



Russian  
Science  
Foundation

# Impact of COVID-19 on research in Russia and RSF

**Alexander Makarov**

Chair of RSF Expert Council

e-mail: [aamakarov@eimb.ru](mailto:aamakarov@eimb.ru)

December 14, 2020

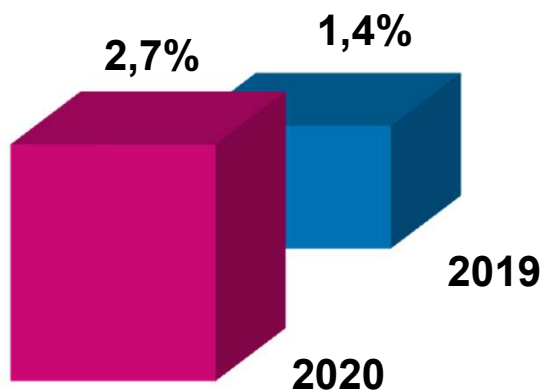
## RSF measures to minimize stress

- In view of the impacts of the coronavirus pandemic on research activities, the RSF has introduced some new guidelines for grantholders
- Researchers could find the latest information about special measures in response to the Covid-19 crisis and current calls on our website that is continuously updated
- **Interim reports submissions and project durations:** can not be changed
- **Inability to perform certain research works:** new fields in scientific reports added, subject of evaluation by RSF expert councils
- **Flexible costs management:** travel cancellations and other “sunk costs” considered as eligible costs
- **Immunity** against normal sanctions for PIs who can not run project
- **Possibility** to transfer some of mobility requirements from 2020 to 2021

RSF successfully adopted a remote mode of work and attempted to mitigate the impacts of the COVID-19 crisis on the grant holders by offering a range of quick and flexible solutions in different programs

## Limited Change on Project Portfolio

2020 applications with «SARS-CoV; pandemic; virus»  
vs. 2019 applications with «pandemic; virus»



- In 2020 we experienced about 10% increase in applications. However, thematic distribution of the applications has not changed significantly.
- In 2020, due to inability of PI to manage the project, 58 PIs' were substituted, 3 projects were terminated. Most of them are foreign scientists or Russian researchers temporarily based abroad.

RSF have not sensed (yet) any significant impact of COVID-19

## The following topics will be addressed

**The role of scientists as experts**

**Enhanced priority of biomedicine**

**Young scientists are key to success**

**Transforming international collaboration**

**Problems with exchange of samples in collaborations**

**Research articles underpin fight against pandemic**

**Changing scientific priorities for the future**

**Collaboration between scientific and clinical institutions**

**The role of Twitter in research**

## **The new role of scientists as experts**

The pandemic has raised the importance of science to a new level. Today, scientists are not only obliged to confront a new challenge by developing and validating diagnostic tests, drugs and vaccines, but also to fulfill the demands of society. Scientists have to make a significant contribution to the formation of socio-economic government policy. Hence, scenarios for the development of a pandemic are expected from epidemiologists, geneticists and virologists are responsible for data on virus mutations, whereas biochemists and biotechnologists are responsible for medicines and vaccines.

## Enhanced priority of biomedicine

The natural sciences and the biomedicine field are the priority area in pandemic conditions. Undoubtedly, the change in social ties and values in society (social distancing, the fall in economic activity of entire industries), as well as historical experience of overcoming past pandemics will be reflected in human sciences. However, it is the biomedical science that must find a solution to overcome the existing crisis.

## **Young scientists are key to success**

Science has always been made by the hands of young people, but in the current pandemic, the importance of young scientists is greater than ever. The older generation, due to restricted movement and social isolation measures, can only play the role of mentors and experts. Therefore, success in the research and development of anti-covid products will be determined by the activity of the young research team.

## Transforming international collaboration

Quarantine measures rapidly introduced by the states and the suspension of transport communications have radically affected international scientific cooperation. Scientific conferences, expeditions (archaeological, ethnological, zoological, botanical, etc.), internships and visits of scientists, for example, for work on particle accelerators or unique scientific equipment, have been canceled or postponed to an uncertain future. Network communication cannot fully replace the full-fledged interaction of scientists around the world. The main new factor in international collaboration now is the element of unpredictability of timing for both long-term and day-to-day plans for joint work.



## **Problems with exchange of samples, chemical and biological compounds in international collaborations**

Now communication between countries has become more complicated and slowed down. There is no longer an opportunity to travel to laboratory of collaborators and swap with them the necessary samples. The exchange of samples through official channels takes much longer and can be even completely closed during the lockdown. Delivery time for compounds ordered from foreign suppliers has also increased. This breaks down the international "division of labor", which is an important part of many international projects.

## Research articles underpin fight against pandemic

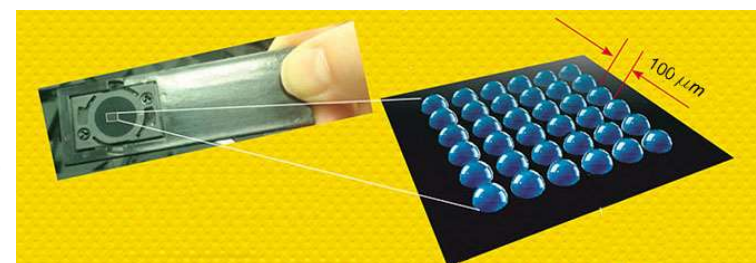
The pandemic has led to the expected explosive increase in the number of articles with the results of studies of the new coronavirus pathogenesis, proposals for diagnosis and treatment of infection. Many journals offer an accelerated version of publication, and the role of scientific repositories ([bioRxiv.org](https://www.biorxiv.org/), [medRxiv.org](https://www.medrxiv.org/), etc.) has grown exponentially. Finally, a considerable number of articles with unconfirmed data on large-scale samples were refuted by subsequent evidence. This is well illustrated by the evolution of treatment protocols for coronavirus infection with the use and subsequent withdrawal of hydroxychloroquine, kaletra (a combination of lopinavir and ritonavir), interferon-beta 1a and other drugs. This situation affects both the priorities of biopharmaceutical companies and the government policy in the field of combating the pandemic.

## Changing scientific priorities in the future

The current pandemic will have a major impact on research priorities. The development of preventive measures to combat such pathogens, obviously, should be included in the list of such priorities.

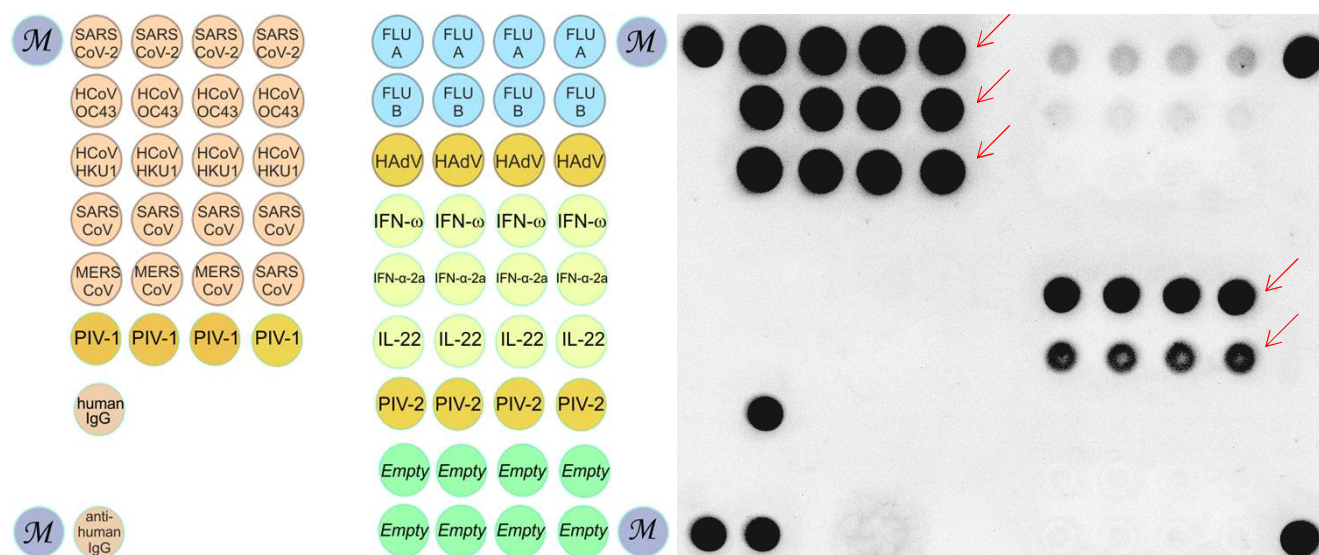
Clinically proven hydrogel biochip technology can serve as a platform for rapid identification of pathogens with pandemic potential. The technology is based on the adaptation of multiplex immune analysis on hydrogel microarrays, that was done in EIMB within the framework of the RSF grant. We developed a new approach for screening of antibodies against various pathogenic coronaviruses of the present and the past, influenza A and B viruses, etc.

Moreover, the biochip will include new biomarkers, discovered by EIMB in cooperation with the National Center of Endocrinology within the framework of another RSF grant. We have shown that autoantibodies, that were found in patients with autoimmune polyglandular syndrome, can block the production of interferon in patients with COVID infection that lead to life-threatening pneumonia. Thus, we have developed the new biochip which is able not only to detect the causative agent of respiratory infection, but also to identify markers of unfavorable development of COVID-19.



## Hydrogel Protein Microarray for Detection of IgG antibodies to Viruses causing Severe Acute Respiratory Infections and Autoantibodies to the type 1 Interferons

### Analysis of Serum Sample from COVID-19 Patient in Intensive Care



Microarray contains antigens of:

- human pathogenic coronaviruses – SARS-CoV-2, HCoV-OC43, HCoV-HKU1, SARS-CoV, MERS-CoV
- Influenza A and B viruses (FLU-A, FLU-B)
- human adenovirus (HAdV), parainfluenza viruses type 1 (PIV-1) and 2 (PIV2)

Microarray also contains interferon- $\omega$  (IFN- $\omega$ ), interferon- $\alpha$ -2a (IFN- $\alpha$ -2a), interleukin 22 (IL-22) to autoantibodies against type I interferons in patients with life-threatening COVID-19

## **Collaboration between scientific and clinical institutions has become complicated**

The increased epidemic danger made the transfer of patients' samples - biological fluids, biopsy specimens, autopsy material, and therefore such collaboration, almost impossible. The greatest obstacles were encountered in working with patients at risk for coronavirus infection. As part of the work under the grant of the RSF, our laboratory studies autopsy samples of brain tissue obtained from patients with Alzheimer's disease. Most of the patients are people over 65, for whom Covid-19 is especially dangerous. Specialized organizations where such patients are observed, such as neuropsychiatric dispensaries, neurological hospitals, have dramatically limited external contacts and cooperation. As a result, our clinical partners could not provide any samples for the research during the pandemic.

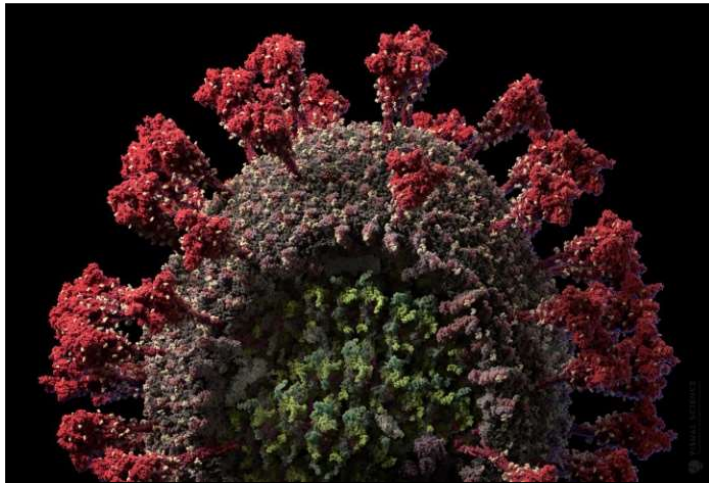
## The role of Twitter in rapid development of ELISA assay for detection of antibodies of the novel coronavirus

A group of virologists noted the unknown infection as early as in the last days of 2019 and suggested that it does belong to *Coronaviridae* family. Florian Krammer, a professor of Mount Sinai School of Medicine, proposed to create test-systems for detection of antibodies. His lab rapidly constructed plasmids for expression and purification of the viral antigen - Spike protein. When he shared this info in Twitter, we asked for these plasmids and in an hour received a positive reply. The plasmids were delivered in a week's time.

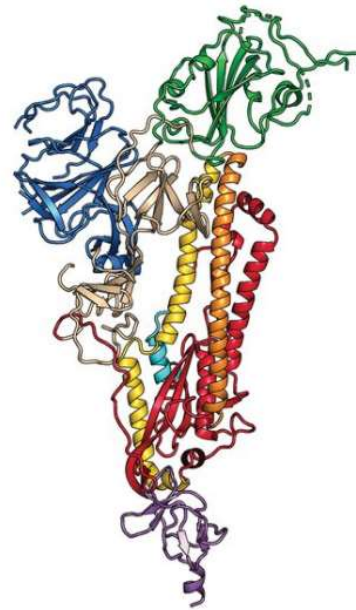
The EIMB team quickly developed the ELISA-based assay for detecting IgG antibodies to the SARS-CoV-2, and its performance in terms of diagnostic sensitivity and specificity was proven to be very high. Further work bringing it to production level at the National Center of Hematology, and the involvement of industrial partners allowed us to get the IVD approval and start the application of diagnostic kit as soon as possible. Today, this kit is used in many diagnostic laboratories for assessing population immunity and searching for blood plasma donors.



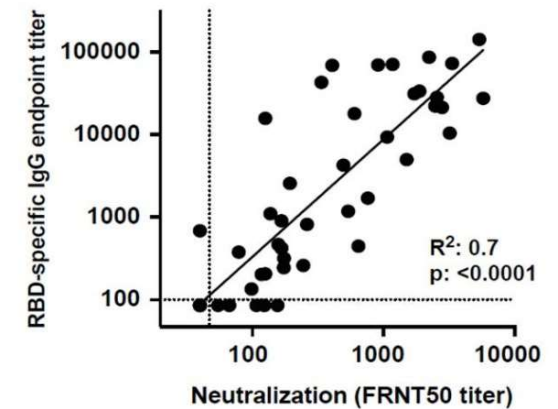
## As an antigen, we chose a receptor-binding domain (RBD) of the Spike protein since:



1. Spike protein is localized on a surface of a virion (**red**), in contrast to nucleocapsid protein (N) (**green**)



2. RBD domain (**green**) interacts with ACE2 receptor...



JUTHAR MS, et al. <https://www.medrxiv.org/content/10.1101/2020.05.03.20084442v1?fbclid=IwAR2WunE7sg6FirbQ1pM44ys5gYT3Q9kvLu9h7q5myAoAlrtuklUGWQik>

3 ...thus conferring neutralizing activity of anti-RBD antibodies

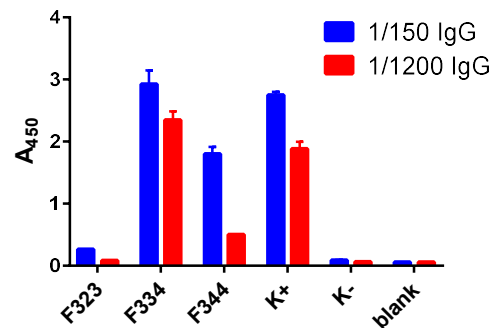
(levels of **anti-RBD antibodies** correlate with titers of **neutralizing antibodies**)

## We also established a collaboration with Prof. Baklaushev

from The Federal Scientific and Clinical Center of Specialized types of Medical Care and Medical Technologies of the Russian  
Federal Medical and Biological Agency

**Goal:** search for donors of convalescent plasma for treatment of patients with severe COVID-19

Donors were selected basing on high titers  
of antibodies  
(i.e. high signal at 1/1200 dilution)

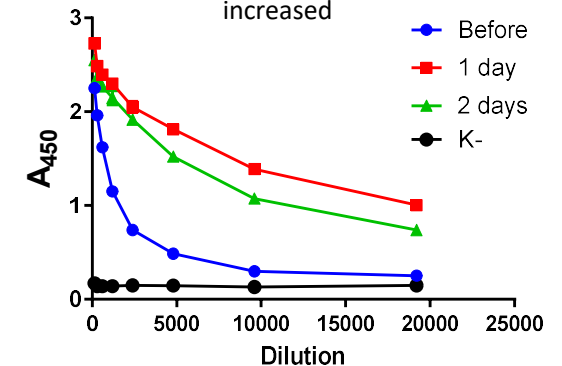


More that 100 former COVID-19 patients  
donated their plasma, many of whom –  
several times



In a clinical trial two portions of plasma  
were injected to each patient with severe  
COVID-19 who had low levels of  
antibodies.

As a result, the levels of antibodies were  
increased



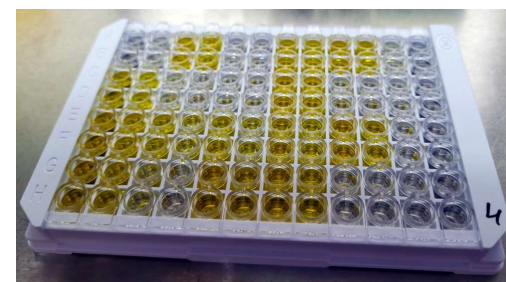
The result: in **75%** patients the convalescent plasma prevented development of respiratory distress syndrome resulting from cytokine storm



## The ELISA test-system was developed in collaboration with Dr. Efimov from National Center of Hematology (Moscow)



The test-system received a registration  
certificate on April 30, 2020 (PY №P3H  
2020/10219)



The test-system allows detection of IgG to RBD  
with **95%** sensitivity and **98%** specificity

And immediately it became available for  
community by several private clinical laboratories  
including

**INVITRO**

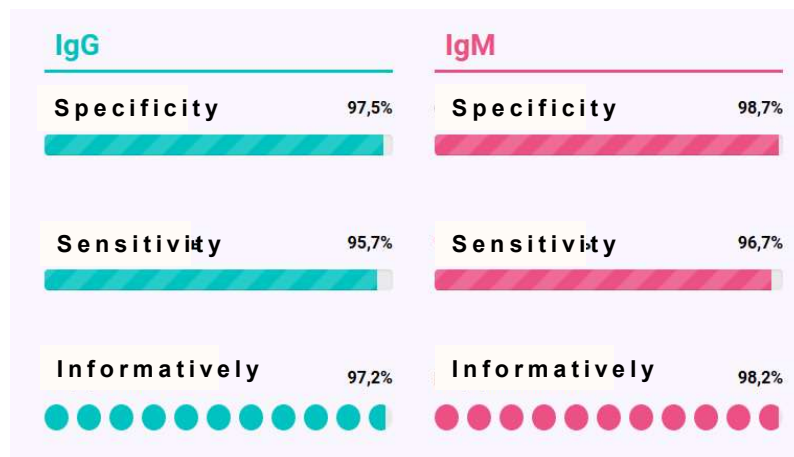
**HELIX**  
Лабораторная служба Хеликс

## Additional collaboration was established with a biotech company **Genetico:**

our group elaborated a protocol that allowed Genetico to develop a «Coronapass» system that detects IgG and IgM to SARS-CoV-2 RBD protein

 **CORONAPASS**

*future inside*  
**Genetico®**





Florian Krammer



Grigory Efimov



Alexander Ivanov  
and  
Vladimir Valuev-Elliston  
Olga Ivanova  
Olga Smirnova



Artur Isaev



Vladimir Baklaushev

# Thank you!



 mfpape

 mfpape

 mfpape



russian science foundation



russian\_science\_foundation  
rscf.ru