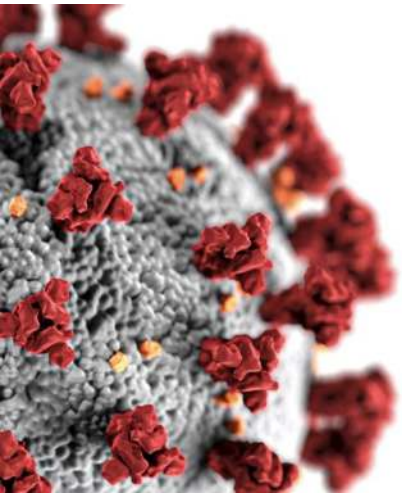

Research Symposium on Coronavirus

6 May 2020 online

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Societat Catalana de **BIOLOGIA**

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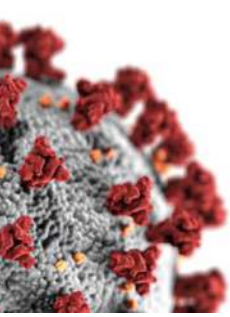
Abstracts Book



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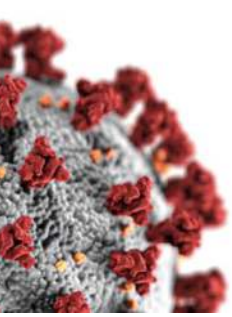

Research Symposium on Coronavirus

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9.00 **Welcome and presentation**

Robert Fabregat
Director of Research and Innovation in Health of the Generalitat de Catalunya
Montserrat Corominas
UB, President of the Societat Catalana de Biologia (SCB)

Session 1. Chairs: Albert Jordan (IBMB-CSIC) and Eduard Torrents (IBEC, UB)

9.15-9.30 **Júlia Vergara-Alert** (IRTA CReSA)
Animal models for the study of SARS-CoV2

9.30-9.45 **Julià Blanco** (IGTP, IrsiCaixa)
SARS-CoV-2 Vaccines. Who, How and When?

9.45-10.00 **Joan Joseph** (VHIR)
CoVIIIRvac. VIIIR vaccine model for SARS-CoV-2

10.00-10.10 **Israel Fernández-Cadenas** (IIB Sant Pau)
INMUNGEN-CoV-2 genetic variants as determinants of COVID-19 severity

10.10-10.30 **Jordi Serra-Cobo** (IRBio)
Eco-epidemiological works in CoV reservoirs

10.30-10.50 **Antoni Trilla** (Hospital Clínic de Barcelona, UB)
Epidemiology and control of COVID-19

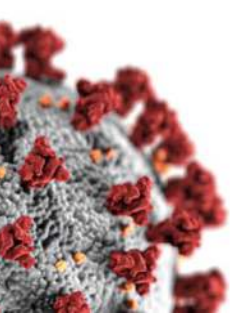
10.50-11.00 **Raquel Villar-Hernández** (IGTP)
Tuberculosis in times of COVID-19

Session 2. Chairs: Montserrat Sala (ICM-CSIC) and Fina Climent (Bellvitge University Hospital, IDIBELL)

11.30-11.45 **Albert Bosch** (UB)
Early warning tool to assess the circulation of SARS-CoV-2 among the population through comprehensive surveillance in wastewater

11.45-12.00 **Lluïsa Pedro-Botet** (Hospital Germans Trias i Pujol)
Olfactory paper-based test as an approach for early detection of COVID-19

12.00-12.20 **Bonaventura Clotet** (IrsiCaixa, Hospital Germans Trias i Pujol)
Where to direct the current research in the fight against coronavirus?



12.20-12.30 **Susana Otero** (Vall d'Hebron University Hospital)
Test performance evaluation of SARS-CoV-2 serological assays: experience from Vall d'Hebron University Hospital

12.30-12.40 **Sílvia Vidal** (IIB Sant Pau)
Immune response to SARS-CoV-2 in hospital workers

12.40-12.50 **Raul Bescos** (University of Plymouth)
Detection of SARS-CoV RNA in saliva samples and assessment of salivary lactate and nitrite as prognostic factors

12.50-13.05 **Rafael Máñez** (Bellvitge University Hospital, IDIBELL)
Elicitation of protective immunity against SARS-CoV-2 by selective removal of non-neutralizing antibodies used by the virus to enhance its infectivity

13.05-13.20 **Gemma Moncunill** (ISGlobal)
Levels and seroprevalence of antibodies against SARS-CoV-2 in health care workers measured by a Luminex-based assay

Session 3. Chairs: Marc Martí-Renom (CNAG-CRG) and Núria Busquets (IRTA-CReSA)

14.30-14.40 **Tanja Ducic** (ALBA Synchrotron)
Synchrotron-based infrared microspectroscopy studies in an interaction virus-infected cells

14.40-14.50 **Juan José López-Moya** (CRAG)
Plant biotechnology contributions to fighting SARS-CoV-2: from therapy to vaccine development

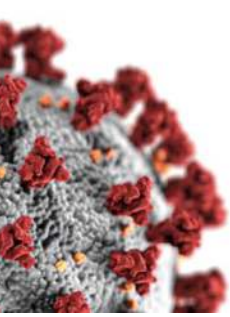
14.50-15.00 **Laia Fernández-Barat** (IDIBAPS)
Identification of epitopes and anti-COVID-19 IgG isolation to produce monoclonal antibodies for treatment

15.00-15.15 **Patrick Aloy** (IRB Barcelona)
Bioactivity profile similarities to expand the repertoire of drugs against COVID-19

15.15-15.30 **Jordi Rodon** (IRTA CReSA)
Search for SARS-CoV-2 inhibitors in currently approved drugs to tackle COVID-19 pandemia

15.30-15.40 **Marta Monguió-Tortajada** (IGTP)
Current immunotherapy approaches for COVID-19

15.40-15.50 **Sandra Acosta-Verdugo** (UPF)
Organoids for drug repurposing in COVID-19



Session 4. Chairs: Roderic Guigó (CRG) and Modesto Orozco (IRB Barcelona, PCB)

16.15-16.30 **Fernando González-Candelas** (UV FISABIO)
Genomic epidemiology of SARS-CoV-2 in Spain. The SeqCOVID-Spain consortium

16.30-16.45 **Eva Maria Novoa** (CRG)
Integrative analysis of SARS-COV-2 RNA modifications using nanopore direct RNA sequencing datasets and our pipeline MasterOfPores

16.45-17.00 **Francisco Martínez-Jiménez** (IRB Barcelona)
Mutational landscape of SARS-CoV-2 across human hosts and its interplay with Human Leukocyte Antigen recognition

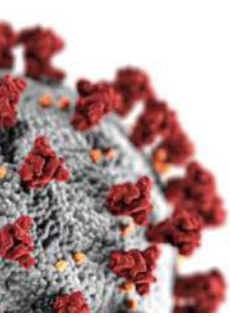
17.00-17.10 **Jonathan Mudge** (EBI, EMBL)
Manual re-annotation and analysis of human protein coding genes linked to COVID-19 pathology

17.10-17.20 **Josep Quer** (VHIR)
Whole-Genome Sequencing of SARS-CoV-2 using Next Generation Sequencing

17.20-17.30 **Andrej Bugrim** (Silver Beach Analytics, Inc.)
Global network analysis of viral-human protein interactions reveals potential mechanism of lung injury by SARS-CoV-2 infection and suggests targets for drug repurposing

17.30-17.45 **Xavier Hernández-Alias** (CRG)
Translational adaptation of human viruses to the tissues they infect

17.45 **Closure**



Animal models for the study of SARS-CoV-2

Júlia Vergara-Alert[1], Jordi Rodon[1], Nuria Izquierdo-Useros[2,5], Bonaventura Clotet[2,5,6], Alfonso Valencia[3,4], Víctor Guallar[3,4], Julià Blanco[2,5,6], Jorge Carrillo[2], Joaquim Segales[7,8]

[1]IRTA, Centre de Recerca en Sanitat Animal (CReSA, IRTA-UAB), Campus de la UAB, 08193 Bellaterra (Cerdanyola del Vallès), Spain
[2]IrsiCaixa AIDS Research Institute, 08916, Badalona, Spain
[3]Barcelona Supercomputing Center
[4]Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain
[5]Germans Trias i Pujol Research Institute (IGTP), Can Ruti Campus, 08916, Badalona, Spain
[6]University of Vic–Central University of Catalonia (UVic-UCC), Vic, Spain
[7]UAB, CReSA (IRTA-UAB), Campus de la UAB, 08193 Bellaterra (Cerdanyola del Vallès), Spain
[8]Departament de Sanitat i Anatomia Animals, Facultat de Veterinària, UAB, 08193 Bellaterra (Cerdanyola del Vallès), Spain

Coronaviruses are a threat for humans, as evidenced in 2002/2003 with the infection by the severe acute respiratory syndrome coronavirus (SARS-CoV), and with the Middle East respiratory syndrome coronavirus (MERS-CoV), which emerged in 2012. Recently, a novel coronavirus (named SARS-CoV-2) is causing a large pandemic and has spread around the world, being the responsible of more than 4,000.000 cases and nearly 300,000 deaths (May 2020). These highly pathogenic coronaviruses crossed the species barrier to infect humans and have taught us that they do not recognize international borders. Finding an animal model of disease is key to develop vaccines or antivirals against such emerging pathogens and to understand its pathogenesis. In this presentation experimental data on potential animal models for SARS-CoV-2 is reviewed, from rodents to non-human primates. Any ideal animal model should reflect clinical signs, viral replication and pathology resembling those in humans. Advantages and limitations of different animal models are evaluated in relation to viral pathogenesis and transmission studies.

FINANCIAL SUPPORT: The research of CBIG consortium (constituted by IRTA-CReSA, BSC, & IrsiCaixa) is supported by Grifols pharmaceutical. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

SARS-CoV-2 Vaccines. Who, How and When?

Julià Blanco[1,2,3], Jorge Carrillo[1], Nuria Izquierdo-Useros[1], Alfonso Valencia[4], Alba Lepore[4], Victor Guallar[4], Joaquim Segalés[5], Júlia Vergara-Alert[5], Bonaventura Clotet[1,2,3]

[1]Institut de Recerca de la SIDA-Caixa, IRSICAIXA
[2]Institut Germans Trias i Pujol, IGTP
[3]UVIC-UCC
[4]Barcelona Supercomputing Center, BSC
[5]IRTA-CReSA, UAB

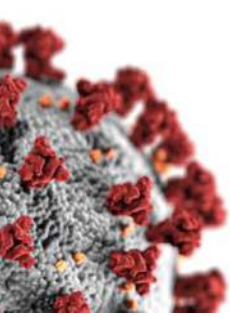
There is a general consensus that a vaccine would be the crucial defense against SARS-CoV-2 and the best strategy to go back to normal life after COVID-19 pandemic. This idea has prompted an unprecedented international effort to develop as soon as possible a safe and effective vaccine with more than 60 initiatives covering all the current known vaccine technologies, including attenuated viruses, VLPs, viral vectors, recombinant proteins and nucleic acid delivery strategies.

However, this global effort is facing an unexpected situation, in which the necessity and the regulatory control would need to find a new balance to overcome constricted vaccine development timings. Classical vaccine development requires different periods of academic/discovery research, preclinical development, clinical phases and large-scale manufacturing before approval and worldwide distribution. These steps usually take 10-15 years.

Shortening this schedule is a seemingly premade decision that will need to manage the risks associated to each step. Namely:

- Shortening academic research by trusting in information retrieved from other human coronaviruses (SARS, MERS)
- Shortening preclinical research by developing previous vaccine platforms with solid safety records in humans
- Accelerating clinical phase in agreement with regulatory bodies according to an urgency/safety equilibrium
- Promoting large-scale production in a joint public/private effort that will finally coordinate the
- worldwide distribution

This presentation will address current knowledge in academic research, which is the starting point and the major strength of an efficient vaccine. However, the preclinical, clinical and regulatory aspects that follow basic research will be also discussed, as they will be also determinant for the success of the different vaccine initiatives.



INMUNGEN-CoV2 Project. Genetic predisposition for COVID-19 outcome

Israel Fernández-Cadenas[1], Natalia Cullell[1,2], Laia Llucia Carol[1,2], Miquel Lledós[1], Jordi Pérez-Tur[3], Anna Planas[4]

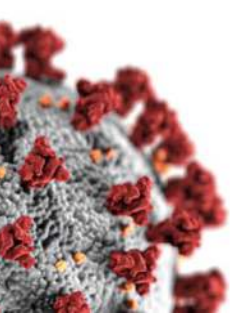
[1]Stroke Pharmacogenomics and Genetics group, Sant Pau Research Institute, Barcelona.
[2]Neurology Unit, Mutua de Terrassa Hospital, Fundació Docència i Recerca MutuaTerrassa.
[3]Institut de Biomedicina de València-CSIC CIBERNED.
[4]Institut d'investigacions BIomèdiques de Barcelona (IIBB-CSIC).
[5]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS).

Background: SARS-CoV2 infection displays inter-individual clinical variability, ranging from silent infection to hospitalization in ICU units. Genetic predisposition could modulate this clinical variability. To find genetic risk factors associated with COVID-19 severity is important to find potential drug targets and to elucidate the biological mechanisms associated with the COVID-19 outcome.

Methods: We aim to study 2.000 with confirmed SARS-CoV-2 infection patients using Genome-Wide Association (GWAs) analysis and 400 patients with Whole Exome Sequencing (WES). The study will compare patients either asymptomatic or developing mild symptoms with patients with severe Covid-19. For the GWAs analysis we will use the Axiom Spain Biobank array (Thermofisher) that can analyse 700.000 single nucleotide variants (SNVs) across the genome. Imputation analysis using Michigan server or TOPMED data will be used to obtain more than 4M SNVs. Impute2, R, SNPtest, VEGAS-2, software among others will be used for the genetic analysis.

Results: Five Spanish hospitals have been included in the study. First round of genotyping will be performed during the following month.

Acknowledgment: Financed by CSIC (Intramural Project nº 202020E086).



Tuberculosis in times of COVID-19

Raquel Villar Hernández

Servei de Microbiologia, Hospital Universitari Germans Trias i Pujol. Institut d'Investigació Germans Trias i Pujol, Badalona, Spain. CIBER Enfermedades Respiratorias, CIBERES, Instituto de Salud Carlos III, Madrid, Spain. Universitat Autònoma de Barcelona, Barcelona, Spain.

Tuberculosis (TB) is an infectious disease caused by bacilli from the *Mycobacterium tuberculosis* complex. Bacteria from this complex, usually affect the lungs, producing pulmonary TB, but can also cause extrapulmonary disease. TB is the first cause of death worldwide due to a single infectious agent, accounting for 1.5 million deaths in 2018 and affecting millions of people each year with an estimate of 10 million new cases in 2018. The recent COVID-19 pandemic has risen several concerns regarding the potential worsening of TB, not only due to the effects of interrupting TB diagnosis and treatment to focus on the new respiratory infectious agent (SARS-CoV-2) but also due to the implications that TB and COVID-19 coinfection may have. Lung damage present in TB patients may induce more aggressive forms of COVID-19 and at the same time, COVID-19 lung injuries may also affect TB infection susceptibility and disease outcome. In addition, less COVID-19 severity has been recently correlated with BCG vaccination. Due to its novelty, COVID-19 is greatly understudied, poorly understood and its implications on TB are a worldwide concern that needs to be addressed.

Olfactory paper-based test as an approach for early detection of COVID-19

M. Luisa Pedro-Botet[1,2,3], Bonaventura Clotet[1,4], Joan Francesc Julian[1,3], Juan Lorente[5], Alexy Inciarte[6], Isam Alobid[6], Antonio María de Lacy[6], Susana Santos[7], Rita Dominges[7], Olga Serrano Arjona[8], Núria Íbáñez[8], Pau Turon[8]

[1]Hospital Germans Trias i Pujol
[2]Centro de Investigación Biomédica en Red
[3]Universitat Autònoma de Barcelona
[4]IrsiCaixa
[5]Hospital Universitari Vall d'Hebron
[6]Hospital Clínic de Barcelona
[7]NasumTECH
[8]B. Braun

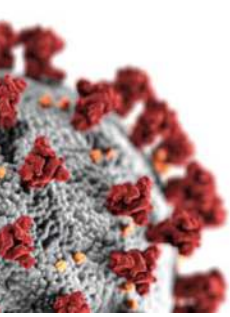
Based on the American Academy of ORL register and Head and Neck Surgery on anosmia/ageusia COVID-19 related symptoms, anosmia was present in 73% of subjects prior to COVID-19 diagnosis and was the initial symptom in 26.6%. The occurrence of smell dysfunction in viral infections is not new. Many viruses may lead to olfactory dysfunction through an inflammatory reaction of the nasal mucosa and further development of rhinorrhoea. The spread of the COVID-19 infection in Europe has highlighted a new atypical presentation of the disease related to dysfunctions in olfactory and gustatory senses. In a recent study, over a population of 417 patients, the authors reported that 85.6% of the infected patients had olfactory dysfunction related to the infection and that this appeared before respiratory symptoms in up to 12%.

In order to clarify if an anosmia test could be useful to control the spread of the virus, we wondered if an olfactory paper-based test could be faster and cheaper than rRT-PCR as a pre-screening approach for COVID-19 infection. To achieve such an objective a clinical validation of the anosmia test was proposed.

A prospective multicentre diagnostic study will be developed in three University hospitals located in Barcelona (H. Germans Trias i Pujol, H. Clínic and H. Vall d'Hebron). The primary objective is to assess the sensitivity and specificity of an olfactory paper-based test for the diagnosis of COVID-19 infection. The olfactory test is based on four validated anosmia chemical components and a control without smell. The validation will be performed in two different environments: a) Emergency Department (in symptomatic and asymptomatic patients for COVID-19) and, b) Hospital corporate setting (asymptomatic health care professionals). In each branch, 1,050 people (350/hospital) will be involved. Every patient or professional will be provided with the olfactory test. A self-test will be performed every 48 h for 32 days. The results of each daily test

will be uploaded to a digital platform that will collect date for further assessment. For the validation, the gold standard will be the RT-PCR for SARS-CoV-2 antigens. To calculate the sensitivity, we will evaluate how many patients do have a positive rRT-PCR among those with a positive (anosmia or hyposmia) olfactory test. For the specificity, as the ability to correctly identify those patients without the disease, it will be assessed how many patients do have a negative olfactory test (normal olfact) compared those with a negative rRT-PCR.

As predictions about the evolution of the pandemic are uncertain, health care systems shall be prepared for a second COVID-19 wave. Thus, if the olfactory test validation is adequate, a massive spread of olfactory tests among the population would be recommended to detect asymptomatic cases and its geographical location. As a consequence, the virus transmission could be stopped by isolating and treating the infected patients in an early stage.



Test performance evaluation of SARS-CoV-2 serological assays: experience from HUVH

Susana Otero-Romero[1]; Juliana Esperalba[2], Ricardo Zules[1], Fernando Velasquez[2], Irene Torrecilla[1], Laia Pinós[1], Tomas Pumarola[2] and Magda Campins[1]

[1]Servei de Medicina Preventiva i Epidemiologia. Hospital Universitari Vall d'Hebron
[2]Servei de Microbiologia. Hospital Universitari Vall d'Hebron

Background: Serological (immunocromatography and ELISA) test can be an important tool in de-escalation phase of the Covid-19 pandemic and external validation is essential. Aim: to evaluate the performance of a rapid immunocromatography test (*Hangzhou All Test Biotech*®) at the HUVH hospital setting.

Methods: we conducted 3 sub-studies: 1) Case – control study in hospitalized Covid-19 patients; 2) Seroprevalence study in asymptomatic healthcare workers (HCW); 3) Case – control study in asymptomatic/paucisymptomatic Covid-19 healthcare workers. A finger prick sample and a questionnaire (demographic, clinical and epidemiological data) was performed in all 3 studies.

Results: the global test performance in 25 Covid-19 hospitalized patients and 24 PCR negative controls was: 96% sensitivity (IC 95% 80.46 - 99.29%) and 100% specificity (IC 95% 86.20% - 100.00%). The global seroprevalence in 144 HCW was 2.8% (IC95% 0.8 to 7.0). Finally, the test performance in 13 paucisymptomatic patients and 24 PCR negative controls was 69.2% Sensitivity (IC 95% 42.4 - 87.3%) and 100% Specificity (IC 95% 86.2% - 100%).

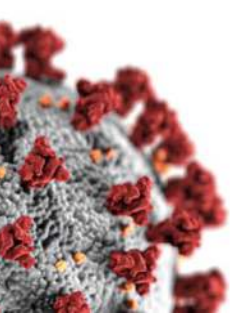
Conclusions: The performance specifications of immunochromatography tests in the manufacturers' brochure may not be applicable to other populations. In asymptomatic and paucisymptomatic Covid-19 cases is lower than in hospitalized patients.

Humoral response to SARS-CoV-2 in hospital workers

Sílvia Vidal[1], Josep F. Nomdedeu[2]

[1]Grup de Malalties Inflamatòries-Immunologia (Institut Rec. Hospital de la Santa Creu i Sant Pau)
[2]Servei Hematologia (Hospital de la Santa Creu i Sant Pau)

Antibodies against SARS-CoV2 can be produced following an exposure to the virus, generating an effective protection against another virus infection. Collecting serum from health professionals at three time points and analyzing the IgM and IgG antibody titers against N, S1 and S2 proteins by commercial and inhouse ELISAs, we will be able to 1) Identify susceptible and immunized professionals, 2) Define dynamics of effective immune response in COVID-19 and 3) Identify potential donors for passive hyperserum treatments. With the corresponding results, we will analyze the association between pattern of antibodies and type of disease.



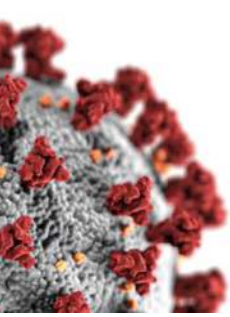
Salivid-19 study: detection of SARS-CoV-2 in saliva samples

Raul Bescos[1], Toni Gabaldón[2,3,4]

[1]University of Plymouth (Plymouth, United Kingdom)
[2]Institute for Research in Biomedicine (IRB, Barcelona)
[3]Barcelona Supercomputing Centre (BSC, Barcelona)
[4]Catalan Institution for Research and Advanced Studies (ICREA)

Current Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) test relies on naso or oropharyngeal swabs for real-time reverse transcription polymerase chain (RT-PCR). However, this method has important limitations (invasive, self-collection, repeat testing and high risk of transmission) that can be significantly mitigated with saliva sampling. Thus, the main aim of this study will be to validate the use of saliva for diagnosing SARS-CoV-2. Additionally, the analysis of salivary biomarkers such as lactate and nitrite may be useful to predict the clinical progress of the patient. Blood levels of both metabolites are commonly used as a prognostic marker for community-acquired pneumonia and sepsis, which are also complications related to SARS-CoV-2 infection. Lactate and nitrite are also found in saliva, but their concentration may vary according to metabolic and immune changes as well as the activity of oral bacteria. Thus, the oral microbiome is another important factor to pay attention, and even more considering that changes in the microbial community due to antiviral immune responses can significantly alter the immune response. The oral cavity is a major entry-door for the virus and changes in the oral ecosystem may facilitate the progress of the infection to the respiratory tracts. Thus, a secondary aim of this study will be to investigate saliva lactate and nitrite concentration, as well as, the oral microbiome composition in regard to SARS-CoV-2 diagnosis and clinical outcome.

To study this, we aim to collect a saliva sample from people that are tested using the standard protocol (nasopharyngeal swabs) to diagnose SARS-CoV-2 infection. We will analyse SARS-CoV-2 RNA in saliva samples to compare it with nasopharyngeal swabs. Furthermore, we will analyse lactate, nitrite and bacterial composition in saliva to compare the positive and negative people and to follow up the clinical progress of those testing positive.

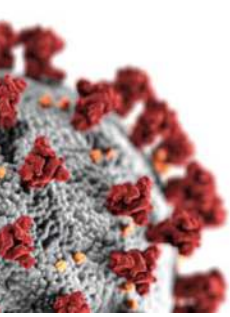


Elicitation of protective immunity against SARS-CoV2 by the selective removal of non-neutralizing antibodies used by the virus to enhance its infectivity

Sara Olivera[1], Daniel Bello-Gil[1], **Rafael Máñez**[1,2,3]

[1]RemAb Therapeutics
[2]Hospital Universitari de Bellvitge
[3]Institut d'Investigació Biomèdica de Bellvitge (IDIBELL)

The phenomenon of the antibody-dependent enhancement (ADE) of infection has been described for almost all human viral infections. It appears to occur when a previous infection or vaccination leads to the presence of non-neutralizing antibodies in serum against the infecting virus. The pathogenic effect of ADE is widely acknowledged for severe dengue infection and mainly occurs in re-infected patients and infants with maternal antibodies following a secondary infection with another serotype different from the first infection. We have been working on the identification and removal of antibodies facilitators of microbial infections. We demonstrated that Gram-negative bacteria might use natural polyclonal antibodies found in the sera of all humans, which bind to α-Galactosyl (αGal) structures, as shields to impair serum-mediated killing and facilitate the survival of the bacteria. The intracorporeal removal of these antibodies using a synthetic and non-immunogenic polymeric glycoconjugate of αGal (RA-01), is a new method to boost serum-killing capacity and prevent infections caused by these pathogens. We are now working on expanding this approach to develop a therapy to treat SARS-CoV2 infection. The treatment is based on the removal of non-neutralizing antibodies that facilitate virus infectivity. The research group is already collaborating with two Saudi Arabian research institutions to identify and eliminate non-neutralizing antibodies that promote MERS-CoV infections. We plan to determine antibody levels in controls and patients against SARS-CoV2 and MERS-CoV; analyze the profile of anti-glycan antibodies of controls and patients infected with SARS-CoV-2 and MERS-CoV; identify significant non-neutralizing anti-glycan antibodies "used" by the virus to enhance its infectivity; design and produce glycoconjugates with a binding capacity to non-neutralizing antibodies; and evaluate *in vitro* the impact of the removal of non-neutralizing antibodies on SARS-CoV and MERS-CoV replication.



Levels and seroprevalence of antibodies against SARS-CoV-2 in health care workers from Hospital Clínic measured by a Luminex-based assay

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Background

Health care workers (HCW) are a high-risk population to acquire SARS-CoV-2 infection from patients or other fellow HCW. At the same time, they can be contagious to highly vulnerable individuals seeking health care. This study aims at assessing the levels seroprevalence of antibodies against SARS-CoV-2 and associated factors in HCW from Hospital Clínic de Barcelona.

Methods

From 28 March to 9 April 2020, we recruited a random sample of 578 HCW from the human resources database of Hospital Clínic in Barcelona. We collected blood for plasma antibody quantification and a nasopharyngeal swab for direct SARS-CoV-2 detection through real time reverse-transcriptase polymerase chain reaction (rRT-PCR). IgM, IgG and IgA antibodies to the receptor-binding domain of the spike protein were measured by using an in-house Luminex-based assay. The cumulative prevalence of infection (past or current) was defined by a positive SARS-CoV-2 rRT-PCR and/or antibody seropositivity.

Results

Of the 578 total participants, 39 (6.7%, 95% CI: 4.8-9.1) had been previously diagnosed with COVID-19 by rRT-PCR, 14 (2.4%, 95% CI: 1.4-4.3) had a positive rRT-PCR at recruitment, and 54 (9.3%, 95% CI: 7.2-12.0) were seropositive for IgM and/or IgG and/or IgA against SARS-CoV-2. The assay had a 97% sensibility and 98% specificity. Of the 54 seropositive HCW, 21 (38.9%) had not been previously diagnosed with COVID-19, although 10 of them (47.6%) reported past COVID-19-compatible symptoms. The odds of being seropositive was higher in participants who reported any COVID-19 symptom (OR: 8.84, 95% CI: 4.41-17.73). Antibody levels in seropositive participants were highly variable. IgM levels positively correlated with age (rho=0.36, p-value=0.031) and were higher in participants with more than 10 days of symptoms (p-value=0.022). IgA levels were higher in symptomatic than asymptomatic subjects (p-value=0.041) and were detected as early as 6 days after onset of symptoms.

Conclusions

The seroprevalence of antibodies against SARS-CoV-2 among HCW was lower than expected. Thus, being a high-risk population, we anticipate these estimates to be an upper limit to the seroprevalence of the general population. Approximately, forty per cent of seropositive participants had not been previously diagnosed with COVID-19, which calls for active periodic rRT-PCR testing among all HCW to minimize potential risk of hospital-acquired SARS-CoV-2 infections.

Synchrotron-based infrared microspectroscopy studies in an interaction virus-infected cells

Tanja Ducic and Ibraheem Yousef

MIRAS beamline - ALBA synchrotron light source, Barcelona

Synchrotron-based Fourier-transform infrared (SR-FTIR) microspectroscopy is an important subset of vibrational spectroscopy which is being increasingly employed in the study of biochemical changes within biological samples [1]. This method can be used to study the local chemical structure in a single cells or tissue without any staining, labelling or cutting artefacts [2]. It is considered as a sensitive technique for the investigation and detection of molecular changes of virus infection of cells and tissues [3]. The main advantage of SR-FTIR microspectroscopy is that it allows inspection of restricted regions of a single cell or a tissue with a spatial resolution down to 3μm. Moreover, it is a fast method to obtain important biochemical information of diverse biological systems.

In this talk, we would like to propose the possibility to apply SR-FTIR microscopy and spectroscopy as a sensitive and effective assay for the detection of cells or tissues infected with virus or virus particles. Possible detectable and significant spectral differences between control and infected cells can be evident at different stages of the infection and evaluated with powerful statistical tools. Changes in several bio-macromolecular signature can be traced in detail in order to identify particular cellular metabolism changes in different stages of the infection, thus could provide deeper insight into cellular rearrangements after the virus-cell interactions.

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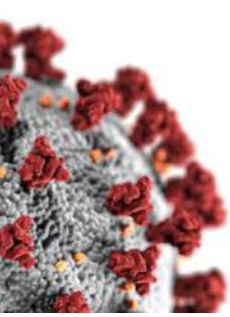

Plant biotechnology contributions to fighting SARS-CoV-2: from therapy to vaccine development

Miguel Aranda[1], María Coca[2], José Antonio Darós[3], Marta López de Diego[4], **Juan José López-Moya**[2], Diego Orzáez[3] and Adrián Valli[4] [alphabetic order]

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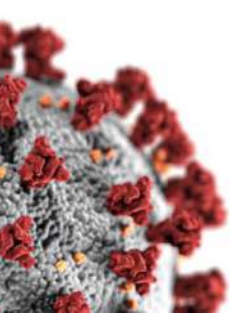
Green biotechnology using plants as bio-factories might contribute to the fight against SARS-CoV-2 by different means. Molecular pharming approaches could provide high yields of valuable compounds for therapeutic uses, or of selected antigens for the development of vaccines. Among other advantages, production in plants is considered a safe technology because, if properly managed, they are free of human pathogens, and production is easy to scale up to reach the expected high demand. Furthermore, if required, plant biotechnology might provide solutions to optimize downstream processes, including purification steps.

For therapeutic treatments, plants can be used as platforms to express human recombinant monoclonal antibodies against SARS-CoV-2 antigens, potentially including cross-reactive reagents for diagnostics and neutralizing antibodies for treatments based in passive immunization. For vaccine development, we propose to explore the production in plants of selected SARS-CoV-2 antigens, in particular domains of the Spike glycoprotein (S1 and S2), and the Nucleoprotein (N), as well as combinations of them which might enhance the capacity to induce adaptive humoral and cellular immune responses after vaccination. To maximize the chances of producing sufficient amounts of the antigens, different plant virus-based vectors for transient expression will be tested by the participant teams, including vectors based on the tobamovirus *Tobacco mosaic virus* (TMV), the potexvirus *Pepino mosaic virus* (PepMV), or the potyviruses *Lettuce mosaic virus* (LMV) and *Endive necrotic mosaic virus* (ENMV). Also, different host plants will be targeted, such as the model species *Nicotiana benthamiana*, a fast-growing and highly susceptible host for many plant viruses, as well as edible plants such as lettuce or chicory.

The validation of the different SARS-CoV-2 antigens for safety and immunogenicity will be assessed in mice, analyzing antibody and T cell responses by different methods. Also, mice will be evaluated for humoral and cellular immune responses after being fed with lettuce or chicory expressing selected antigens. Finally, neutralizing antibodies in mouse sera or produced in plants will be tested by microneutralization assays using cell cultures and infectious virus under BSL3 conditions.



Bioactivity profile similarities to expand the repertoire of drugs against COVID-19

Miquel Duran-Frigola[1], Martino Bertoni[1], Roi Blanco[2], Víctor Martínez[2], Eduardo Pauls[1], Víctor Alcalde[1], Gemma Turon[1], Núria Villegas[1], Adrià Fernández-Torras[1], Carles Pons[1], Lídia Mateo[1], Oriol Guitart-Pla[1], Pau Badia-i-Mompel[1], Aleix Gimeno[1], Nicolas Soler[1], Isabelle Brun-Heath[1], Hugo Zaragoza[2] and **Patrick Aloy**[1,3]

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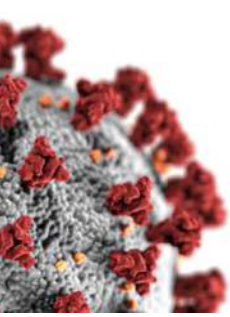
Until a vaccine becomes available, the current repertoire of drugs is our only therapeutic asset to fight the SARS-CoV-2 outbreak. Indeed, emergency clinical trials have been launched to assess the effectiveness of many marketed drugs, tackling the decrease of viral load through several mechanisms. In this talk, I shall present an online resource, based on small-molecule bioactivity signatures and natural language processing, to expand the portfolio of compounds with potential to treat COVID-19. By comparing the set of drugs reported to be potentially active against SARS-CoV-2 to a universe of 1M bioactive molecules, we identify compounds that display analogous chemical and functional features to the current COVID-19 candidates. Searches can be filtered by level of evidence and mechanism of action, and results can be restricted to drug molecules or include the much broader space of bioactive compounds. Moreover, we allow users to contribute COVID-19 drug candidates, which are automatically incorporated to the pipeline once per day. The computational platform, as well as the source code, is available at https://sbnb.irbbarcelona.org/covid19.



Search for SARS-CoV-2 inhibitors in currently approved drugs to tackle COVID-19 pandemia

Jordi Rodon[1], Marc Noguera[2], Itziar Erkizia[2], Alfonso Valencia[3,4], Victor Guallar[3,4], Jorge Carrillo[2], Julià Blanco[2,5,6], Joaquim Segalés[7,8], Bonaventura Clotet[2,5,6], Júlia Vergara-Alert[1,*], Nuria Izquierdo-Useros[2,5,*]

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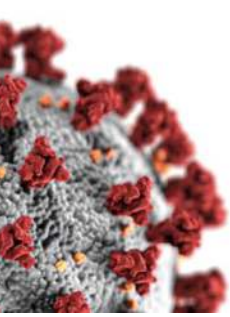
Different treatments are currently used for clinical management of SARS-CoV-2 infection, but little is known about their efficacy yet. Here we present ongoing results to compare all the currently available drugs to avoid SARS-CoV-2-induced cytopathic effect *in vitro.* Our goal is to prioritize antiviral activity to provide a solid evidence-driven rationale for forthcoming clinical trials. Since the most effective antivirals are usually based on combined therapies that tackle the viral life cycle at different stages, we are also testing combinations of drugs that may be critical to reduce the emergence of resistant viruses. We will provide results as soon as they become available, so data should be interpreted with caution, clearly understanding the limitations of the *in vitro* model, that may not always reflect what could happen *in vivo.* Thus, our goal is to test all active antivirals in adequate animal models infected with SARS-CoV-2. In turn, the efficacy of the antivirals identified using this approach could be assessed in clinical trials as treatments for infected patients, but also as pre-exposure prophylaxis to avoid novel infections until an effective and safe vaccine is developed.

Current Immunotherapy approaches for COVID-19

Marta Monguió-Tortajada

ICREC Research Program and REMAR-IVECAT Group, Health Science Research Institute Germans Trias i Pujol (IGTP), Can Ruti Campus, Badalona, Spain
Cardiology Service, Germans Trias i Pujol University Hospital, Badalona, Spain

Evidence suggests that the acute respiratory distress syndrome (ARDS) observed in severe COVID-19 patients, and part of COVID-19 mortality, may be due to a cytokine release syndrome (CRS) triggered by the immune response against the virus. In turn, prognostic markers related to coagulation and inflammation (d-dimer, ferritin, IL-6) have been found to allow early patient stratification as critical COVID-19. Thus, therapies focused on modulating this exacerbated inflammation in patients predicted as critical could reduce the number of patients with respiratory failure with the need for mechanical ventilation, and then decrease COVID-19 death rate. To this end, different immunotherapies are currently studied in different clinical trials, based on previous experience on CRS-related diseases such as autoimmune flares, sepsis, graft-versus-host disease or CAR-T cell therapies. A summary of the most promising strategies will be given, with special attention to our proposal of the use of extracellular vesicles (EV) derived from mesenchymal stem cells (MSC) as a cell-free therapy to modulate the immune response in COVID-19.



3D human organoids for treatment assessment biomarker and identification in COVID-19

Mª Carmen Puertas[1], Isabel Turpín[2], Patrica Resa Infante[1], Oscar Lao[3], Javier Martínez-Picado[1], **Sandra Acosta**[2]

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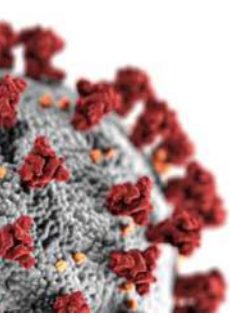
The emergence and spread of a novel and highly pathogenic coronavirus (SARS-CoV-2), which causes COVID-19, has posed a serious global public health emergency. SARS-CoV-2 exploits the angiotensin-converting enzyme 2 receptor to infect cells of multiple body organs including lung, kidney and intestines. Therefore, effects of the infection are acute respiratory tract infection, gastrointestinal symptoms and neurological manifestations ranging from hyposmia to loss of involuntary control over breathing, suggesting viral neurotropism. The urgent need for effective antiviral therapies has prompted the testing of new and repurposed drugs in valid in vitro experimental models. Human Organoids are in vitro complex 3D structures that recapitulate in vivo organs. We propose to use high-throughput analysis in SARS-CoV-2 infected human derived 3D brain, intestine and lung organoids linked to the newly established 3D organoid based AI screening tool to i) evaluate SARS-CoV-2 infection and assess drug combinations efficiency and ii) identify biomarkers system that can be used as outcome prognostic in patient blood samples. The main advantage of our proposal is the ability to analyze, within a few weeks, the efficacy of multiple drug combinations, along with the ability to evaluate the impact of the infection at the single cell level in diverse tissues and the versatility of the system to detect biomarkers that later on can be applied to the clinic.



Genomic epidemiology of SARS-CoV-2 in Spain. The SeqCOVID-Spain Consortium

Fernando González Candelas[1,2], Iñaki Comas[3], on behalf of the SeqCOVID-Spain Consortium

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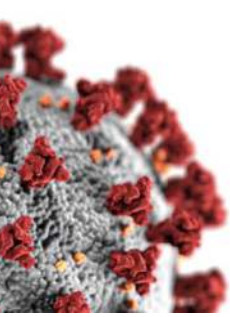
In less than four months, COVID-19 has spread from a small focus in Wuhan, China to more than 3 million people in almost every country in the world, dominating the concern of most governments and public health systems. The social and political distresses caused by this epidemic will certainly affect our world for a long time to come. Researchers all over the world are using many different approaches to confront this pandemic. In our case, we think that in order to understand, control and eventually anticipate and prevent further spreads of the virus it is essential to analyze its evolution. This is best achieved through the analysis of its complete genome sequence which can be obtained readily from remnants of diagnostic samples. This is the basis of a strategy to implement genomic epidemiology surveillance in collaboration with more than 40 hospitals, research groups, and public health administration that have led to the funding of the SeqCOVID-Spain Consortium by CSIC and ISCIII. In this presentation, we will describe the procedures we have started to use in the consortium along with the first conclusions derived from the analyses of about 300 viral genome sequences obtained from hospitals in the Comunitat Valenciana.



Integrative analysis of SARS-CoV-2 RNA modifications using nanopore direct RNA sequencing

Anna Delgado-Tejedor[1,2], Luca Cozzuto[1], Toni Hermoso[1], Oguzhan Begik[1,3,4], Leszek Pryszcz[1], Huanle Liu[1], Julia Ponomarenko[1], **Eva Maria Novoa**[1,2,3]

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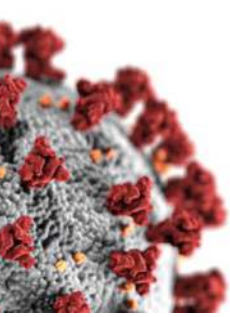
Many single-stranded (ssRNA) viral RNA genomes, such as coronaviruses- are heavily enriched in multiple RNA modifications. While the role of specific RNA modifications in viral RNAs is largely unclear, several studies have pointed towards RNA modifications playing a role in recognition as "self", avoiding a cellular response to fight infection.

Full length sequencing of single viral RNA particles is now possible thanks to the emergence of the direct RNA nanopore sequencing technology, which is the only technology that can currently sequence native RNA molecules, instead of its complementary cDNA. As such, this technology can also reveal which and where RNA modifications are located in RNA transcripts and viral RNA genomes. However, a major challenge in the field is the lack of uniform pipelines to analyze direct RNA sequencing data, leading to non-comparable results and outputs, and inconsistent predictions of viral RNA modifications across public datasets.

To overcome this limitation, here we have gathered publicly available direct RNA nanopore sequencing SARS-CoV-2 datasets, and have uniformly processed them using our pipeline for analysis of direct RNA nanopore sequencing data, termed *MasterOfPores* (https://github.com/biocorecrg/master_of_pores). To make the results accessible to all users, we have created a publicly available resource (https://covid.crg.eu) where we have placed both raw and processed data (mapped data, per-transcript abundances, RNA modification predictions, polyA tail length predictions). Moreover, we have embedded in the resource IGV visualization tools that will allow the user to examine the mapped viral RNA tracks without having to download the full datasets.

We hope this tool will serve the whole community to examine the unbiased SARS-CoV-2 transcriptome with single molecule resolution, and with full information on its RNA modifications, to better comprehend how and why RNA modifications are used by the virus to avoid immune responses and/or to increase its infectivity.



The mutational landscape of SARS-CoV-2 across human hosts and its interplay with Human Leukocyte Antigen recognition

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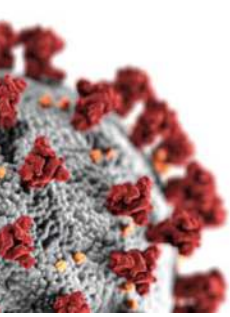
SARS-CoV-2 is an RNA coronavirus responsible for the COVID-19 pandemic. Understanding the mutational processes of the virus is essential to pinpoint how the virus is evolving across the human population. We leveraged more than 16000 SARS-CoV-2 genomes sequenced to define the occurrence and type of mutations observed in the virus across the human infected population.

We observed that the mutational spectra of the virus is not random where C>T, G>A transitions and G>T transversions dominate the viral mutational landscape. This spectrum is very unlikely attributable to the selective forces and it is very consistent across independent branches of the viral evolutionary tree across human populations. Finally, we exemplify how we can leverage the background mutation rate to compute the deviation from the expectation of the immunogenicity of viral mutations across human Human Leukocyte Antigen recognition.



Manual re-annotation and analysis of human protein coding genes linked to COVID-19 pathology

Jonathan M. Mudge[1], Julien Lagarde[2], Sílvia Carbonell[2], Carme Arnan[2], Adam Frankish[1] and Roderic Guigó[2]

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The challenges presented by the SARS-CoV-2 pandemic have led to an unprecedented refocusing of global scientific efforts along multiple lines. It is particularly important to elucidate the method by which the virus infects the body and the molecular processes that lead to COVID-19 disease. A core goal will be to establish which human genes are relevant to COVID-19 pathology: several hundred candidate genes have already been identified, and it is anticipated that more will emerge. The next step will be to examine these potential linkages in more detail. To support this vital work, the GENCODE project are reanalysing the annotation for each gene linked to COVID-19. In general, we find that the annotation for a given gene can typically be updated along several lines. Firstly, we can usually add more transcript models, using long read transcriptomics data that was not available when the gene was originally annotated. For example, we are able to integrate the datasets produced by our bespoke 'capture long-read-seq' pipeline, alongside other public resources. We can also use such data to improve the structures of existing models, especially by extending 'incomplete' models to their full lengths. We will also re-appraise the 'functional' annotation of each gene, considering in particular whether our inferences into the protein isoforms expressed by the various alternatively spliced transcripts are appropriate. We have so far reanalysed the annotation of over 100 genes, adding or updating more than 1500 transcripts. Here, we will present the initial results of this work, focusing on improvements to the annotation of specific genes of interest. This will include ACE2, a gene of likely importance in clinic as it encodes the membrane protein that the virus uses to gain access to the cell.

Whole-Genome Sequencing of SARS-CoV-2 using Next Generation Sequencing

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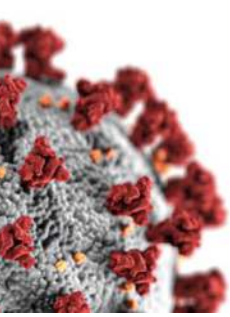
On April 1st our group from VHIR-HUVH was able to complete the whole genome sequence of SARS-CoV-2 strains from two laboratory-confirmed patients (29,893 and 29,890 nucleotides, respectively) with very high quality and without any gap or any indetermination (N). Both genome sequences have been uploaded into GISAID (https://www.gisaid.org/, named EPI_ISL_418861 and 418860) and GenBank (accession numbers MT359895 & MT359866). Comparing our two sequences with the original Wuhan-Hu-1 sequence (MN908947.3) reveals that our sequences have fixed only 5 and 9 nucleotide changes (Andres C et al. manuscript submitted) and fell within the genetic clade G based on the phylogenetic analysis, one of the four currently circulating. This result suggests that the virus is spreading, acquiring nucleotide substitutions but without any selective pressure limitation due to the lack of human population immunity and the use of antivirals or vaccines. Consensus sequences are key points for molecular epidemiology and surveillance studies.



Global network analysis of viral-human protein interactions reveals potential mechanism of lung injury by SARS-CoV-2 infection and suggests targets for drug repurposing

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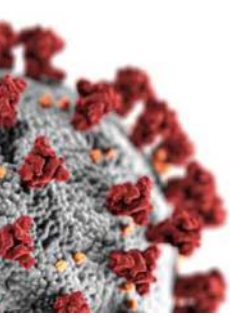
Interactions between viral and host proteins is a potential source of pathogenicity and, at the same time they can be exploited for drug development or repurposing of the existing drugs. Since the biological impact of SARS-CoV-2 on human host cells remains poorly understood, we have performed global network analysis of such interactions in order to reveal potential mechanisms of pathogenic reactions and to suggest targets for drug interventions. In our analysis we relied on recently reported list of over three hundred human proteins that can interact with viral proteins expressed upon SARS-COV-2 infection. The proteins from this list were mapped onto the global network of protein interactions and functional associations and used as seeds to perform the random walk with restart. This algorithm ranks all human proteins in the network by their relevance to the set of direct interactors. The activity/function of proteins that are highly scored is likely to be altered in the course of viral infection, even though they do not have direct contact with viral proteins. Our analysis revealed that one of the top-scoring proteins, ABCG1 is related to impaired surfactant metabolism in lungs. It is closely associated with SCRAB1, a direct interactor with viral SARS-CoV2 nsp7. While impaired surfactant metabolism was earlier reported as potential cause of lung injury during SARS-CoV-2 infection, our finding points to its specific molecular mechanism. Additionally, our analysis revealed several known drug targets in close network proximity to viral proteins which could be further investigated for drug repurposing.



Translational adaptation of human viruses to the tissues they infect

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Viruses need to hijack the translational machinery of the host cell for a productive infection to happen. However, given the dynamic landscape of tRNA pools among tissues, it is unclear whether different viruses infecting different tissues have adapted their codon usage toward their tropism. In this work, we collect the coding sequences of over 500 human-infecting viruses and determine that tropism explains changes in codon usage. Using an *in-silico* model of translational efficiency, we validate the correspondence of the viral codon usage with the translational machinery of their tropism. In particular, we propose that the improved translational adaptation to the upper respiratory airways of the pandemic agent SARS-CoV-2 coronavirus could enhance its transmissibility. Furthermore, this correspondence is specifically defined in early viral proteins, as upon infection cells undergo reprogramming of tRNA pools that favours the translation of late counterparts.