

## IN BRIEF

## COVID-19

## Will we see protection or reinfection in COVID-19?

There is rising concern that patients who recover from COVID-19 may be at risk of reinfection. In this preprint, Bao et al. investigated acquired immunity to SARS-CoV-2 in rhesus macaques. Four rhesus monkeys were infected with SARS-CoV-2 and two were reinfected after confirmed recovery. After primary infection, viral replication was detected in the nose, pharynx, lungs and gut, with histopathological evidence of lung damage. Sera collected from recovered monkeys before reinfection exhibited neutralizing activity against SARS-CoV-2. Upon reinfection, viral replication was not detected in nasopharyngeal or anal swabs, and reinfected monkeys did not show any signs of COVID-19 disease recurrence. This suggests that immunity acquired following primary infection with SARS-CoV-2 may protect upon subsequent exposure to the virus.

**ORIGINAL ARTICLE** Bao, L. et al. Reinfection could not occur in SARS-CoV-2 infected rhesus macaques. Preprint at *bioRxiv* <https://doi.org/10.1101/2020.03.13.990226> (2020)

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## Macrophages: a Trojan horse in COVID-19?

Patients with severe COVID-19 exhibit marked lymphopenia. This preprint by Feng et al. used immunohistochemistry and immunofluorescence to characterize hilar and subscapular lymph nodes and spleens post-mortem from six patients who died from COVID-19. In addition to splenic and lymph node atrophy and necrosis, the authors reported significant lymphocytic apoptosis. Of note, ACE2-expressing CD68<sup>+</sup>CD169<sup>+</sup> macrophages were detected in the splenic marginal zone and in marginal sinuses of lymph nodes, and these macrophages contained SARS-CoV-2 nucleoprotein antigen and showed upregulation of IL-6. Virally infected tissues also showed higher expression of FAS. This suggests that CD169<sup>+</sup> macrophages could contribute to viral spread, excessive inflammation and activation-induced lymphocytic cell death during SARS-CoV-2 infection.

**ORIGINAL ARTICLE** Feng, Z. et al. The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) directly decimates human spleens and lymph nodes. Preprint at *medRxiv* <https://doi.org/10.1101/2020.03.27.20045427> (2020)

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## A map of SARS-CoV-2 and host cell interactions

Currently, little is known about the molecular interactions between SARS-CoV-2 and its host. In this preprint, Gordon et al. cloned, tagged and expressed 26 of 29 SARS-CoV-2 proteins individually in HEK293T cells and used mass spectrometry to measure protein-protein interactions. They identified 332 interactions between viral and host proteins, and several viral proteins (including N, nsp9, nsp13, nsp15, ORF3a and ORF6) were found to directly target cellular proteins involved in innate immune signalling. Furthermore, they noted 69 existing drugs known to target host proteins or associated pathways that interact with SARS-CoV-2. Overall, this 'SARS-CoV-2 interaction map' paves the way to better understand how the virus hijacks its host during infection and provides promising therapeutic candidates.

**ORIGINAL ARTICLE** Gordon, D. E. et al. A SARS-CoV-2-human protein-protein interaction map reveals drug targets and potential drug-repurposing. Preprint at *bioRxiv* <https://doi.org/10.1101/2020.03.22.002386> (2020)

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(encoded by *Slc40a1*), the authors next looked at the role of ferroportin in the intestine. Mice expressing a hepcidin-resistant ferroportin variant (*Slc40a1*<sup>C326Y</sup>) specifically in macrophages and neutrophils had impaired intestinal repair after DSS withdrawal, which indicates that these cells are a crucial target for CDC-derived hepcidin in the gut.

So what is the mechanism of hepcidin-mediated intestinal repair? *Hamp*<sup>ΔCD11C</sup> mice had higher levels of non-haem iron in the intestinal lumen after DSS administration than control mice. This likely reflects, in the absence of hepcidin, the ferroportin-mediated efflux of iron from intestinal macrophages that have phagocytosed erythrocytes. The extracellular iron chelator deferoxamine restored mucosal repair

after DSS withdrawal in *Hamp*<sup>ΔCD11C</sup> mice. In keeping with the known role of iron in modulating microbial populations, *Hamp*<sup>ΔCD11C</sup> mice had altered composition of the intestinal microbiota with increased levels of tissue-infiltrating bacteria, and faecal microbiota transplantation from *Hamp*<sup>ΔCD11C</sup> mice to wild-type germ-free mice transferred the impaired intestinal repair phenotype.

Thus, hepcidin production by intestinal DCs in response to microbial signals limits iron levels in the intestinal lumen, which restrains tissue infiltration by the microbiota to promote intestinal repair.

Kirsty Minton

**ORIGINAL ARTICLE** Bessman, N. J. et al. Dendritic cell-derived hepcidin sequesters iron from the microbiota to promote mucosal healing. *Science* <https://doi.org/10.1126/science.aau6481> (2020)



Importantly, incubation of these platelets with a reporter cell line showed that the virus was replication competent



They isolated platelets from people treated with antiretroviral therapy, 15 of which had a detectable viral load in blood, whereas in 27 people the viral load was below the detection limit. 10 of the 27 people with suppressed viral load had detectable HIV RNA in their platelets with around ten copies per million platelets, which was more than ten times lower than the copy number in platelets from the other group of people with the detectable viral load. Labelling and fluorescence assays confirmed that viral RNA and p24, a capsid component, were present in platelets, suggesting that they contain intact virions. Megakaryocytes also contained HIV,

making them the likely origin of the platelet-associated virus.

Importantly, incubation of these platelets with a reporter cell line showed that the virus was replication competent. Platelets were able to transfer virus to macrophages after phagocytosis, a process that happens during platelet clearance. The macrophages contained integrated HIV DNA and produced infectious virus.

Finally, the people with HIV-containing platelets had lower CD4<sup>+</sup> T cell counts than those with HIV-negative platelets, which suggests a link to disease progression.

In summary, this study shows that platelets harbour replication-competent HIV and as such can perpetuate infection.

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**ORIGINAL ARTICLE** Real, F. et al. Platelets from HIV-infected individuals on antiretroviral drug therapy with poor CD4<sup>+</sup> T cell recovery can harbor replication-competent HIV despite viral suppression. *Sci. Transl. Med.* **12**, eaat6263 (2020)