2nd Edition of
Coronavirus and Research
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Why might haem be a good target for SARS-CoV-2?





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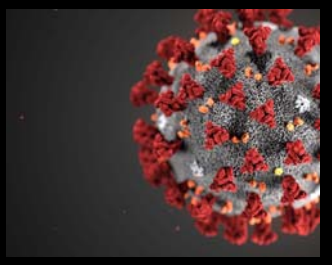
To date, the COVID-19 pandemic has infected 191 million people worldwide, with 4,11 million deaths.

Although a vaccination campaign has been launched, the situation is still not under control.

Many variants, such as English, Brazilian, Indian.. must be considered



During the quarantine period in March 2020, a case report of Slovenian skiers with COVID brought our interest in studying this disease

They found benefit from irradiation of the thoracic region with red to near-infrared radiation (R/NIR) combined with 660 and 920 nm, at a total fluence of 10 J/cm2 (i.e. two 5 J/cm2 sessions per day) (data not published).
The efficacy of this treatment was confirmed a few months later by a Brazilian study in humans [Fernandes AB et al. Photobiomodul. Photomed. Laser Surg.2020], based on an earlier study reporting the effect of light irradiation in mice with pneumonia [Geralde MC et al. Physiol Rep 2017].

The mechanism of action of SARS-CoV-2 is not clear yet.

Principal targets: respiratory and hematopoietic systems and homeostasis.

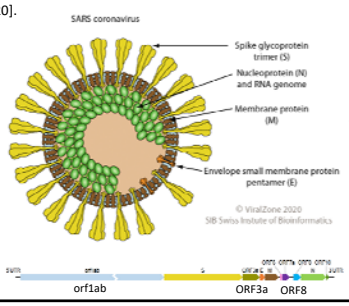
- ↓ Haemoglobin
- ↑ Serum ferritin
- ↑ Erythrocyte sedimentation rate
- ↑ C-reactive protein
- ↑ Lactate dehydrogenase
- ↑ Bilirubin
- ↑ Porphyria

These data support **a link between SARS-CoV-2 and iron metabolism,**
similar with other RNA viruses, such as hepatitis C and B, Ebola, human

In this study, several lines of evidence suggest a potential link between virus and Hb

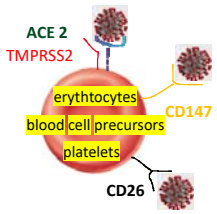
i) women who have lower Hb levels than men are less susceptible to infection COVID;
ii) new-borns of infected mothers do not get sick; the beta chain of Hb appears a few weeks after birth;
iii) at the beginning of the pandemic, there was a very low percentage of clinical cases in many Mediterranean regions, such as Tunisia, Libya, Sardinia, and Sicily. This is possibly due to many patients with beta- thalassemia in these areas, a blood disease caused by abnormalities in the beta-chains of Hb

A molecular docking study found that the viral ORF8 protein and surface glycoprotein bind to porphyrin. At the same time orf1ab, ORF3a proteins could coordinate attack the haem on the 1-beta chain of haemoglobin to dissociate the iron to form the porphyrin [Liu & Li. ChemRxiv 2020].



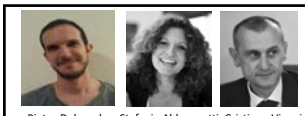
Recent studies confirmed the increase in the production of haem and free haemoglobin and demonstrated the link between SARS-CoV-2 and haem through a **computational-experimental** approach [Paul George AA et al. BMC Bioinform 2020; Lansiaux E. et al. Med Hypotheses 2020

Viral interactions with receptors located on erytrocytes and blood cell precursors



Radzikowska U et al bioRxiv 2020;
Liu & Li. ChemRxiv 2020;
Cosic I et al Appl. Sci 2020
Khawaja UA et al. Einstein Journal 2021
Thomas T et al. J. Proteom. Res 2020

SARS-CoV-2 binds to haem



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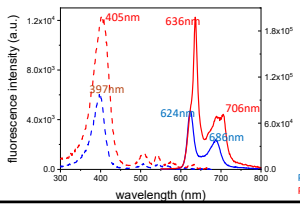
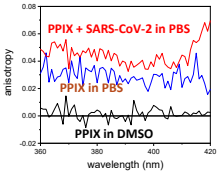
excitation and emission

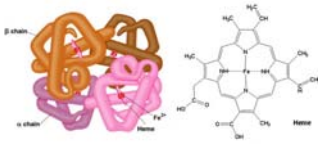


fluorescence anisotropy from excitation spectra



PPIX (250 nM) in PBS
PPIX (250 nM) + SARS-CoV-2 (dil 1:10, ~5nM) in PBS

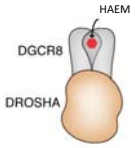
OUR QUESTIONS…



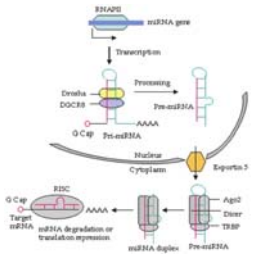
Why would the virus target haem?

What would be the benefit to this?

Haem regulates microRNA processing



Nguyen TA et al NAR 2018
Partin AC et al Nature Commun. 2017



Roles of MicroRNA in DNA Damage and Repair

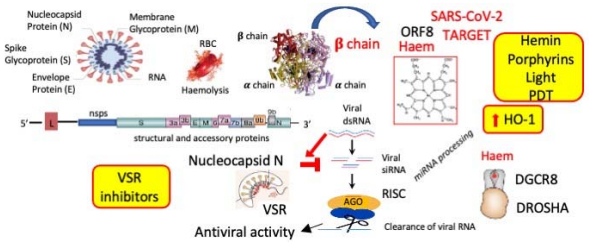
Xinrong Chen and Tao Chen

The Nucleocapsid Protein of Coronaviruses Acts as a Viral Suppressor of RNA Silencing in Mammalian Cells

The SARS-CoV-2-encoded structural protein N displayed VSR activity in cultured human cells.
SARS-CoV-2-N can antagonize RNAi in both initiation (i.e. siRNA biogenesis) and effector (i.e. RISC assembly and target RNA cleavage) steps.

Cui L. J Virol. 2015
Mu J et al . Sci China Life Sci. 2020

OUR DESIGN….with some possible strategies to reduce the virulence of SARS-CoV-2



With the goal of defeating the pandemic triggered by SARS-CoV-2 as soon as possible

THANK YOU FOR YOUR ATTENTION