

Boletim BiblioCovid

Boletim BiblioCovid v.2 n.8, agosto 2021 | Reinfecção da Covid-19

Boletim destinado a apresentação de estratégias e artigos científicos sobre temas relacionados à Covid-19.

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Reinfecção da Covid-19



Vocabulário controlado

MeSH – Medical Subject Headings (NLM/NIH)
DeCS

Bases utilizadas

Medline - (Acesso via portal Regional BVS)

Termos Utilizados (com base no Medical Subject Headings - MeSH):

Descritores e/ou palavras-chave

Reinfecção (DeCS)	Nuevo Coronavirus
Re-infecção (DeCS)	Novo Coronavirus
Reinfection (DeCS)	Coronavirus disease
Recurrent Infection	Enfermedad por Coronavirus
Reactivated Infection	severe acute respiratory syndrome coronavirus 2
New Coronavirus	Severe Acute Respiratory Infections
Novel Coronavirus	Severe Acute Respiratory Infection
covid-19	Infecção recorrente (termos alternativos)
Covid2019	Reativação de infecção (termos alternativos)
covid-2019	acute respiratory disease
covid 2019	mh:Betacoronavirus
2019-ncov	mh:Coronavirus infections
ncov 2019	srag-cov-2

Filtros utilizados

Artigos (tipo de documento)
Medline (base de dados)



Estratégias de busca

((Reinfec* OR Re-infec* OR Reactiv*Infec* OR Recurre*Infec* OR "infecção recorrente" OR "reativação da infecção") (((("2019-2020" OR 2019 OR da:202*) ("New Coronavirus" OR "Novel Coronavirus" OR "Nuevo Coronavirus" OR "Novo Coronavirus" OR "Coronavirus disease" OR "Enfermedad por Coronavirus" OR "severe acute respiratory syndrome coronavirus 2")) OR ((2019-ncov) OR (ncov 2019) OR 2019ncov OR covid19 OR (covid-19) OR covid2019 OR (covid-2019) OR ((srag-cov-2 OR sars-cov-2 OR sars2) OR (sars 2) OR (sars cov 2) OR cov19 OR cov2019 OR coronavirus* OR "Severe Acute Respiratory Infections" OR "Severe Acute Respiratory Infection" OR "Coronavirus 2" OR "acute respiratory disease" OR mh:Betacoronavirus OR mh:"Coronavirus infections" OR mh:"sars virus") AND (tw:2019 OR da:202*) AND NOT da:201*) OR (Wuhan market virus) OR (virus mercado Wuhan) OR "Wuhan Coronavirus" OR "Coronavirus de Wuhan") AND NOT (ti:dromedar*)))

Seleção dos dez artigos mais relevantes, segundo critérios da base de dados Medline, incluindo os filtros "Artigos (tipo de documento)" e "Medline (base de dados)"

1. Establishment of an African green monkey model for COVID-19 and protection against re-infection

[doi:10.1038/s41590-020-00835-8](https://doi.org/10.1038/s41590-020-00835-8)

Resumo

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for an unprecedented global pandemic of COVID-19. Animal models are urgently needed to study the pathogenesis of COVID-19 and to screen vaccines and treatments. We show that African green monkeys (AGMs) support robust SARS-CoV-2 replication and develop pronounced respiratory disease, which may more accurately reflect human COVID-19 cases than other nonhuman primate species. SARS-CoV-2 was detected in mucosal samples, including rectal swabs, as late as 15 days after exposure. Marked inflammation and coagulopathy in blood and tissues were prominent features. Transcriptome analysis demonstrated stimulation of interferon and interleukin-6 pathways in bronchoalveolar lavage samples and repression of natural killer cell- and T cell-associated transcripts in peripheral blood. Despite a slight waning in antibody titers after primary challenge, enhanced antibody and cellular responses contributed to rapid clearance after re-challenge with an identical strain. These data support the utility of AGM for studying COVID-19 pathogenesis and testing medical countermeasures.

Referência

MOLINA WOOLSEY, C. et al. Establishment of an African green monkey model for COVID-19 and protection against re-infection. **Nat Immunol**, v. 22, n. 1, p. 86-98, 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33235385/>. Acesso em: 21 jul. 2021.

2. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study

[doi:10.1016/S0140-6736\(21\)00575-4](https://doi.org/10.1016/S0140-6736(21)00575-4)

Resumo

The degree to which infection with SARS-CoV-2 confers protection towards subsequent reinfection is not well described. In 2020, as part of Denmark's extensive, free-of-charge PCR-testing strategy, approximately 4 million individuals (69% of the population) underwent 10.6 million tests. Using these national PCR-test data from 2020, we estimated protection towards repeat infection with SARS-CoV-2. **Methods** In this population-level observational study, we collected individual-level data on patients who had been tested in Denmark in 2020 from the Danish Microbiology Database and analysed infection rates during the second surge of the COVID-19 epidemic, from Sept 1 to Dec 31, 2020, by comparison of infection rates between individuals with positive and negative PCR tests during the first surge (March to May, 2020). For the main analysis, we excluded people who tested positive for the first time between the two surges and those who died before the second surge. We did an alternative cohort analysis, in which we compared infection rates throughout the year between those with and without a previous confirmed infection at least 3 months earlier, irrespective of date. We also investigated whether differences were found by age group, sex, and time since infection in the alternative cohort analysis. We calculated rate ratios (RRs) adjusted for potential confounders and estimated protection against repeat infection as $1 - RR$. During the first surge (ie, before June, 2020), 533 381 people were tested, of whom 11 727 (2.20%) were PCR positive, and 525 339 were eligible for follow-up in the second surge, of whom 11 068 (2.11%) had tested positive during the first surge. Among eligible PCR-positive individuals from the first surge of the epidemic, 72 (0.65% [95% CI 0.51–0.82]) tested positive again during the second surge compared with 16 819 (3.27% [3.22–3.32]) of 514 271 who tested negative during the first surge (adjusted RR 0.195 [95% CI 0.155–0.246]). Protection against repeat infection was 80.5% (95% CI 75.4–84.5). The alternative cohort analysis gave similar estimates (adjusted RR 0.212 [0.179–0.251], estimated protection 78.8% [74.9–82.1]). In the alternative cohort analysis, among those aged 65 years and older, observed protection against repeat infection was 47.1% (95% CI 24.7–62.8). We found no difference in estimated protection against repeat infection by sex (male 78.4% [72.1–83.2] vs female 79.1% [73.9–83.3]) or evidence of waning protection over time (3–6 months of follow-up 79.3% [74.4–83.3] vs ≥ 7 months of follow-up 77.7% [70.9–82.9]). Our findings could inform decisions on which groups should be vaccinated and advocate for vaccination of previously infected individuals because natural protection, especially among older people, cannot be relied on.

Referência

HANSEN, C. H. et al. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. **Lancet**, v. 397, p. 1204-1212, 2021. Disponível em: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00575-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00575-4/fulltext). Acesso em: 21 jul. 2021.

3. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN)

[doi:https://doi.org/10.1016/S0140-6736\(21\)00675-9](https://doi.org/10.1016/S0140-6736(21)00675-9)

Resumo

Increased understanding of whether individuals who have recovered from COVID-19 are protected from future SARS-CoV-2 infection is an urgent requirement. We aimed to investigate whether antibodies against SARS-CoV-2 were associated with a decreased risk of symptomatic and asymptomatic reinfection. A large, multicentre, prospective cohort study was done, with participants recruited from publicly funded hospitals in all regions of England. All health-care workers, support staff, and administrative staff working at hospitals who could remain engaged in follow-up for 12 months were eligible to join The SARS-CoV-2 Immunity and Reinfection Evaluation study. Participants were excluded if they had no PCR tests after enrolment, enrolled after Dec 31, 2020, or had insufficient PCR and antibody data for cohort assignment. Participants attended regular SARS-CoV-2 PCR and antibody testing (every 2-4 weeks) and completed questionnaires every 2 weeks on symptoms and exposures. At enrolment, participants were assigned to either the positive cohort (antibody positive, or previous positive PCR or antibody test) or negative cohort (antibody negative, no previous positive PCR or antibody test). The primary outcome was a reinfection in the positive cohort or a primary infection in the negative cohort, determined by PCR tests. Potential reinfections were clinically reviewed and classified according to case definitions (confirmed, probable, or possible) and symptom-status, depending on the hierarchy of evidence. Primary infections in the negative cohort were defined as a first positive PCR test and seroconversions were excluded when not associated with a positive PCR test. A proportional hazards frailty model using a Poisson distribution was used to estimate incidence rate ratios (IRR) to compare infection rates in the two cohorts. From June 18, 2020, to Dec 31, 2020, 30 625 participants were enrolled into the study. 51 participants withdrew from the study, 4913 were excluded, and 25 661 participants (with linked data on antibody and PCR testing) were included in the analysis. Data were extracted from all sources on Feb 5, 2021, and include data up to and including Jan 11, 2021. 155 infections were detected in the baseline positive cohort of 8278 participants, collectively contributing 2 047 113 person-days of follow-up. This compares with 1704 new PCR positive infections in the negative cohort of 17 383 participants, contributing 2 971 436 person-days of follow-up. The incidence density was 7.6 reinfections per 100 000 person-days in the positive cohort, compared with 57.3 primary infections per 100 000 person-days in the negative cohort, between June, 2020, and January, 2021. The adjusted IRR was 0.159 for all reinfections (95% CI 0.13-0.19) compared with PCR-confirmed primary infections. The median interval between primary infection and reinfection was more than 200 days. A previous history of SARS-CoV-2 infection was associated with an 84% lower risk of infection, with median protective effect observed 7 months following primary infection. This time period is the minimum probable effect because seroconversions were not included. This study shows that previous infection with SARS-CoV-2 induces effective immunity to future infections in most individuals. Department of Health and Social Care of the UK Government, Public Health England, The National Institute for Health Research, with contributions from the Scottish, Welsh and Northern Irish governments.

Referência

HALL, V. J. et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). *Lancet*, v. 397, p. 1459-1469, 2021. Disponível em: <https://www.sciencedirect.com/science/article/pii/S0140673621006759?via%3Dihub>. Acesso em: 21 jul. 2021.

4. Transmission and Protection against Reinfection in the Ferret Model with the SARS-CoV-2 USA-WA1/2020 Reference Isolate

[doi:https://doi.org/10.1128/JVI.02232-20](https://doi.org/10.1128/JVI.02232-20)

Resumo

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has initiated a global pandemic, and several vaccines have now received emergency use authorization. Using the reference strain SARS-CoV-2 USA-WA1/2020, we evaluated modes of transmission and the ability of prior infection or vaccine-induced immunity to protect against infection in ferrets. Ferrets were semipermissive to infection with the USA-WA1/2020 isolate. When transmission was assessed via the detection of viral RNA (vRNA) at multiple time points, direct contact transmission was efficient to 3/3 and 3/4 contact animals in 2 respective studies, while respiratory droplet transmission was poor to only 1/4 contact animals. To determine if previously infected ferrets were protected against reinfection, ferrets were rechallenged 28 or 56 days postinfection. Following viral challenge, no infectious virus was recovered in nasal wash samples. In addition, levels of vRNA in the nasal wash were several orders of magnitude lower than during primary infection, and vRNA was rapidly cleared. To determine if intramuscular vaccination protected ferrets, ferrets were vaccinated using a prime-boost strategy with the S protein receptor-binding domain formulated with an oil-in-water adjuvant. Upon viral challenge, none of the mock or vaccinated animals were protected against infection, and there were no significant differences in vRNA or infectious virus titers in the nasal wash. Combined, these studies demonstrate direct contact is the predominant mode of transmission of the USA-WA1/2020 isolate in ferrets and that immunity to SARS-CoV-2 is maintained for at least 56 days. Our studies also indicate protection of the upper respiratory tract against SARS-CoV-2 will require vaccine strategies that mimic natural infection or induce site-specific immunity. **IMPORTANCE** The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) USA-WA1/2020 strain is a CDC reference strain used by multiple research laboratories. Here, we show that the predominant mode of transmission of this isolate in ferrets is by direct contact. We further demonstrate ferrets are protected against reinfection for at least 56 days even when levels of neutralizing antibodies are low or undetectable. Last, we show that when ferrets were vaccinated by the intramuscular route to induce antibodies against SARS-CoV-2, ferrets remain susceptible to infection of the upper respiratory tract. Collectively, these studies suggest that protection of the upper respiratory tract will require vaccine approaches that mimic natural infection.

Referência

PATEL, D. R. et al. Transmission and Protection against Reinfection in the Ferret Model with the SARS-CoV-2 USA-WA1/2020 Reference Isolate. **Journal of Virology**, v. 95, n. 13, 2021. Disponível em: <https://journals.asm.org/doi/abs/10.1128/JVI.02232-20>. Acesso em: 21 jul. 2021.

5. ACoRE: Accurate SARS-CoV-2 genome reconstruction for the characterization of intra-host and inter-host viral diversity in clinical samples and for the evaluation of re-infections

[doi:https://doi.org/10.1016/j.ygeno.2021.04.008](https://doi.org/10.1016/j.ygeno.2021.04.008)

Resumo

Sequencing the SARS-CoV-2 genome from clinical samples can be challenging, especially in specimens with low viral titer. Here we report Accurate SARS-CoV-2 genome Reconstruction (ACoRE), an amplicon-based viral genome sequencing workflow for the complete and accurate reconstruction of SARS-CoV-2 sequences from clinical samples, including suboptimal ones that would usually be excluded even if unique and irreplaceable. The protocol was optimized to improve flexibility and the combination of technical replicates was established as the central strategy to achieve accurate analysis of low-titer/suboptimal samples. We demonstrated the utility of the approach by achieving complete genome reconstruction and the identification of false-positive variants in >170 clinical samples, thus avoiding the generation of inaccurate and/or incomplete sequences. Most importantly, ACoRE was crucial to identify the correct viral strain responsible of a relapse case, that would be otherwise mis-classified as a re-infection due to missing or incorrect variant identification by a standard workflow.

Referência

DALL'AVA, MARCOLUNGO, L. et al. ACoRE: Accurate SARS-CoV-2 genome reconstruction for the characterization of intra-host and inter-host viral diversity in clinical samples and for the evaluation of re-infections. **Genomics**, v. 113, n. 4, p. 1628-1638, 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33839270/>. Acesso em: 21 jul. 2021.

6. Serum Antibody Profile of a Patient With Coronavirus Disease 2019 Reinfection

doi: <https://doi.org/10.1093/cid/ciaa1368>

Resumo

We recently reported a patient with coronavirus disease 2019 reinfection. Here, we show that serum neutralizing antibodies could be detected during the first episode but not at the presentation of the second episode. During reinfection, neutralizing antibodies and high avidity immunoglobulin G were found within 8 days after hospitalization, whereas immunoglobulin M response was absent.

Referência

TO, K. K. et al. Serum Antibody Profile of a Patient With Coronavirus Disease 2019 Reinfection. **Clin Infect Dis.**, v. 72, n. 10, p. , 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/32966566/>. Acesso em: 21 jul. 2021.

7. Genetic Evidence and Host Immune Response in Persons Reinfected with SARS-CoV-2, Brazil

[doi: 10.3201/eid2705.204912](https://doi.org/10.3201/eid2705.204912)

Resumo

The dynamics underlying severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reinfection remain poorly understood. We identified a small cluster of patients in Brazil who experienced 2 episodes of coronavirus disease (COVID-19) in March and late May 2020. In the first episode, patients manifested an enhanced innate response compared with healthy persons, but neutralizing humoral immunity was not fully achieved. The second episode was associated with different SARS-CoV-2 strains, higher viral loads, and clinical symptoms. Our finding that persons with mild COVID-19 may have controlled SARS-CoV-2 replication without developing detectable humoral immunity suggests that reinfection is more frequent than supposed, but this hypothesis is not well documented.

Referência

FINTELMAN-RODRIGUES, N. et al. Genetic Evidence and Host Immune Response in Persons Reinfected with SARS-CoV-2, Brazil. **Emerging infectious diseases**, v. 27, n. 5, p. 1446-1453, 2021. Disponível em: <https://www.arca.fiocruz.br/handle/icict/47755>. Acesso em: 21 jul. 2021.

8. Genomic Evidence of SARS-CoV-2 Reinfection Involving E484K Spike Mutation, Brazil

[doi:10.3201/eid2705.210191](https://doi.org/10.3201/eid2705.210191)

Resumo

Uncertainty remains about how long the protective immune responses against severe acute respiratory syndrome coronavirus 2 persists, and suspected reinfection in recovered patients has been reported. We describe a case of reinfection from distinct virus lineages in Brazil harboring the E484K mutation, a variant associated with escape from neutralizing antibodies.

Referência

NONAKA, C. K. V. et al. Genomic evidence of SARS-CoV-2 reinfection involving E484K spike mutation, Brazil. **Emerging Infectious Diseases**, v. 27, n. 5, May 2021. Disponível em: <https://www.arca.fiocruz.br/handle/icict/47610>. Acesso em: 21 jul. 2021.

9. Severe Acute Respiratory Syndrome Coronavirus 2 P.2 Lineage Associated with Reinfection Case, Brazil, June-October 2020

doi: [10.3201/eid2707.210401](https://doi.org/10.3201/eid2707.210401)

Resumo

A 37-year-old healthcare worker from the northeastern region of Brazil experienced 2 clinical episodes of coronavirus disease. Infection with severe acute respiratory syndrome coronavirus 2 was confirmed by reverse transcription PCR in samples collected 116 days apart. Whole-genome sequencing revealed that the 2 infections were caused by the most prevalent lineage in Brazil, B.1.1.33, and the emerging lineage P.2. The first infection occurred in June 2020; Bayesian analysis suggests reinfection at some point during September 14-October 11, 2020, a few days before the second episode of coronavirus disease. Of note, P.2 corresponds to an emergent viral lineage in Brazil that contains the mutation E484K in the spike protein. The P.2 lineage was initially detected in the state of Rio de Janeiro, and since then it has been found throughout the country. Our findings suggest not only a reinfection case but also geographic dissemination of the emerging Brazil clade P.2.

Referência

RESENDE, P. C. et al. Severe Acute Respiratory Syndrome Coronavirus 2 P.2 Lineage Associated with Reinfection Case, Brazil, June–October 2020. **Emerging Infectious Diseases**, v. 27, n. 7, p. 1789-1794, July 2021. Disponível em: <https://www.arca.fiocruz.br/handle/icict/47920>. Acesso em: 21 jul. 2021.

10. Respiratory Viral Shedding in Healthcare Workers Reinfected with SARS-CoV-2, Brazil, 2020

doi: [10.3201/eid2706.210558](https://doi.org/10.3201/eid2706.210558)

Resumo

We documented 4 cases of severe acute respiratory syndrome coronavirus 2 reinfection by non-variant of concern strains among healthcare workers in Campinas, Brazil. We isolated infectious particles from nasopharyngeal secretions during both infection episodes. Improved and continued protection measures are necessary to mitigate the risk for reinfection among healthcare workers.

Referência

AMORIM, M. R. et al. Respiratory Viral Shedding in Healthcare Workers Reinfected with SARS-CoV-2, Brazil, 2020. **Emerg Infect Dis**, v. 27, n. 6, p. 1737-1740, 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33871331>. Acesso em: 21 jul. 2021.



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Expediente

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Diagramação

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