA (Xetra:MRK), Halix B.V., Advent s.r.l. and Cobra Biologics AB to manufacture its vaccine (see “Oxford Adds to Surge of Pandemic Deals”). Oxford has launched a 1,112-person Phase I trial of its ChAdOx1 nCoV-19 vaccine and has stated that it could have doses ready for emergency use this year. The university has stated that it will not seek patents or other intellectual property protection for the vaccine. SII’s manufacturing facilities are certified by the WHO but have not been licensed by FDA or EMA. The company does not plan to seek FDA or EMA licensure for its COVID-19 vaccines and will market products only in developing countries. While a vaccine manufactured by SII would be sold in India, it is less than certain that India would have unrestricted access at an affordable price to COVID-19 vaccines manufactured in the U.S. or Europe.

7. 新型冠状病毒 HCoV-19 刺突蛋白和人 ACE2 的质谱分析揭示了多糖修饰和独特的翻译后修饰

Mass spectrometry analysis of newly emerging coronavirus HCoV-19 spike S protein and human ACE2 reveals camouflaging glycans and unique post-translational modifications

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发布时间：2020-04-29
链接：https://www.biorxiv.org/content/10.1101/2020.04.29.068098v1
第一作者：Zeyu Sun
通讯作者：李兰娟
通讯作者单位：浙江大学
DOI 或 PUBMED ID：
编译者：王玮
中文摘要：
引起肺炎的 COVID-19 爆发，促使全世界努力了解新发现的 HCoV-19 病毒的生物学和临床特征。本研究采用 LC-MSMS 技术对重组 HCoV-19 刺突蛋白和 hACE2 的翻译后修饰（PTM）进行了表征。发现这两种蛋白都被一定比例的 N-聚糖亚型高度修饰。HCoV-19 刺突蛋白中 21 种可能的糖基中，有 20 种被 N-聚糖完全占据，其中以低聚甘露糖聚糖最为丰富。hACE2 中所有 7 个可能的糖基化位点大部分被复杂的 N-聚糖占据。然而，我们发现糖基化并不直接影响 SARS-CoV 刺突蛋白与 hACE2 的结合亲和力。此外，该研究还鉴定了两种蛋白质中的多个甲基化位点，并且 hACE2 中的多个脯氨酸被转化为羟基脯氨酸。在最近发表的 HCoV-19 刺突

蛋白和 hACE2 的 cryo-EM 结构中加入 N-聚糖和 PTMs，在两种蛋白的结合面附近产生糖基化位点，最后建立了精细的结构模型。HCoV-19 刺突蛋白和 hACE2 的 PTM 和聚糖图谱为研究宿主附着机制、刺突蛋白和 hACE2 介导的免疫应答以及开发当今急需的药物和疫苗提供了额外的结构细节。

编者注：相关文章，4 月 17 日简报中第 11 篇文章《糖胺聚糖在刺突糖蛋白 S1/S2 水解位点的结合模体可能会促进新冠病毒对宿主的入侵》讲到类似的研究。

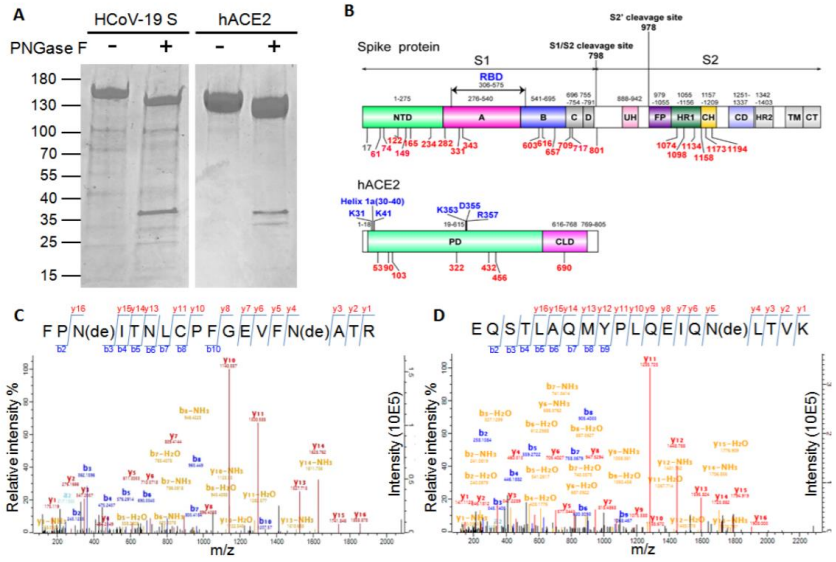

Figure. 1. Potential glycosylation sites in HCoV-19 spike protein and hACE2. A: 15% SDS-PAGE analysis of intact and deglycosylated form of HCoV-19 spike protein and hACE2. Molecular weight markers are shown on the left. B: schematic representation of functional subunits and domains of HCoV-19 spike protein (upper panel) and hACE2 (lower panel). CD, connector domain; CH, central helix; CT, cytoplasmic tail; FP, fusion peptide; TM, transmembrane domain; UH, upstream helix; HR1/2, heptad repeat 1/2. Blue indicated sites possibly responsible for interaction between the S protein and hACE2. Potential glycosylation sites within in each domain were listed in braces. Red indicated identified glycosylated sites in this study. Mass spectra of identified deglycopeptide containing N331 and N343 in HCoV-19 spike protein (C) and deglycopeptide containing N90 in hACE2 (D).

Abstract:

The pneumonia-causing COVID-19 pandemia has prompt worldwide efforts to understand its biological and clinical traits of newly identified HCoV-19 virus. In this study, post-translational modification (PTM) of recombinant HCoV-19 S and hACE2 were characterized by LC-MSMS. We revealed that both proteins were highly decorated with specific proportions of N-glycan subtypes. Out of 21 possible glycosites in HCoV-19 S protein, 20 were confirmed completely occupied by N-glycans, with oligomannose glycans being the most abundant type. All 7 possible glycosylation sites in hACE2 were completely occupied mainly by complex type N-glycans. However, we shown that glycosylation does not directly contribute to the binding affinity between SARS-CoV spike protein and hACE2. Additionally, we also identified multiple sites methylated in both proteins, and multiple

prolines in hACE2 are converted to hydroxylproline. Refined structural model were built by adding N-glycan and PTMs to recently published cryo-EM structure of the HCoV-19 S and hACE2 generated with glycosylation sites in the vicinity of binding surface. The PTM and glycan maps of both HCoV-19 S and hACE2 provide additional structural details to study mechanisms underlying host attachment, immune response mediated by S protein and hACE2, as well as knowledge to develop remedies and vaccines desperately needed nowadays.

8. 整合分析多组学数据和单细胞测序数据证明COVID-19感染里面血液动力学改变的分子来源，解释了老年病人里的凝血和死亡

Integrated analysis of bulk multi omic and single-cell sequencing data confirms the molecular origin of hemodynamic changes in Covid-19 infection explaining coagulopathy and higher geriatric mortality

来源：biorxiv

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链接：https://www.medrxiv.org/content/10.1101/2020.04.26.20081182v1

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通讯作者: Ishaan Gupta, Deepali Jain

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DOI：

编译者：蒋立春

中文摘要：

除了严重的呼吸窘迫，最近的报道表明 COVID-19 病人中血小板的数据和病人的生存率强相关。和诸如凝血时间变长、纤维降解产物以及 D 二聚体水平升高等等血流动力学的改变相随，也观察到更多单核细胞发生形态改变。

通过整合分析 COVID-19 病人来源的 RNA-seq 和肺组织单细胞测序数据，作者们发现大部分对基因表达有改变的细胞是血液系统来源细胞。作者们也发现 COVID-19 病人里的差异表达基因很显著有一群是表达在吞噬细胞比如单核细胞和血小板中的基因。有意思的是， 当作者们观察到 COVID-19 病人里单核细胞信号的富集，作者们发现里面并不包括 FCGRA3+单核细胞的信号。进一步的，作者在单核细胞和血小板中发现与年龄相关的基因和炎症相关，印证了 COVID-19 病人里的基因表达变化。这提示老龄化过程中促炎性信号通路可能会导致老年 COVID-19 病人病情恶化。作者们鉴定到 20 个基因在 COVID-19 感染和老化的细胞中变化方向一致，这些基因可能可以作为治疗的靶点。最有意思的是在血小板中表达的 IL2RG,GNLY 以及 GMZA，这些基因促进单核细胞和血小板通过相互作用而激活细胞因子信号通路。

为了理解病毒感染是否可以直接改变单核细胞和血小板的生物学过程，研究者们推测不表达 ACE2 的细胞可能通过吞噬途径感染病毒。作者们观察到和 COVID-19 病毒相互作用的基因在吞噬细胞比如单核细胞，T 细胞以及血小板中表达水平更高。作者推论说这些细胞类型在病毒的致病过程比如导致凝血中积极而不是被动地发挥了作用。该研究的结果从分子层面证明从抗炎和抗凝血两方面来对病人特别是老年病人进行治疗可能会收到更好的疗效。

Abstract

Besides severe respiratory distress, recent reports in Covid-19 patients have found a strong association between platelet counts and patient survival. Along

with hemodynamic changes such as prolonged clotting time, high fibrin degradation products and D-dimers, increased levels of monocytes with disturbed morphology have also been identified. In this study, through an integrated analysis of bulk RNA-sequencing data from Covid-19 patients with data from single-cell sequencing studies on lung tissues, we found that most of the cell-types that contributed to the altered gene expression were of hematopoietic origin. We also found that differentially expressed genes in Covid-19 patients formed a significant pool of the expressing genes in phagocytic cells such as Monocytes and Platelets. Interestingly, while we observed a general enrichment for Monocytes in Covid-19 patients, we found that the signal for FCGRA3+ Monocytes was depleted. Further, we found evidence that age-associated gene expression changes in Monocytes and Platelets, associated with inflammation, mirror gene expression changes in Covid-19 patients suggesting that pro-inflammatory signalling during aging may worsen the infection in older patients. We identified more than 20 genes that change in the same direction between Covid-19 infection and aging cells that may act as potential therapeutic targets. Of particular interest were IL2RG, GNLY and GMZA expressed in Platelets, which facilitates cytokine signalling in Monocytes through an interaction with Platelets. To understand whether infection can directly manipulate the biology of Monocytes and Platelets, we hypothesize that these non-ACE2 expressing cells may be infected by the virus through the phagocytic route. We observed that phagocytic cells such as Monocytes, T-cells, and Platelets have a significantly higher expression of genes that are a part of the Covid-19 viral interactome. Hence these cell-types may have an active rather than a reactive role in viral pathogenesis to manifest clinical symptoms such as coagulopathy. Therefore, our results present molecular evidence for pursuing both anti-inflammatory and anticoagulation therapy for better patient management especially in older patients.

9. CovidNLP：一个使用自然语言处理技术提取 COVID-19 疫情的系统性影响的 Web 应用程序

CovidNLP: A Web Application for Distilling Systemic Implications of COVID-19 Pandemic with Natural Language Processing

来源：medRxiv

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链接：https://www.medrxiv.org/content/10.1101/2020.04.25.20079129v1

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DOI 或 PUBMED ID：

编译者：宋珂

中文摘要：

对于 COVID-19 疾病的研究，存在大量不一致的结论。这说明人类对 COVID-19 的相关问题仍未完全了解。尽管 COVID-19 的流行程度很高，并有超过 14000 篇关于 COVID-19 的研究论文发表，但临床医生和研究人员仍在努力汲取有价值的信息，以提升临床管理和研究质量。在

这项研究中，作者借助自然语言处理技术，开发了名为“CovidNLP”的网络应用，用以帮助目标用户群体，如：临床医生，研究人员和政策制定者加快知识发现。WHO 已经建立了一个有关 COVID-19 的信息库，其中存储了流行病学，临床特征，诊断，治疗，社会因素和经济学等各方面大约 5000 余篇，经过同行评审和仔细挑选的研究文章。作者通过提取文章的节选，总结了 WHO 数据库中的所有内容。然后使用 word embedding 方法对特征空间进行了探索，并将文本中与 COVID-19 有关联的内容进行汇总，最终将结果可视化。临床医生，研究人员和政策制定者不仅会发现 COVID-19 的直接结果，而且还会发现系统性的影响。例如，作者的模型强调，由于进出口停止而无法获得药品，导致预期结核病的感染率和癌症死亡率的上升。现有结果证明，利用自然语言处理技术对海量文献进行挖掘，从而快速提炼和更新知识的实用性。这可以帮助用户整合和理解经过同行评审的有关 COVID-19 的可用信息，并采取快速行动。现有模型将随着新的文献产生而不断更新，且 CovidNLP 会以用户友好的形式对公众开放：http://covidnlp.tavlab.iiitd.edu.in/。

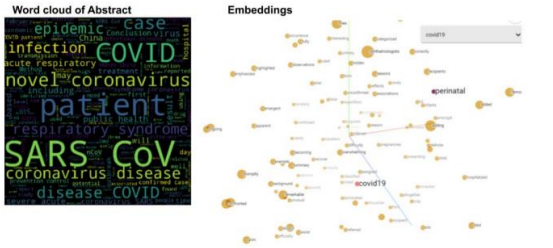

*Fig2: **Word** cloud generated by frequency count of words in the abstract of title and embedding of words generated by word2Vec and visualized on the CovidNLP dashboard.*

Abstract:
The flood of conflicting COVID-19 research has revealed that COVID-19 continues to be an enigma. Although more than 14,000 research articles on COVID-19 have been published with the disease taking a pandemic proportion, clinicians and researchers are struggling to distill knowledge for furthering clinical management and research. In this study, we address this gap for a targeted user group, i.e. clinicians, researchers, and policymakers by applying natural language processing to develop a CovidNLP dashboard in order to speed up knowledge discovery. The WHO has created a repository of about more than 5000 peer-reviewed and curated research articles on varied aspects including epidemiology, clinical features, diagnosis, treatment, social factors, and economics. We summarised all the articles in the WHO Database through an extractive summarizer followed by an exploration of the feature space using word embeddings which were then used to visualize the summarized associations of COVID-19 as found in the text. Clinicians, researchers, and policymakers will not only discover the direct effects of COVID-19 but also the systematic implications such as the anticipated rise in TB and cancer mortality due to the non-availability of drugs during the export lockdown as highlighted by our models. These demonstrate the utility of mining massive literature with natural language processing for rapid distillation and knowledge updates. This can help the users understand, synthesize, and take pre-emptive action with the available peer-reviewed evidence on COVID-19. Our models will be continuously updated with new literature and we have made our

resource CovidNLP publicly available in a user-friendly fashion at http://covidnlp.tavlab.iiitd.edu.in/.
编者注：我们在 3 月 20 日的简报介绍了针对 COVID-19 进行自然语言处理的 kaggle 挑战，包含更多的文献，已经有不少挑战者公开了自己的解决方案，可以参考。

10. 病毒星球计划：科普

链接： http://worldofviruses.unl.edu/
单位：内布拉斯加林肯大学
支持单位：NIH
编译者：蒋立春
中文摘要：

病毒星球计划是一个内布拉斯加林肯大学（University of Nebraska Lincoln，是巴菲特的母校）社会学系主办的一个关于病毒的科普教育项目。获得过 NIH 的科学教育合作奖，在 2007 到 2012 年间获得专项基金支持。

如下图网页主页截图所示，包括漫画（pdf 可免费下载），手机电脑 APP，有声故事，书，图片，K12 教育课程等等相关内容。其中中国读者最熟悉的应该是《病毒星球》这本科普读物。这本书由在芝加哥大学取得分子、遗传及细胞生物学博士学位专业的刘旸博士翻译，广西师范大学出版社于 2019 年 4 月出版第一版（编者还未开始阅读，暂无评论）。
其中 K12 教育内容丰富，既涵盖了常见的比如流感病毒，也涵盖了相对新发的 SARS，西非尼罗病毒等。网站里包括详细的课程设计内容和评估办法，值得我们在相关科普和基础教育中学习和推广。也是非生物医药人士进行科普阅读了解病毒和相关疾病的好选择。