Government-supported R&D&I projects to handle the epidemiological situation

The development of a hACE2-Fc fusion protein that is suitable for therapeutic application

Eötvös Loránd University (ELTE), University of Pécs (PTE), Richter Gedeon Nyrt., Immunogenes Kft.

The main objective of the consortium was to develop the most effective therapeutic solution against the SARS-CoV-2 virus in Hungary. With the cooperation of the consortium members, Richter Gedeon Nyrt. will produce a biological agent that neutralizes the virus inside the infected patient's body and destroys the cells that have been infected with the virus. Based on currently available data, the ACE2-Fc fusion protein could be the most suitable for this purpose. There are several ongoing clinical trials that use a recombinant ACE2 as medication to treat acute respiratory distress syndrome (ARDS). These trials suggest that the application of ACE2 is safe and an additional beneficiary characteristic of ACE2-Fc fusion protein could be that it reduces the severity of the occasionally fatal ARDS caused by the coronavirus. The objective of the project is the expression of the ACE-2 fusion protein for the development of required medication, the preparation of a productive cell line and the launch of a pre-clinical program.

The development of a mechanical ventilator

Budapest University of Technology and Economics

In order to avert the consequences of a human epidemic resulting in mass infections that poses a threat to life and assets, to safeguard the life and health of Hungarian citizens, the Hungarian government ordered a state of danger for the entire country with Government Decree 40/2020 (III. 11.) on the Declaration of State of Danger. Jointly commissioned by the Ministry of Interior and the Ministry for Innovation and Technology, during the state of danger the Budapest University of Technology and Economics is developing a mechanical ventilator to mitigate the challenges caused by the coronavirus. The project is currently entering the stage of series production.

Mathematical modelling, analysis and projections of the spread of the COVID–19 pandemic in Hungary

University of Szeged

The project was started in mid-March 2020 for the mathematical modelling, epidemiological analysis and projections of the regional spread of the pandemic caused by the COVID-19 virus. Its objective is to support decision makers in evidence- and calculation-based decision-making in order to slow the spread of the virus, to decrease the rate of severe complications and epidemic-related mortality and to mitigate the burden of the epidemic on the healthcare system. The project leader, Dr. Röst Gergely is the associate professor of the University of Szeged and the researcher of the Department of Applied and Numerical Mathematics. His research interests include nonlinear dynamics, bifurcation theory and different areas of applied mathematics, including the mathematical modelling of epidemics.

Development of anti-coronavirus candidate drugs by directed evolution

EvolVeritas Biotechnológiai Kft.

The first step in the process of the coronavirus infection is the entry of the virus into human cells. The novel coronavirus (SARS-CoV-2) uses two cell surface proteins in the host. One of them is the angiotensin-converting enzyme 2 (ACE2) that acts as a cell surface receptor for the virus. The virus binds to the ACE2 receptor through its own spike (S) proteins. However, in order to bind to the ACE2 receptor, the S viral protein must be cleaved at a specific location. This cleavage is performed by another membrane-anchored protein of the host, the TMPRSS2 (transmembrane protease, serine 2) protease enzyme. The aim of the project is to develop a specific, highly effective inhibitor of the TMPRSS2 protease to treat and possibly prevent the coronavirus infection. To develop a novel specific inhibitor that inhibits the function of the TMPRSS2 enzyme. High-efficiency, specific inhibitors of the TMPRSS2 protease could result in new, patentable anti-coronavirus drugs. TMPRSS2 is a promising drug target also because as a human protein, it is not as prone to changes as the viral proteins.

Hyperacute anti-COVID–19 serum in the treatment of the virus infection

OrthoSera Kft.

The first scientific data from the COVID–19 pandemic demonstrated that in critically ill patients, the virus triggers the overactivation of the immune system the patients' blood resulting in "cytokine storm syndrome". Cytokine storm syndrome is much milder in the survivors' blood and the body produces antibodies that defeat the virus. The blood of survivors has been used in medicine for decades for passive immunization to support critically ill patients – this therapy has also been approved by the FDA and urgently introduced in the treatment of COVID–19. The patented hyperacute serum technology of the OrthoSera Kft. might have supplementary therapeutic effects in addition to the antiviral antibodies: their research suggests that it can counter the excessive cytokine response, as well. The project involves a wide-ranging cooperation: the Modernization Institute of the Hungarian Defense Force, the virology workforce of the University of Pécs and the Department of Translational Medicine of the Semmelweis University, as well as multiple experts and companies have joined to rapidly complete the subtasks of the project. The necessary development, production and phased clinical introduction might produce results against the epidemic as soon as in 2020.

Favipiravir development

Eötvös Loránd Research Network (ELKH) Research Centre for Natural Sciences consortium leader, Első Vegyi Industria Zrt., Richter Gedeon Nyrt., MEDITOP Gyógyszeripari Kft.

The aim of the project is to develop a manufacturing process capable of manufacturing favipiravir-containing pharmaceutical products. During the project, the laboratory, large laboratory and scale-up process capable of manufacturing the active ingredient will be developed together with the appropriate analytical processes and the summaries based on these. Multiple task forces will be established during the project to efficiently coordinate the work of the consortium members: in addition to analytical and clinical task forces, a task force for the

development of the active ingredient and a task force for formulation development will also be formed.

The clinical testing of favipiravir – stage II (clinical, application phase)

University of Pécs, ELKH Research Centre for Natural Sciences, INTEGRA Consulting Zrt.

The consortium, that is led by the University of Pécs, will implement the testing of the pharmaceutical product that is manufactured with the process that is developed under the direction of the Research Centre for Natural Sciences. The project involves the HECRIN Consortium (Hungarian European Clinical Research Infrastructure Network). The clinical task force will ensure compliance with the tight deadlines, monitor the tests and rapidly deal with the necessary professional and official consultations. Professionals from the National Institute of Pharmacy and Nutrition of Hungary will provide support so that the clinical trials could start as soon as possible, and in case of confirmed efficacy, the treatment could be available as soon as possible.

Multicentric, non-interventional clinical trial to identify the genetic factors that determine the course of the COVID–19 infection caused by the novel coronavirus, and prepare their pharmacogenetic applications

University of Pécs (Genomics and Bioinformatics Facility)

Researchers of the University of Szeged and the University of Pécs (geneticists, laboratory experts, clinicians) have started a multicentric study that includes the state-of-the-art genetic analysis of COVID–19 patients with the objective to identify genetic factors that determine the course of the infection and to prepare the (pharmacogenetic) applications of the individual drug response determined by the genetic factors. There are multiple known case reports that suggest that genetic predisposition is one of the factors that determine the course of the disease. Identifying the genetic factors (of both the virus and the patient) that determine the course of the COVID–19 infection will be of great importance in the accurate exploration of the course of the disease, in the identification of the pharmacogenomic factors of the therapies that are under development and in the development of patient-tailored treatments.

Development of a flagellin-based novel fusion protein vaccine molecule – stage I

University of Pannonia (Research Institute of Bio-nanotechnology and Chemical Engineering), TargetEx Kutató-Fejlesztő Kft., Ceva-Phylaxia Oltóanyagtermelő Zrt.

In connection with the fight against the coronavirus epidemic, this project aims to develop a novel protein-based vaccine that simultaneously stimulates the innate and acquired immunity, thus rendering the body resistant to the attack of the real virus. The idea is to combine two proteins in the vaccine: the first is a part of flagellin (a protein making up the motor system of the Salmonella bacterium) that has been demonstrated to be a beneficial carrier or adjuvant increasing the efficacy of vaccines; and the second is the part of the “spike” protein (it identifies the host cell) that binds to the cell surface. Building the receptor-binding domain of the

coronavirus (it directs its cellular invasion) into the flagellin offers a promising option to build an efficient vaccine.

Studying the spread, the current state and the subsidence of COVID–19 by analyzing different wastewaters

University of Pannonia (Research Institute of Bio-nanotechnology and Chemical Engineering), University of Pécs

The aim of the project is to analyze municipal wastewaters to estimate the extent of coronavirus infection within a given community. SARS-CoV-2 can be detected in wastewater 3 days after the infection, even before the onset of symptoms. By analyzing viral specimens, the local spread of the infection can be detected in its early stage and the necessary measures to stop its transmission can be introduced in time before a widespread outbreak. Wastewater analysis can also be a useful tool to detect the re-emergence of the infection. The project includes the creation of a database and the adoption of methodology for COVID–19, that can be later used to follow the spread of the virus and predict potential hotbeds of the infection.

A unique medical device with CPAP and BIPAP ventilation modes that is capable of both invasive and non-invasive respiratory support

Semmelweis University, Femtonics Kft., 77 Elektronika Kft., 3D Center of the University of Pécs

The objective is to develop a unique medical device that has CPAP and BIPAP ventilation modes, that is capable of invasive and non-invasive respiratory support and that is efficient in the treatment of the particular respiratory failure occurring in COVID–19. The advantage of the planned, COVID–19-specific medical equipment over other ventilators is that it can be cost-efficiently manufactured in a large number of series in a short period of time. Filtering the extract air of the device provides safety for healthcare professionals (doctors, nurses) in the frontline of care and excludes the infectious potential that occurs during the care of patients requiring respiratory support.

The development of a mechanical ventilator (MassVentil project)

Óbuda University

The objective of the MassVentil project is to develop the working prototype of a modular mass-ventilator to more efficiently manage patients who fell sick due to the novel coronavirus. The aim of a modular mass-ventilator is to develop a ventilator that can be used by as many patients as possible with the lowest requirements for infrastructure investment and installment. It can be used to simultaneously ventilate a large number (5–10) of patients even in out-of-hospital settings. One of the winning projects of the EU hackathon!
