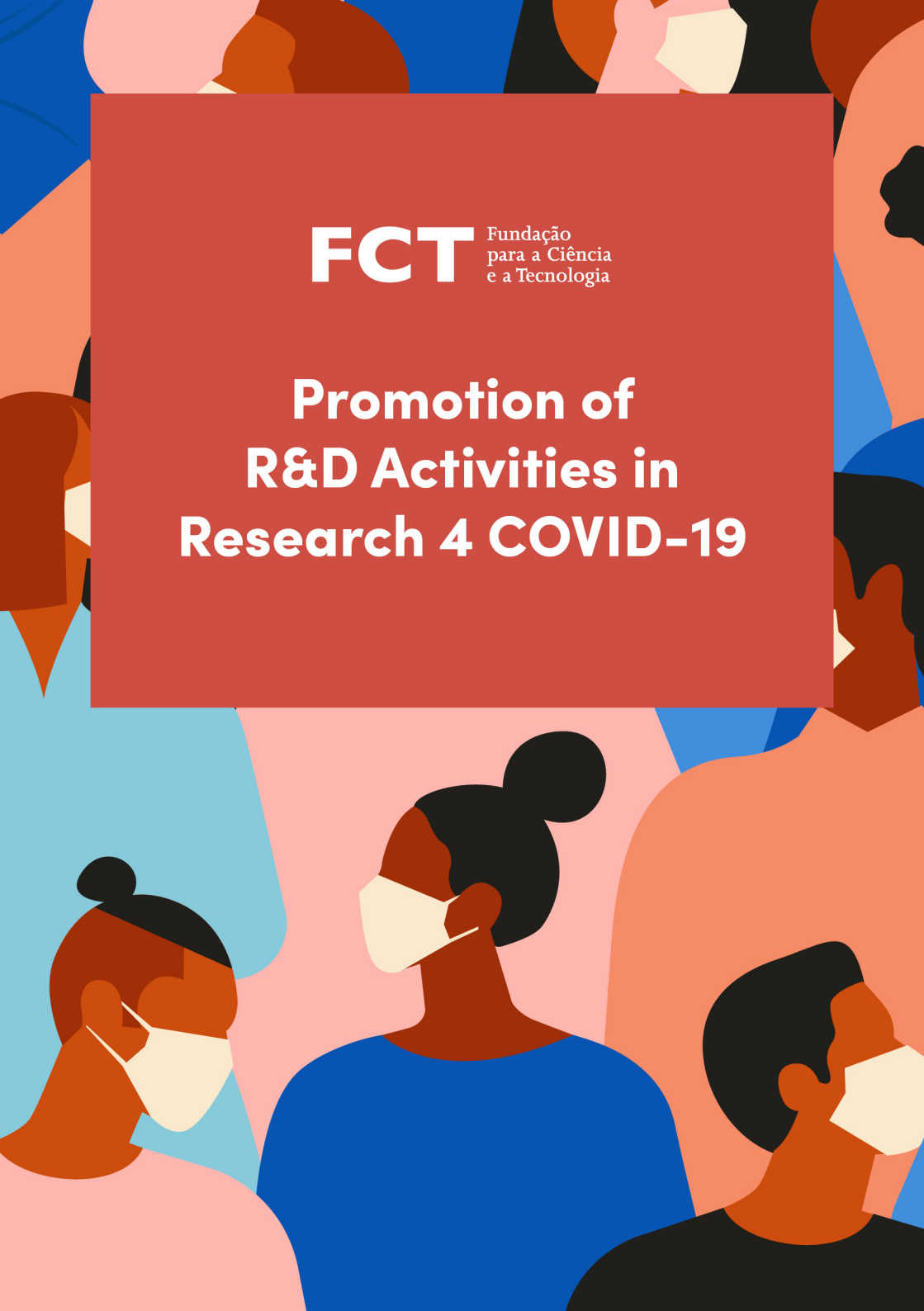
FCT Fundação para a Ciência e a Tecnologia

Promotion of R&D Activities in Research 4 COVID-19



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Introduction

Introduction

Since the beginning of 2020, the world is submerged in a unique and global reality. A new corona virus strain, SARS-CoV-2, that has not been previously identified in humans, emerged in Wuhan city, China, as the cause of an epidemic respiratory disease COVID-19. The rapid and global spread due to its high infection rate, associated to the mortality numbers, led the World Health Organization to declare the outbreak as a pandemic on March 11th. At this date, more than 118 000 cases had been reported in 114 countries, and 4 291 deaths recorded. By mid-March, the European region became the epicentre of the epidemic, reporting over 40 % of globally confirmed cases. As of April 28th, 63 % of global mortality from the virus was from this region.

The lack of knowledge on the virus, of inoculation or effective treatment for the COVID-19 forced the imposition of social distance, the only effective measure known to stop the spread of infectious diseases. On March 13th, the Portuguese government declared a general lock down. The protection of human life being mandatory, resources were directed to respond to health emergencies, social protection and minimizing the impact on the economy.

Life as we knew it changed abruptly. Public spaces were closed or heavily conditioned, the only open spaces were for the purchase of essential goods and with restrictions. We adopted home school and, when possible, home office; in general, the Portuguese society was confined in-doors. Feelings of anxiety, emotional instability and financial worries began to emerge. At the time, the common sense was that we were simply avoiding a catastrophic situation and not eliminating it because of lack of knowledge on the virus and on the disease that could allow better solutions to deal with them.

The Fundação para a Ciência e Tecnologia (FCT), as the Portuguese agency for the funding of research and technological development, acted promptly to contribute to leverage the national R&D Units and their research and innovation expertise into developing targeted work aiming at quick solutions to some of the more urgent problems of our health system in relation with the pandemic. A quick process of launching research initiatives was designed while complying with the openness, competitiveness and evaluation procedures that are the framework reference for FCT.

In this context, on March 24th, the FCT in collaboration with Agência de Investigação Clínica e Inovação Biomédica (AICIB) launched a first call of a special support "Research 4 COVID-19" to R&D initiatives that could in the short-term respond to needs of the National Health Service (SNS) in the framework of this and future pandemics. The response of the scientific community was extraordinary, in spite of the short application period, and the results were made public one month later.

A second call of RESEARCH 4 COVID-19 was released on April 30th, also with an even greater number of applications, and the results were given after less than an one month.

In both calls, the applications were evaluated by external evaluators from the academia and knowledge in the areas under appreciation who very generously contributed to this effort. Their work is gratefully acknowledged.

In both calls, the proposals had to contribute to a response improvement of health systems to the impact of COVID-19 in line with the National Plan for readiness and response to the disease by the new coronavirus of the Direção Geral da Saúde (DGS). The first call focused on stimulating the retargeting of activity in the R&D units supported by FCT towards R&D initiatives that responded to the needs of SNS and to strengthen collaboration with health care institutions. The second call focused on the pandemic evolution and its impact on health services and society, as well as in the optimization of the response at different levels of the society.

A total of 121 projects are being funded with an investment of 3.8 million Euros. From these two calls for expression of interest, the research initiatives cover the following areas:

- Prevention: with 33 projects,
- Diagnostic: with 32 projects.
- Therapeutics: with 14 projects,
- Clinical and epidemiological studies: with 27 projects,
- 15 projects in other associated areas.

Of the 121 approved projects, 70 will be developed in Universities and Polytechnic Institutes, 39 in Research and Development Centers, Associations and Institutes, 5 in Hospital Centers, 5 in private research Foundations, 1 by the Portuguese Society of Oncology and other in Agência Regional para o Desenvolvimento da Investigação Tecnologia e Inovação. Most of these R&D institutions are based in the Lisbon and Porto region.

RESEARCH 4 COVID-19 was one of the several initiatives launched by FCT in response to this emergency environment. Different calls were launched in this period: Gender Research 4 COVID-19, AI 4 COVID-19 call (Data Science and Artificial Intelligence in Public Administration), and the DOCTORATES 4 COVID-19 PhD scholarships. FCT also increased the capacity of RCTS - Rede Ciência, Tecnologia e Sociedade, which supports connections to internet from the teaching and research community to strengthen the capacity of services that provide distance learning and teleworking in the academic and scientific community (Colibri, NAU, Educast, Videocast). The Science 4 COVID-19 portal was also created aimed at gathering information directly or indirectly related to the R&D that is being issued in relation with the pandemic.

FCT understands how important it is to inform the society on the response given by the national scientific community to increase knowledge and develop solutions to mitigate the epidemic and serve as a basis for future public policy decisions.

In this line of thought, FCT presents here all the initiatives that are under development within the scope of the projects approved in the RESEARCH 4 COVID-19 calls.

Promotion of R&D Activities in Research 4 COVID-19

Prevention

PIC 4 COVID-19

PRINCIPAL INVESTIGATOR	Manuel José Lopes
LEADING INSTITUTION	Universidade de Évora
FUNDING	€ 30 000

With the objective to assure safe housing of COVID-19 patients, with a personalized care plan, integrated and continuous given the personalized clinic information, we propose the development of a digital tool, named Individual Care Plan (ICP). ICP is a tool that provides fundamental decisions to the patient and the caregiver. Through the CPU we may promote the literacy, the functional state, the self-care, the effectiveness to quality of life and security of medication as well as reduce the use of health services, the hospital admissions, and mortality of housed COVID-19 patients. ICP is also of unquestionable use for all those who are in need of care in hospitalization context. In these cases, if the professionals have a decision support system that proposes a specific sequence of personalized actions, and based on technical guidelines, they have gained time and intervention precision.
The algorithms that support the ICP, as well as all of its decision and intervention suggestions, are supported by validated scientific evidence, with reference to different environmental factors of the Portuguese population, namely: Signs and symptoms of COVID-19 for the population over 65 years old; Pharmacological options for the treatment and prevention of COVID-19, as well as its complications; early detection of signs and symptoms that enhance mental illness; and the associated social determinants.
In order to integrate all the information collected and analyzed, work was done focused on automating the decision on the various aspects resulting from previous work. Through the use of standard protocols of the triple crown of the Object Management Group (OMG): BPMN, CMMN and DMN, we proceed with the modeling of the surveyed workflows and the respective manual decision processes. The various simple decision nodes were modeled using algorithms provided by the researchers according to the DMN 1.2 standard and implemented using jBPM 7.39.
In the end, we will have a device that integrates into the logic of the decision support systems of caregivers and that, in addition, constitutes a guarantee of integration and continuity of care.

Desenvolvimento de Equipamentos de Proteção Individual (EPIs) com propriedades melhoradas de conforto e possibilidade de reutilização, mantendo as propriedades de proteção inalteradas

PRINCIPAL INVESTIGATOR	Carla Silva
LEADING INSTITUTION	Centro Tecnológico das Indústrias Têxtil e do Vestuário de Portugal
FUNDING	€ 30 000

Several Personal Protective Equipment items (PPEs) are used every day by healthcare personnel to protect themselves, patients, and others when providing care. The project RE-COVER-ALL main ambition is the development of a new line of protective clothing, namely PPEs, to be used by healthcare personnel exposed to COVID-19. This new line of PPEs are designed to be re-used after a suitable cleaning procedure and must ensure the protection of the worker throughout their lifetime. Contrarily to the disposable PPEs, that are typically produced in nonwoven polypropylene fabric laminated with a polymeric membrane or film, this new line of protective clothing will be made in a coated or laminated woven or knitted textile fabric. Therefore, these PPEs will be more comfortable, breathable, ergonomic and sustainable than disposable PPEs, whereas their protection characteristics like liquid penetration and mechanical resistance will be the kept as defined by the legislation in place (EN 13795, EN 14605, EN 14126 and EN ISO 13688). After use, these PPEs will be subjected to a suitable cleaning procedure, which will allow them to be re-used again safely to protect the healthcare personnel from the many hazards encountered in the healthcare facilities. This solution represents an important approach for the control of PPE shortages in our national healthcare system, for improved personnel working conditions due to the increased comfort and for important economic and environmental savings while helping sustaining the Portuguese SMEs operating in the clothing industry. The project is organised into four main tasks. Laminated membranes and films were explored in Task 1 and polymeric coatings in Task 2, for waterproofing different textile fabrics while keeping their breathability. Regarding the textile fibres, both synthetic, artificial and natural fibres were explored, were bio-based solutions further investigated in Task 3 for accessing comfort, performance and washing fastness, due to their enhanced environmental parameters. Finally, in Task 4, two models for a surgical gown were built with the developed fabric materials and are at this stage ready to be validated in a real hospital environment by healthcare personnel.

Produção de Viseiras de Proteção por Moldagem por Injecção

PRINCIPAL INVESTIGATOR	João Manuel Carvalho Gomes
LEADING INSTITUTION	CENTITVC - Centro de Nanotecnologia e Materiais Técnicos, Funcionais e Inteligentes
FUNDING	€ 30 000

Mould2Protection project will develop a new design for protective visors, employing injection moulding processes to manufacture the fixing ring and visor components of the final visor structure. Additional protection will be provided via integration of antiviral and anti-fogging functionalities on the visor, thus increasing the level of protection for the user.
The structural design of the final solution will allow an increase in comfort and ease of use, with a circularity/sustainable design targeting reutilization and reuse of both the concept solution and the polymeric base materials, thus improving the product's environmental sustainability. The new design will increase the mechanical strength of the protection visor structure, providing greater comfort and safety to the user.
Further evaluation of ergonomic parameters and utilization requirements may result in the inclusion of more features to increase adaptability and versatility.
The production of the visor components via injection moulding process enables a considerable reduction of the cycle production time necessary processing, assembly and implementation of the product on the market.
The application of antiviral and anti-fog coatings, as well as material compounding and functionality integrated, leading to an increase of protection level for the users, enabling its use for longer periods in safer conditions.
The selection of materials and design will be thought in the sense that the visor can be reutilized, withstanding sanitization via frequent disinfection and sterilizations, and contributing to the sustainability of resources and costs, maintaining a high level of performance.

Assisting the prevention and control of COVID-19 with 3D printing solutions

PRINCIPAL INVESTIGATOR	Jorge Américo de Oliveira Pinto Belinha
LEADING INSTITUTION	INEGI - Instituto de Ciência e Inovação em Engenharia Mecânica e Engenharia Industrial
FUNDING	€ 30 000

This project is a joint venture of two research centres - INEGI and INESC-TEC - and two academic institutions – University of Porto and Polytechnic Institute of Porto. The outputs of the project are continuously tested and validated by two partners of the Portuguese national health system (PNHS): "Centro Hospitalar Vila Nova de Gaia/Espinho" and "Administração Regional de Saude do Norte".
The project aims to design and produce medical and health-care devices using 3D printing technology to prevent COVID-19 dissemination. It is also expected that the outputs of this project can be used to assist and improve the existing therapies. Although not suitable for mass production, 3D printing can be used to design/produce real-scale prototypes to be tested/calibrated by clinical partners in a real scenario. Next, the prototypes will be mass-produced by injection moulding technologies by the industrial partner. This project is sub-divided in many sub-projects, responding to distinct needs. Thus, it is expected to develop and produce by 3D printing several solutions to reduce COVID-19 dissemination in hospitals. 3D printing allows the rapid production of urgent medical devices with low tech level, such as visor holders, nasal swabs and hand-free devices (for doors and gels). Nevertheless, high-tech level components are also within the scope of the present project, such as ventilator parts that will be enhanced and manufactured by demand. A secure web-based information and decision support system was implemented, allowing to manage all the data regarding the participants, resources, materials and locations. It is capable to support, in real-time, the planning of collection and delivery, optimising production and routes: https://3dlog.inesctec.pt/ Presently, the project already produced several devices and new ideas. Up to now, 5 000 visor holders were produced by 3D printing and delivered to hospitals and health centres. Presently, those visor holders are being produced by the industrial partner with a production capacity of 8 000 units/day. New designs for nasal saws and ventilator parts were developed and prototypes were produced for testing and validation in the PNHS institutions. Also new prototypes for disinfectant gel dispensers, ear-savers and hands-free door openers are being developed and produced. These devices are being designed using advanced computational simulation.

R4COVID.1.098/2020

Desenvolvimento de uma escala de risco COVID-19 através de uma análise I&D probabilística de Monte Carlo de forma a dotar o Hospital de Ovar de planos de contingência adaptados para gestão de casos de pandemia

PRINCIPAL INVESTIGATOR	Ricardo Cruz Correia
LEADING INSTITUTION	Faculdade de Medicina da Universidade do Porto
FUNDING	€ 29 996

The PRiSACovid - Predictive Risk Scale Analysis for Covid in Healthcare Facilities tool was developed with the aim of tackling foreseeable logistical and operational constraints by using an epidemiological simulation (SIR model) which provides input for the material and staff needs of Hospital Dr. Francisco Zagalo - Ovar. This project stemmed from the intense strain the hospital suffered when the COVID-19 pandemic first hit the region of Ovar, in mid March, leading to a rapid overload of the hospital's resources and capacity. The relevance of predicting future straining of healthcare services and having in place a contingency plan to fight it was therefore understood and approached.
An investigation was conducted in order to gauge the most relevant performance indicators regarding the provision of all the services in the hospital.
The resulting product now consists of a ready-to-ship standalone digital tool that simulates the propagation of the pandemic and allows for monitoring of the relevant indicators. The user, typically a board member of the hospital, has the ability to tinker with parameters ranging from the epidemiology variables to human resources and Personal Protective Equipment (PPE) constraints, thus crafting a model of the institution. This model presents relevant information (i.e. days until shortage of PPE, risk assessment in the next 60 days, predicted demand of hospital beds) in a graphical way, drawing from the Theory of Constraints to establish a red-yellow-green buffer for every relevant measure. Alongside the monitoring dashboard, contingency plans were devised to tackle risk scenarios on different areas of hospital activity, with the help of the personnel responsible for implementing them.
This tool presents the potential for rapid action when an upcoming capacity stress wave is detected and is simple and user-friendly enough to be provided to hospital managers with little training. Future iterations, combining real-time data from national health authorities and a web-based interface, will prove scalable to other hospitals and settings.

RADAR R4COVID.1.091/2020

Robô Autónomo para Desinfeção em Ambiente hospitalaR

PRINCIPAL INVESTIGATOR	António Paulo Gomes Mendes Moreira
LEADING INSTITUTION	INESC TEC - Instituto de Engenharia de Sistemas e Computadores, Tecnologia e Ciência
FUNDING	€ 29 965

The RADAR project was born from the willingness to help combat COVID-19. RADAR is the acronym for Autonomous robot for disinfection in health care institutions and is designed for indoor virus prevention. It consists of a mobile robot equipped with cutting-edge technology that allows it to map the environment, navigate autonomously, irradiate short-wave UVC light, and detect the presence of people through infrared and motion sensors.
Impacts:
- Prevent and reduce the transmission of infectious diseases caused by virus and bacteria
- No-touch automated disinfection eliminates human error in the disinfection process
- Allow human resources to be redirected to other duties
- Reduce cleaning staff exposure to toxic and corrosive agents used in traditional processes
- Chemical-free process and leaves behind no residue
- Requires no transportation and storage or handling of toxic or corrosive chemicals

The effectiveness of the disinfection by means of UVC light is related to the radiation power, the exposure duration and the distance to the light source. According to the International Ultraviolet Association, some microorganisms are more susceptible than others, but all the hundreds of microorganisms tested so far (including other types of coronavirus) can be inactivated with the proper dose of UVC radiation.
UVC radiation has been used the past 40 years for disinfection of potable water, air, hospital surfaces and pharmaceutical products.
UVC light inactivates microorganisms by damaging their DNA. The longer the dose of UVC radiation, the greater is the DNA damage. When the damage is too extensive to be fixed, the cells cannot carry out their normal functions and are directed to programmed cell death (apoptosis).

SARSBLOODsafe R4COVID.1.021/2020

SARS-CoV-2 and blood donation safety in Portugal: a shift to screening?

PRINCIPAL INVESTIGATOR	João Rodrigo Gonçalves Goiana Mesquita
LEADING INSTITUTION	Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto
FUNDING	€ 29 880

The SARS-CoV-2 emerged in early December 2019 and rapidly spread to many countries around the globe, with the number of confirmed cases increasing every day. Although emerging coronaviruses infect the respiratory tract, studies have shown that viral RNA could be detected in plasma and serum of patients infected with SARS-CoV and MERS-CoV, and the more recent SARS-CoV-2. As growing numbers of asymptomatic infections (circa 80% of all COVID-19 infections) are being found among COVID-19 cases, considerations on blood safety with regards to SARS-CoV-2 are urgent and to the time of writing this project, no study has evaluated the presence of SARS-CoV-2 in the blood of blood donors.
In order to evaluate if blood donations in Portugal can pose a risk to COVID-19 in blood recipients, blood samples from donors will be tested for IgM anti-SARS-CoV-2 (evidence of recent/ongoing COVID-19 infection) by ELISA and for SARS-CoV-2 RNA (current infection) by real-time RT-PCR.
Plasma samples (anonymized clinical analysis remnants) from blood donations (n=500, 1ml) will be collected from the Blood Bank of the Centro Hospitalar de Vila Nova de Gaia/Espinho. After transport to ICBAS, all samples will be screened for IgM anti-SARS-CoV-2 using a commercial enzyme-linked immunosorbent assay (ELISA) (Wantai SARS-CoV-2 IgM ELISA), according to the manufacturer's instructions. Additionally, all plasma samples will be screened for SARS-CoV-2 RNA. Viral RNA extraction will be performed using QIAamp Viral RNA Mini kit and viral extracts will be screened by real-time RT-PCR assay using a commercially available CE&FDA approved kit (EURORealTime SARS-CoV-2, Germany) targeting two genomic regions of SARS-CoV-2 by use of specific primers and probes, according to the manufacturer's instructions.
Results from this project will provide extremely valuable baseline data that will assist in transfusion medicine in Portugal.
This project is currently awaiting approval decision by the Ethics Comission of the Instituto de Saúde Pública da Universidade do Porto, under the reference no. CE20146.

R4COVID.1.113/2020

REUSE: Bio-decontamination of filtering facepiece respirators and masks for reuse

PRINCIPAL INVESTIGATOR	Fernando Antunes
LEADING INSTITUTION	FCiências.ID - Associação para a Investigação e Desenvolvimento de Ciências
FUNDING	€ 29 500

As the pandemic is disrupting healthcare systems, stepping up efforts to protect those on the frontline is crucial to further combat the deadly COVID-19 disease. The pandemic revealed the healthcare systems to be unable of protecting healthcare personnel as Personal Protective Equipment (PPE) has been lacking in hospitals. It put healthcare workers at an immense risk of contracting the virus while treating the COVID-19 patients. Additionally, a worldwide shortage limited the use of PPE by the rest of the society, which could otherwise slow down the spread of the virus. In the USA only, over 10,000 health professionals contracted the virus and 821 died. There is no sign of relief as PPE stocks for hospitals will not be enough for the next several months, when the COVID-19's second wave hits.
To address this critical problem, the consortium headed by Centro de Química Estrutural from Faculdade de Ciências da Universidade de Lisboa brings together the start-up Delox, Centro de Investigação da Academia Militar, Laboratório de Defesa Biológica da Unidade Militar Laboratorial de Defesa Biológica, Hospital das Forças Armadas and Instituto Dom Luiz also from Faculdade de Ciências da Universidade de Lisboa, to develop REUSE, a project that aims at decontamination of PPE such as respirators, masks and gowns. Once decontaminated, PPE can be safely reused, thus reducing waste and costs, and ultimately decreasing the shortage.
The project is an adaptation of Delox's technologies. The company developed a dry Vaporized Hydrogen Peroxide (dryVHP), a highly efficient decontamination agent which allows designing affordable, compact and easy-to-operate devices that spread the bio-decontamination agent in the environment, removing 99.9999% of all the bacteria and virus.
The consortium is finalizing building a portable decontamination chamber where the current Delox device (Delox BOX) is used to decontaminate between 100-200 PPE pieces at a time. Simultaneously, a much smaller device was already built by the REUSE consortium for decontamination of up to 5 PPE pieces. It may not only be used at healthcare facilities, but also in households.

Mental Health in COVID-19

PRINCIPAL INVESTIGATOR	Teresa Caldas de Almeida
LEADING INSTITUTION	Instituto Nacional de Saúde Dr. Ricardo Jorge
FUNDING	€ 29 500

The project Mental Health in COVID-19 (SM-COVID19) is promoted by the National Institute of Health Doutor Ricardo Jorge (INSA), through its Department of Health Promotion and Prevention of Noncommunicable Diseases, in collaboration with the Environmental Health Institute of the Faculty of Medicine of the University of Lisbon (ISAMB) and the Portuguese Society of Psychiatry and Mental Health (SPPSM).
To assess the impact of the pandemic on the Mental Health (MH) and Well-Being (WB) of health professionals, other professionals at the forefront and the general population.
Specific objectives of the study are: 1. to evaluate the impact on the MH and general WB in the following target groups: health professionals and other professionals at the forefront, individuals in isolation, quarantine and in social distancing. 2. to identify the protective and risk factors for MH during the pandemic. 3. to assess perceived access to health services and individual protection measures.
Study design: This is a cross-sectional study with a non-probabilistic sample, targeted at people residing in Portugal, aged 18+ years; Data collection was carried out through an online survey, between May and July 2020; The survey consists of 52 items. Validated scales were used to assess the MH dimensions considered in this study: anxiety, depression, post-traumatic stress, resilience, presentism and burnout; and The chosen dissemination strategy was through social networks and institutional emails at a national level.
A second moment of data collection was carried out, through the completion of a simplified version of the original survey. Participants who consented on a later contact for this purpose were invited via email.
Expected results: The evidence thus obtained will serve as the basis for the production of timely recommendations and Policy Briefs. These are aimed at guiding and strengthening the response of health services in the cases of Mental Health issues identified in the most vulnerable groups.
Expected Products: Website with dashboard; Recommendations; Policy briefs; Final report.
More information about the project at https://sm-covid19.pt/

Response to the COVID-19 pandemic in the context of social inequalities in health: a cross-sectional study among the native and immigrant population of Amadora

PRINCIPAL INVESTIGATOR	Maria Rosário Fraga Oliveira Martins
LEADING INSTITUTION	Universidade Nova de Lisboa
FUNDING	€ 28 277

COVID-19 is cruelly exposing the existing and persistent health inequalities in our society. In this context, health systems must be prepared for the needs arising from the economic and social changes caused by the pandemic. With little evidence on how the pandemic is affecting the immigrant population in Portugal, it is essential within this context to analyse the socioeconomic dynamics and identify the difficulties in accessing health care for these families.
In this quantitative study, we are conducting telephone interviews during the month of July with 217 immigrant families and 203 natives living in Amadora Municipality in order to describe and analyse changes in material deprivation, income and employment status of households; moreover, we are also investigating their living experiences during social confinement and possible increased difficulties in accessing health care.
Immigrant families are mostly from Cape Verde, Angola, Brazil, Guinea-Bissau and S. Tomé and Príncipe. Regarding socioeconomic dynamics, preliminary results (6 July) suggest that 40% of immigrant families reported that someone in their household was unemployed versus only 4.2% of native; and 83% reported a decrease in household income compared to 54.2% of the natives. Regarding access to health care, 38% of immigrants reported that someone in their family had to go to the emergency room in the last month (versus 25% natives) and that they had increased access difficulties because of the pandemic; about 70% of the interviewees reported that they had to cancel or postpone a medical appointment or treatment, with no difference between immigrants and natives; difficulty in accessing medication was reported more frequently by native families (12%) than by immigrants (9%).
However, these results cannot yet be generalized since they correspond to only 100 questionnaires.
We expect to have impact at the NHS, by complementing clinical information already existing at ACES Amadora; at the population level, especially on immigrant's households, by identifying more adequate public health responses.

COMPRIME R4COVID.1.099/2020

COnhecer Mais PaRa Intervir MElhor

PRINCIPAL INVESTIGATOR	Paulo Sousa
LEADING INSTITUTION	Universidade Nova de Lisboa
FUNDING	€ 28 000

The project COMPRIME, have the main objective to identify the dynamics of the spread of the SARS-CoV-2 virus, in its relation with the demographic and socioeconomic profiles of territories, at the county level, identifying the determinants of this propagation. The study was carried out in three stages: in the first we did a descriptive statistical analysis of epidemiological data, associated with the spatial distribution of the total number of cases per 100.00 inhabitants; a second stage, in which four analysis of multiple linear regression were developed, related to four temporal moments, using about 60 indicators representative of the three dimensions; third stage where nonlinear analysis was applied using the artificial neural network, for the same moments and indicators. As main preliminary conclusions we highlight: i) the pattern of regional evolution started in metropolitan areas, but it quickly extended to the municipalities of the non-metropolitan coast north of Lisbon and the northern and central coastal territories. The Alentejo and the Algarve have registered, only in the most recent period, higher incidence of the phenomenon. The population dimension and density were always present on the linear regression model. Other variables were added, on the 1st moment, factors related to the existence of an export dynamic; in the 2nd moment, the resumption of activities, the presence of people working in the production support services, as well as the students of the third cycle; in the 3rd moment, activities related to construction and migration dynamics stand out; and in the 4th moment, the daily mobility dynamics of the population in greater daily commuting is counted. The prediction model adds new data, which allows to identify the counties where the verified values are above the expected values, highlighting the question of population density, which adds to the mobility of the population outside the municipality and the presence of migrant communities. Thus explaining the estimated values above the expected ones, mainly in the metropolitan Lisbon area, including the municipalities of Lisbon, Amadora, Odivelas, Sintra, Loures. The knowledge resulting from this study will help to support decision-making in relation to initiatives aimed at controlling the spread of SARS-CoV-2, the typology of the restriction measures and their adaptation to territorial characteristics, allowing also to support the preparedness and response strategy to new pandemic waves.

R4COVID.1.053/2020

Occupational Health Interventions in healthcare workers exposed to SARS-CoV-2 during the recovery from COVID-19 pandemic

PRINCIPAL INVESTIGATOR	Florentino Manuel dos Santos Serranheira
LEADING INSTITUTION	Universidade Nova de Lisboa
FUNDING	€ 27 500

Occupational Health Service (OHS) of CHULN had difficulties in the management of healthcare workers (HCW) during the pandemic and after, in pandemic recovery. Monitorizing the health of the HCW must be supported by effective mechanisms, in order to prevent contagion and keep them active in the face of the expected exhaustion of the teams. It is essential to manage the process of deciding the HCW fitness for work in the Hospitals Occupational Health Services and other Health Units, so it was proposed to design a dashboard for the health surveillance of the HCW.

Project steps and objectives:

1. To collect and analyze the existing data from the decision-making process of fitness for work, along the pandemic progression, including the HCW with greater susceptibility to serious illness.
2. To analyze the confirmed cases among the HCW: Demographic characteristics (age, sex, profession, seniority); Epidemiological link, service and underlying likely exposure; Clinical evolution (initial symptoms, incubation time in view of the likely exposure identified, time elapsed between suspected exposure and positive analytical test, duration of symptoms, performed therapy); Time elapsed until the analytical remains negative for fulfilling return to work criteria; and Incidence.
3. To collect and analyze data on suspected HCW cases: Demographic characteristics of suspected cases (age, sex, profession, seniority); Suspected cases, by confirmed case, identified by management according to Health Policy (HP) criteria; Suspicious cases corrected by OH, after interview, according to HP criteria for confirmed case; and Rate of suspicious cases that evolve to confirmed case.

It is expected to create a procedure to be implemented in the Occupational Health Services, based on the health surveillance of healthcare workers, which allows to obtain information in a systematic way in the hospital, to process the data of health professionals and to communicate with the various entities, in the contribute to preventing contagion and monitoring those infected with COVID-19, during and after the COVID-19 pandemic.

Desenvolvimento de espaços para a esterilização por irradiação ultravioleta-C (UV-C) em larga escala de Equipamentos de Proteção Individual (EPIs) nos hospitais para a sua reutilização

PRINCIPAL INVESTIGATOR	Andrea Zille
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 20 000

In their proper use, personal protective equipment (PPE) are discarded or immediately autoclaved after use, as they might be infected. This type of protection is fundamental when diseases have a nosocomial transmission such as SARS (2003), H1N1 (2009), MERS (2012) and COVID-19 (2019).
Reprocessing non-reusable PPEs has been attracted researchers' attention in the literature, especially after the market shortage. Four groups of reprocessing methods exist: thermal, chemical, radiation and energetic. Reprocessing these PPEs cause uncertainty on which method to choose, since it can affect the efficiency and integrity of PPEs, reducing its barrier capacity. There is no universal alternative for sterilizing all PPEs. Then, the method's selection should consider both PPEs' materials and topology, as available resources and market acceptance. Energetic methods are mainly based on ultraviolet germicidal irradiation (UVGI), and widespread in food and water industries. Ultraviolet C (UV-C), among the UVGI, is able to damage biological structures via the photodimerization process. UV-C is suitable due to its low cost, high throughput, ease to use and do not leave chemical residues. UV-C has shown some limitations related to thermal deformation, diminishing of electrostatic charges and shadowing or absorption effects. However, these results are strongly dependent on irradiation level, material quality and production technology.
Thus, this research aims to create a certifiable system and protocol for sterilizing non-reusable gowns and masks using UV-C. The project will be developed in 5 main steps: i) Development of the UV-C system using a whole room approach for PPEs; ii) Validation of the PPEs' microbiological sterilization after UV-C irradiation; iii) Test the PPEs' mechanical integrity after using UV-C's sterilization method up to 5 reuse cycles; iv) Define the PPEs' sterilization protocol parameters and v) Create an UV-C sterilization chamber prototype. Due to the scarcity of PPE on the world market during a pandemic emergency, this solution represents a safe, fast, low-cost and environmental-friendly alternative.

FollowMyHealth

PRINCIPAL INVESTIGATOR	Ana Aguiar
LEADING INSTITUTION	Universidade do Porto
FUNDING	€ 11 000

Epidemiological evidence reveals that the SARS-CoV-2 virus spreads through close contact with infected people, through aerosols, which can stay in the air for several hours in poorly ventilated spaces, as well as through surfaces. In this context, knowledge about the various means of virus transmission, risk factors, and the clinical picture of the disease are relevant Public Health issues, as well as timely information to support action or response planning. The aim of this project is to investigate and validate how smartphones and the location they can provide may be used in response to an epidemic. In conjunction with ISPUP Public Health and FPCEUP Psychology experts, with the collaboration of USF Valongo, we designed solutions to support the response of health authorities. Adopting privacy by design, we gave special attention to preserving the privacy of application users and other aspects of socio-economic impact of the use of location. Studies based on questionnaires to collect information on the impact of the evolution of the pandemic in the population behavior and emotional state were also integrated. These solutions explore the possibility of using citizens as sampling agents to better understand what is happening on the ground on a daily basis. The main result is the CovidMonitor data donor application, available for Android OS on the PlayStore in a beta release, which will allow to 1. create a daily map of symptoms aggregated by geographic area for early detection of possible outbreaks; 2. send by email the history of visited places and reported symptoms to facilitate recall during contact tracing, as well as symptom monitoring in self-surveillance and over-active surveillance; 3.assess the risk of environmental transmission for different types of locations; 4. collect data on the psychological impact of social detachment, and give feedback on emotional state to users; 5. understanding the behavior of the population, the risk factors and the clinical picture of COVID-19; and 6. gather data on the adoption and robustness of collective protection measures
We currently await the opinion of CNPD on a prior communication recommended by the data protection officers (DPO) of UP and ISPUP. This will be followed by the consultation with the ISPUP Ethics Committee, before moving to the field studies in Valongo and University of Porto.

Maré R4COVID.2.344/2020

Mobilização Anónima de Regresso à normalidade para mitigar a Epidemia de COVID-19

PRINCIPAL INVESTIGATOR	Nuno Jardim Nunes
LEADING INSTITUTION	IST-ID- Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento - Universidade de Lisboa
FUNDING	€ 40 000

Maré's vision is that digital technology can play an essential role in mitigating the COVID-19 pandemic. The ubiquity of mobile computing enables a widespread deployment of solutions to promote the necessary behavior change to contain the virus spread.
Maré goal is to build a citizen-centric mobile platform that mobilizes the population to fight COVID-19 though engagement, gamification, and citizen science. Through a multiplatform App that stores all the information on citizen's devices, Maré brings to the broader public multiple technological solutions: i) anonymous feedback on social distancing; ii) targeted gamification; iii) territorial risk models; iv) planning of daily activities under unconfinement measures.
While many of the proposed solutions focus on the health system needs and the early response to control the virus during the lockdown, Maré focuses on the transition to unconfinement. During this stage, that could take months, mobilizing and engaging citizens will be critical to keeping the virus spread under control.
Maré takes a human-centered design approach by designing and deploying a novel citizen App which supports the following goals: i) anonymous feedback on social distancing based on existing reliable proximity services for mobile devices which use a combination of Bluetooth, WiFi and ultrasound; ii) gamification strategies targeting different population groups (e.g. children, young adults, risk groups, etc.) and promoting safety and confidence; iii) planning of daily activities under gradual unconfinement measures and taking into consideration risk individual and spatial risk models and also providing feedback on the occupancy of public spaces and transportation; iv) voluntary sharing of anonymous citizen science data for planning and scientific purposes.
Maré leverages anonymous citizen engagement and, therefore, will not include proximity tracing and data sharing with public authorities as described in other projects (e.g., DP-3T, PEPP-PT, and Apple and Google APIs). Because these approaches raise technical, privacy, and adoption issues, Maré attempts to complement the need for widespread support of citizen's needs and their voluntary collaboration via citizen science.

nano2Prevent R4COVID.2.247/2020

Nanoparticles to prevent SARS-CoV-2 transmission

PRINCIPAL INVESTIGATOR	Salette Reis
LEADING INSTITUTION	REQUIMTE - Rede de Química e Tecnologia - Associação
FUNDING	€ 40 000

The high incidence of transmission of the virus SARS-CoV-2 in hospitals and nursing-houses demands the correct disinfection of personal protective equipment (PPE) and bed linens, as well as virus detection in surfaces. Strategies to prevent contamination of healthy people, particularly from most vulnerable population (the elderly) and high-risk groups (health professionals), are urgent!
nano2Prevent aims to prevent SARS-CoV-2 transmission through the development of 3 solutions based in nanoparticles towards (i) virus inactivation in locus, namely in PPE and bed linens, upon incorporation within the textiles; (ii) specific visual detection of the virus on surfaces, by pulverization; and, (iii) a combination of both solutions in a unique formulation for the simultaneous detection and inactivation of the virus, in medical facilities, enabling the elimination of the virus while identifying contamination outbreaks. Research team expertise and multi-disciplinarity contribute to the design of gold nanoparticles able to inactivate the virus and polymeric nanoparticles for colorimetric visualization of the virus on surfaces, and thus stop virus transmission within the community.
nano2Prevent team is coordinated by Salette Reis, research group coordinator at LAQV and Professor at the Faculty of Pharmacy of the University of Porto, and is composed of several PhD researchers from LAQV, namely Catarina Seabra, Sofia Costa Lima, Cláudia Nunes, Joana Magalhães, Marina Pinheiro, and Tânia Moniz. Furthermore, nano2Prevent also includes a sustained network that enables expected results within 6 months, with the participation of Helena Felgueiras from the Centre for Textile Science and Technology from the University of Minho (2C2T) and Carla Silva from the Technological Centre for the Textile and Clothing Industry of Portugal (CITEVE).
The successful outcomes of nano2Prevent project will allow to eliminate the virus when using a PPE or bed linens and to identify infections focus on surfaces or in the textiles by pulverization. In the end, nano2Prevent will strengthen the National Health System with ready-to-use solutions for the control of the SARS-CoV-2 transmission in high-risk groups, that could be further employed by the population in general. These tools will play an important role in lowering the risk of virus transmission, minimizing the impact of this pandemic outbreak.

SafeS4Life R4COVID.2.483/2020

Long-term active surface protection to SARS-CoV-2 contamination

PRINCIPAL INVESTIGATOR	Andreia de Almeida Rosatella
LEADING INSTITUTION	FARM-ID - Associação da Faculdade de Farmácia para a Investigação e Desenvolvimento
FUNDING	€ 40 000

Healthcare settings are epicentres for SARS-CoV-2 transmission, by direct aerosol contamination, and also due to contact with contaminated surfaces where the virus can remain active for days. Disinfection of these surfaces, especially, on high-touch ones, like doorknobs, light switches, etc, can be quite challenging since the available disinfectants loses activity just after cleaning, resulting in rapid recontamination and virus spreading. SafeS4Life aims towards creating a novel, biodegradable and non-corrosive disinfectant spray that can be applied on high-touch surfaces in healthcare settings, or householding environments to inactivate the virus and avoid its spread. SafeS4Life spray can be easily applied in different surfaces, like glass or plastic, porous or not. The novelty of SafeS4Life spray is that it can remaining active for a long period on the surface.

SAFE Coating R4COVID.2.562/2020

Anti viral coating for widespread use

PRINCIPAL INVESTIGATOR	Carlos Alberto Alves Cordeiro
LEADING INSTITUTION	FCiências.ID - Associação para a Investigação e Desenvolvimento de Ciências
FUNDING	€ 40 000

Imagine a world where SARS-CoV-2 can no longer remain viable outside its human host. A world where hospital rooms, airplane seats and coffee tables, among other surfaces, are shielded. This will be a safer world concerning the present pandemic caused by SARS-CoV-2 and a more resilient one towards future threats caused by similar coronaviruses. This world can be made possible through the combination of extreme resolution mass spectrometry (FT-ICR-MS at Ciências ULisboa, one of the ten European Laboratories with this analytical instrumentation), an antiviral surface coating technology (Biomimetx, a company that innovates in surface coating for antifouling) and a real life test setup (Hospital de Curry Cabral, an hospital that was solely dedicated to the COVID-19 response). This is the vision of SAFE Coating - anti viral coating for widespread use project. We will use mass spectrometry to uncover SARS-CoV-2 inactivation at the molecular level, with a special emphasis on the S-protein, responsible for host cell recognition on different surfaces coated with an antiviral technology developed by Biomimetx. Small scale experiments with recombinant S-protein will be used to characterize and validate the antiviral coating approach that will be followed by coating optimization experiments, aiming to obtain stable, effective and long lasting surface protection against SARS-CoV-2.
Once optimized, large surfaces will be painted with the developed protective coating in different environments and exposed to S-protein to allow time course monitorization of the coating protective action. Once the project is successfully concluded, the next step will be to evaluate the surface coating effect on SARS-CoV-2 viability and infectivity.
The team believes that once developed, tested and proven to be effective, SAFE Coating will be of paramount importance primarily for the resilient and cost effective protection of critically exposed environments in hospitals and health care units, vehicles for the transport of infected people and, at a next stage, objects and surfaces of common use. Imagine the possibilities of using again, unrestrictedly, computer keyboards, airplane seats and regaining a daily life in a SAFEly Coated environment.

Development of a Lateral Flow Assay working prototype for detection of antibodies to SARS-CoV-2

PRINCIPAL INVESTIGATOR	Duarte Prazeres
LEADING INSTITUTION	IST-ID- Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento - Universidade de Lisboa
FUNDING	€ 40 000

Portugal is the midst of the COVID-19 pandemic. Antibody tests are key to define how the SARS-CoV-2 virus is spreading across the population. Laboratory-based tests (ELISA) are in-place that yield quantitative results but they need skilled workers and take several hours to complete. Further, as the pandemic advances, central labs will be flooded by requests for testing. Lateral flow assays (LFA) on the contrary are executed at the time/place of patient care and produce results within minutes. This can help optimize decision-making, avoid referrals and decrease costs. While COVID-19 LFAs are available from foreign firms, access to them is hindered by a huge worldwide demand. Clearly, Portugal would benefit from having the capacity to manufacture LFAs instead of relying on imports.
The Institute for Bioengineering and Biosciences of Instituto Superior Técnico (iBB-IST) and Instituto Gulbenkian de Ciência (IGC) have joined efforts to set-up and validate a working prototype of a LFA to detect antibodies to SARS-CoV-2 virus in human samples. The project builds upon the Covid-ELISA expertise of the Serology4Covid (S4C) consortium, established by IGC, IMM, CEDOC, ITQB and IBET, and combines it with the know-how of iBB-IST in the area of rapid diagnostics. Jointly, iBB-IST and IGC will investigate the possibility of establishing a reliable LFA test. The LFA performance will be further characterized and validated with preCovid and Covid sera (% of false/true positives/negatives). The ultimate goal is to create an LFA that can be manufactured at scale by national companies, independently of global markets.
The majority of LFA are qualitative (yes/no result), small and portable. The conventional LFA format consists of a small rectangular strip of overlapping materials that are mounted on a card, combined with specific reagents for recognition and encased in a cassette. We will design an LFA test to provide a visual indication (i.e., a red line) of the presence or absence of antibodies against the virus in the serum of patients. These tests will use high-performing viral antigens prepared by the S4C consortium, which will hopefully translate into an LFA with superior performance to the ones available. Once a working prototype is available, we will actively search for national companies that could manufacture the LFA at large scale, independently of global markets.

A practical assay for routine detection of neutralizing antibodies against SARS-CoV-2 that bypasses requirements for high biosafety laboratory usage

PRINCIPAL INVESTIGATOR	Maria João Lopes Gonçalves de Brito Amorim
LEADING INSTITUTION	Fundação Calouste Gulbenkian - Instituto Gulbenkian de Ciência
FUNDING	€ 40 000

The Severe Acute Respiratory Syndrome virus 2 (SARS-CoV-2) was first identified in humans in December 2019 in China, from where it spread, causing a pandemic outbreak. After 6 months, SARS-CoV-2 infected 11.5 million people worldwide, killing 534,500, and is still rampant. Urgent development of ways to treat, prevent and control SARS-CoV-2 pandemics are needed. The design of efficient strategies for the epidemiological control of SARS-CoV-2 requires the knowledge of whether people can be reinfected and, in that case, if infection will be more or less severe. This is relevant for immediate contingency measures but also for assessing the need of repeated vaccination programs and implement ways to surveille the status of protecton in the population. It is well known that humans develop a wide range of immunity upon viral challenge. Measles and chickenpox, for example, trigger long-lasting immunity, that results in lifelong protection against reinfection. In the opposite spectrum, dengue virus leads to an immune response that does not prevent reinfection, and, in addition, the disease is more severe in a second attack. Other coronaviruses capable of infecting humans, lead to a temporary immune response, that does not prevent reinfections, but we lack information on alterations in disease severity. At the heart of the protection from reinfection are a special type of antibodies, called neutralizing antibodies (nAb), that impede viral binding to human cells, and hence viral entry and replication. In this project, we proposed to establish an easy assay to detect nAbs in the population upon SARS-CoV-2 infection and test whether mutations occurring naturally during SARS-CoV-2 evolution lead to loss of protective immunity. Our assay is based on the use of viral particles that, although not infectious, mimic SARS-CoV-2 viral entry, and thus the assay bypasses the need for high biosafety labs that are limited in Portugal. We aim to validate and scale up this method for continued monitoring of the population on their protection status against SARS-CoV-2. By knowing the protected status of the population, governments can allocate appropriate healthcare resources, and hence, better respond to SARS-CoV-2 emergence.

R4COVID.2.679/2020

Environmental monitoring of SARS-CoV-2 in an hemodialysis unit: a quest for preventing transmission in healthcare facilities

PRINCIPAL INVESTIGATOR	Gil Roberto Correia Lopes
LEADING INSTITUTION	IST-ID- Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento - Universidade de Lisboa
FUNDING	€ 40 000

The starting point for the project is the investigation of the contamination inside a health unit with COVID-19 patients. Transmission between individuals occurs mainly by contact and via air. Contact transmission can take place by direct transmission between people or by contacts with surfaces. Air transmission is possible by droplets or by aerosols in certain circumstances. Personal protective equipment is essential to prevent the transmission of the virus, but it is also essential to ensure the safety of healthcare facilities and to reduce the likelihood of transmission between users, both patients and professionals. The project intends to detect critical points of contamination on different surfaces, in the environment air and inside Heating, ventilation and air conditioning (HVAC) systems and to determine the effectiveness of the hygiene measures implemented in a health unit, in this case in a hemodialysis unit. For this, we will collect samples with swabs on various surfaces such as tables, chairs, medical equipment, door handles and others in order to detect and quantify the presence of the virus on them. We will also make several air samples to determine the degree of contamination of the indoor air by the virus and we intend to collect samples from the inside of the ventilation system to ensure that there is no virus emission by this system. We also propose to evaluate the efficiency of two air purification equipments, one that uses UVC radiation, other HEPA filters, in inactivation/removal of this virus in the air. Multiple samples will be collected at different times to assess the places most prone to viral deposition. All samples will be done in duplicate, before and after cleaning processes. In this way, we intend to confirm the effectiveness of cleaning and disinfection processes. The project aim is to create and evaluate a Monitoring Program for detection of environmental contamination with SARS-CoV-2 in Healthcare units. This work integrates a translational research that proves that academic and basic research can play a very important role in solving problems and developing strategies for clinical settings with strong relevance for society. The goal of our team for this project is that it can constitute a model of quality program in the monitoring of the implemented infection control measures in different Health Units across our Public Health Service (SNS).

SerCOVID-19 R4COVID.2.754/2020

Sero-prevalence of SARS-CoV-2 antibodies: Tools for population-based epidemiological studies.

PRINCIPAL INVESTIGATOR	Mónica Bettencourt-Dias
LEADING INSTITUTION	Faculdade de Medicina da Universidade de Coimbra
FUNDING	€ 40 000

On preparation for large serological studies this project aims to integrate and fine-tune the tools required to obtain rigorous estimates of sero-prevalence of SARS-CoV-2 antibodies at the population level. Using a multidisciplinary team we will put together a set of statistical, epidemiological, immunological and data analysis methodologies covering all needed tools to implement these studies. The project includes field tests in different population settings that will serve as pilot studies to identify improvement opportunities and to refine the tools, the methods and approaches.

Background work for this project (https://gulbenkian.pt/ciencia/ptpt/noticias/roteiro-serologico-nacional/) provided the grounds for a study design based of random participant selection based on households. Also, an epidemiological questionnaire was constructed to ascertain possible risk factors involved in viral exposure in the community (including age of co-habitants, contacts with suspected and cases, usage of protection equipment, usage of public transportation). An ELISA assay was implemented in the context of a consortium of Portuguese biomedical institutes (Serology4COVID) was calibrated to detect IgG/IgM antibodies recognizing SARS-CoV-2 spike antigen and determine appropriate cut-offs for prevalence studies.

Using these tools we engaged in a serological study of a rural municipality (Almeirim). The implementation model was based on the cooperation of the municipal capacities for participant recruitment and logistics, the local health authorities for sample collection and the IGC capacity for antibody testing. This pilot study analyzed 283 individuals engaged in frontline activities (including health workers, firemen, etc.) and 270 individuals from 121 households randomly selected in the municipality.

Preliminary results show that IgG anti-SARS-CoV-2 sero-prevalence in the population was 3.88% (CI 1.87-7.08) while only 0.9% of the frontline workers were positive. Further analysis related to associated factors is ongoing. The next step is to run a similar pilot study in an urban municipality that is currently in the planning phase.

The results of these pilot studies will provide a comprehensive set proven options and tools to be applied in larger studies at national level.

R4COVID.2.798/2020

Development of an inexpensive, simple and open-source device for SARS-CoV-2 detection

PRINCIPAL INVESTIGATOR	César S. Mendes
LEADING INSTITUTION	Universidade Nova de Lisboa - Faculdade de Ciências Médicas
FUNDING	€ 40 000

Molecular testing is amongst the most efficient approach to prevent the spread of COVID-19 within a community, in addition to increase positive outcomes amongst symptomatic patients. It is thus critical to maximise our testing capacity. Currently, diagnostics aim to identify the genetic material of SARS-CoV-2 through high-sensitivity molecular biology tools such as RT-PCR. These tests have been further optimized at CEDOC | NOVA Medical School in order to produce a colorimetric readout providing a quick response. Nevertheless, they still require expensive and complex devices that prevent their use by a large number of entities. In this proposal we aim to overcome this hurdle by designing an affordable, simple to use, precise and open-source device capable to execute sensitive thermocycling protocols.
We expect to execute this project in multiple steps:
First, to develop a prototype comprising all the electronic components and an aluminium tube holder for at least 48 samples. The setup would be pre-programmed (via USB cable) to run the proper thermocycling protocol.
Second, once a prototype is built, we will test the COVID-19 detection protocol currently being used at CEDOC | NOVA Medical School using our device. Here we will access the reliability of our prototype by re-testing samples already tested using current laboratorial conditions
Third, once a final product is designed, we will look for partners capable to mass-produce and distribute this device amongst entities interested in executing COVID-19 testing. Moreover, we will share the blueprints and code in public repositories.
The successful execution of this proposal will decentralize, expand and lower the costs associated with COVID-19 testing. This will reduce the testing burden allocated to the SNS and increase overall COVID-19 testing capacity, which will minimize the spread of the virus, reduce the number of patients requiring hospitalization and enhance survival chances. This will also provide testing capabilities to developing countries and communities unable to acquire the hardware necessary to execute testing at the desired scale. This system will build on existing high-sensitivity PCR testing protocols, maximizing the chances of adoption and minimizing implementation costs.

R4COVID.2.804/2020

Work, Telework and Social Distancing under a Pandemic

PRINCIPAL INVESTIGATOR	Tiago Santos Pereira
LEADING INSTITUTION	CoLABOR - Laboratório Colaborativo para o Trabalho, Emprego e Proteção Social
FUNDING	€ 40 000

In view of the COVID-19 pandemic, telework proved to be a central measure supporting social distancing in order to prevent contagion and promote public health. This project aims to assess the ability to implement telework by different sectors of the economy and professional occupations, as well as the corresponding impacts. These results will support the design of strategies for adopting telework in different organizational contexts, the assessment of the territorial distribution of the risk of contagion in the workplace and the design of local public health interventions.
Work at CoLABOR showed the existing inequalities in access to telework under confinement, and the tensions and ambiguities in the individual experiences of telework, regarding, for example, the organization of work, autonomy, or the articulation of professional and family life. We will survey a representative sample of the working population in Portugal to capture, information relevant to the assessment of the material working conditions and satisfaction levels. Such results will be of particular relevance for policies concerning the uptake of telework, under conditions of confinement as well as under normal conditions of work. In a second activity, we are developing a model to evaluate the permeability of different occupations and sectors of the Portuguese economy to telework. By understanding the task composition of different occupations we will distinguish between occupations with greater, partial or non-existing permeability to telework. By applying this model at a territorial level, the results will be of relevance for the implementation of public health strategies at the territorial level. In a third task we are developing a qualitative study of the experience of teleworking in different organizations, exploring the experience of teleworking before and after the emergence of the pandemic outbreak. These case studies will focus on the individual experiences of workers and managers as well as on organizational standpoint. The results will shed light on the impact of telework on the organization of work, the structures and forms of sociability in the workplace, motivations and concerns related to the continued adoption of telework as a normal mode of work organization, or the impact of telework on health and safety conditions at work with reference to the current pandemic situation.

R4COVID.2.404/2020

Esterilização de EPIs com radiação gama com vista à sua reutilização

PRINCIPAL INVESTIGATOR	Ana Paula Valagão Amadeu do Serro
LEADING INSTITUTION	IST-ID- Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento - Universidade de Lisboa
FUNDING	€ 39 808

In a pandemic context, personal protective equipments (PPEs), such as masks and clothing, are essential to ensure the safety of the general population and in particular the health professionals who face greater inherent risks. Although most PPEs are disposable, many can be reused effectively and safely, with unquestionable advantages both in economic and environmental terms, once they are sterilized and maintain an adequate performance.
The project "Sterilization of PPEs with gamma irradiation regarding their reuse" aims to evaluate the possibility of using gamma irradiation to sterilize essential PPEs to prevent the spread of COVID-19. To this end, several materials (already used in the production of PPEs or with potential for future use) that can be sterilized by this method will be identified, and the ideal sterilization conditions and the number of times that they can be reprocessed will be defined for each one. In some cases, post-sterilization treatments may be required to restore the materials' functionality.
The sterilization method in analysis is recognized by the International Atomic Energy Agency as an effective tool for the elimination of SARS-CoV-2 and has numerous advantages over other methods currently available. Since radiation has a high penetration power, PPEs can be sterilized in sealed packages, reducing the contamination risks associated with handling. It does not generate toxic residues, which allows immediate reuse of PPEs. Processing only takes a few hours and is done at room temperature, with is advantageous for the materials and in terms of energy costs. In addition, it is possible to process large quantities of materials simultaneously, which contributes to cost savings.
Sterilization will be carried out at the CTN-IST radiosterilization unit, an unique infrastructure in the country. A team with extensive experience in sterilization of medical devices, which includes researchers from IST (CQE and IPFN) and LMAEM-Egas Moniz, will work closely with CITEVE and with health professionals from Centro Hospitalar Universitário de Lisboa Central (Hospital de São José) and from Clínica Dentária Universitária Egas Moniz.

MoodUP R4COVID.2.411/2020

A digital platform to accelerate access to Mental Health care for cancer patients amid COVID-19 pandemic

PRINCIPAL INVESTIGATOR	Diana Frasquilho Guerreiro
LEADING INSTITUTION	Fundação D. Anna de Sommer Champalimaud e Dr. Carlos Montez Champalimaud
FUNDING	€ 39 552

The COVID-19 Pandemic is the biggest crisis of our recent history and is threatening people's physical and mental wellbeing as people cope with the disease, disrupted work, personal and social lives, family dynamics, finances and an uncertain future.
Some groups of the population are at higher risk, including individuals with pre-existing physical and/or mental health conditions. Cancer patients are particularly vulnerable to COVID-19 as their immune systems may be compromised due to the cancer itself, or the resulting treatment. Additionally, they also already account for higher rates of depression and anxiety than the general population.
Public health authorities urge for health services to adapt quickly to the "new normal" and react to the challenges of this pandemic. Scaling-up mental health care capacity for cancer patients during the pandemic is thus needed to deal with the likely mental health problems surge. Moreover, the requirement of social distancing is also adding urgency on digital transformation in healthcare. The MoodUP project aims at both increasing mental health care response capacity to the upsurge in depressive and anxiety symptoms and at much-needed care digitalization. Its objective is the creation of an online platform to provide depression and anxiety symptom screening, triage by severity and treatment recommendation based on symptom severity levels for cancer patients in psychological distress amid the pandemic.
The MoodUP platform will be implemented at the Champalimaud Clinical Centre and will allow for tackling the under-detection and under-treatment of depression and anxiety while improving coordination and cooperation between Oncology Care and Mental Health Care teams that would result in reductions in patients' depression and anxiety symptoms. Furthermore, the MoodUP will deliver a software platform that can be independently adapted or expanded to different care and research settings, thus facilitating know-how transfer amongst institutions in the national health system. This will advance scientific and technological knowledge on collaborative mental healthcare and distribute and/or expand the digital tool to improve overall mental health care management to high-risk patients amid COVID-19 pandemic and for future crises.

Spatial Modelling for mapping COVID-19 risk

PRINCIPAL INVESTIGATOR	Maria João Correia Colunas Pereira
LEADING INSTITUTION	IST-ID- Associação do Instituto Superior Técnico para a Investigação e Desenvolvimento - Universidade de Lisboa
FUNDING	€ 38 000

The lack of knowledge about the SARS-CoV-2 combined with a global pandemic crisis, caused by the rapid spread of COVID-19 disease makes the need for the development of tools suited to monitor and evaluate infection risk dynamics. This is valuable information for health authorities for containing and mitigating the spread of the COVID-19 pandemic. With this in mind, this project gathers a multidisciplinary team of experts in geo-spatial data sciences, epidemiology, public health, computer sciences and decision sciences in health to develop a set of tools to model the spatial and temporal evolution of the risk of infection to support decision-making of health and civil protection authorities.
These tools will be coupled in a web-based dashboard where information from various sources and models are represented in an appropriate way for crisis management in terms of health, population safety and logistics, and where methods and data in use are communicated according to the best practices in information visualization. The information to be delivered in this project will be centered on COVID-19 risk maps with high spatial resolution for the mainland Portuguese territory, to be developed under a geostatistical modelling framework. Moreover, geostatistical simulation algorithms will be used to provide a measure of spatial uncertainty attached to the predicted risks. Here it must be underlined the relevance of quantifying spatial uncertainty shown by COVID-19 risks maps to support decision-making (e.g., to set local lockdowns). The project will use data concerning the number of positive tests for COVID-19 as provided by the Direcção Geral da Saúde. Other auxiliary information such as mobility, socio-demographic and economic factors will be included in the models, improving not only the accuracy of predicted risks but also reducing their spatial uncertainty. The project will demonstrate the benefits of using geostatistical models to assess the effectiveness of the measures to prevent virus propagation during all stages of the pandemic, to balance demand and supply of medical resources required to control the disease and learn lessons ahead of any possible second or third epidemic waves, while developing a vaccine.

Social Sensing & Intelligence for Forecasting Human Response in Future COVID-19 Scenarios, towards Social Systems Resilience

PRINCIPAL INVESTIGATOR	Rui Gaspar
LEADING INSTITUTION	Universidade Católica Portuguesa
FUNDING	€ 37 682

A widely discussed future scenario for the COVID-19 pandemic refers to the creation of a vaccine. But how will citizens respond in other scenarios, e.g. what if there is no vaccine? What if there is no effective therapy? Or even: what if group immunity is not achieved? Irrespectively of the different possible scenarios, human behaviour will always be the most effective mechanism for social control of a pandemic in the absence of a vaccine or other control measures. Understanding it allows to intervene proactively, reducing the burden on the National Health System and increasing its resilience. To do so, the ResiliScence 4 COVID-19 project will identify: 1) predictors of current and future protective behaviours (e.g. mask use) that prevent contagion risks with the new coronavirus; and 2) risk profiles, i.e. psychosocial and socio-demographic characteristics that may increase individuals exposure to risks. Analysis will be grounded on human sensors data, collected through a three-wave longitudinal survey and "smart" anonymized data from smartphones (following RGPD regulations).
The first project stage was implemented grounded on a multimethod approach, to monitor how portuguese citizens evaluate the COVID-19 pandemic across time and geographical locations. This allowed analysing thousands of comments to COVID-19 related posts/news on social networks since January 2020, to calculate a threat level ratio - an indicator of the social system's overall risk(s) perception. These comments were coded as either representing perceived demands to individuals or resources perceived as available. The results enabled public health authorities to create risk and crisis communication materials, social mobilization strategies and resources based on evidence of risk perception changes across time (https://covid19.min-saude.pt/comunicacao-de-crise-e-percecao-de-riscos/). Social media, psychosocial and "smart" data analysis will allow rethinking the National Preparedness and Response Plan (PNPR) for COVID-19 by developing behaviour change strategies and resources to promote citizens social mobilization and resilience, customized to different crisis stages and pandemic scenarios.

INTAKE R4COVID.2.361/2020

INtegrating mobility daTa into spAtial risK modEls

PRINCIPAL INVESTIGATOR	Arlindo Manuel Limede de Oliveira
LEADING INSTITUTION	Instituto de Engenharia de Sistemas e Computadores, Investigação e Desenvolvimento em Lisboa (INESC-ID)
FUNDING	€ 37 524

Despite the relative success of the initial measures adopted for the containment of COVID-19, the next phases of containment will have to be based on intelligent approaches to monitor and control the spread of the pandemic. Tracking solutions, based on the use of BLE beacons or GPS information from cellphones have the potential to enable the tracking and reporting of potential contacts by infected people, but face significant hurdles, amongst which are privacy concerns, battery usage, false alarms and a number of confounding human factors.
On the other hand, telecommunication providers continuously trace the location of individual users, since the connection with the cellular towers is permanent, non-invasive and does not involve abnormal battery usage. The data obtained from this source is potentially very useful to monitor the spread of the epidemic, since mobility data can be used to improve existing models for the spatial dependency of diseases. Such models, for the Portuguese territory, are already available on the web, but they do not take into account detailed mobility patterns. This project will integrate mobility data, gathered and processed by a mobile phone provider which also participates in the project. Specifically, the project will use public data of confirmed COVID-19 cases made available by DGS and mobility data from a mobile operator, duly anonymized to avoid any privacy issues, to improve the prediction of medium-term evolution of the pandemic.
A number of techniques will be used to fit the model to the data. As a baseline, we will include the computation of mobility indexes between municipalities to improve existing geostatistical models. We will then model the evolution in each municipality using state-of-the-art artificial intelligence techniques, namely recurrent neural networks, which will integrate the effects of the epidemic pressure from within the municipality and the neighboring municipalities, by using mobility data as inputs to the networks. This analysis will be used to infer, with higher precision and granularity, the predicted risk for each geography, in the near and medium-term future. The resulting model will be made available to the public and to the relevant authorities, with an interface that can be used to run what/if scenarios, enabling SNS entities to more quickly and efficiently assess the spatial evolution of the pandemic.

R4COVID.2.818/2020

Cost-effectiveness and optimization of the Public Health (PH) effort for COVID-19 Track and Tracing activities in Portugal

PRINCIPAL INVESTIGATOR	Rui Gentil de Portugal e Vasconcelos Fernandes
LEADING INSTITUTION	Instituto de Saúde Ambiental (ISAMB), Faculdade de Medicina da Universidade de Lisboa
FUNDING	€ 37 060

Track and tracing activities are fundamental in low incidence serious infectious diseases, for their ability to prevent secondary cases and containing the transmission. In the situation where a new infection, without immunity at the population level ('herd immunity') evolves towards an endemic equilibrium and community-level transmission, track and tracing activities assume new roles: the protection of vulnerable and at-risk populations, the management of cases in their setting (families, nursing homes, workplace), the reinforcement of containment efforts and collection of critical data for pandemic management.
However, tracking and tracing activities are time-demanding and dependent on the training and proficiency of the public health agent, as well as on the collaboration of the subjects. They also depend on the information system circuits and time-dependent articulation among levels (doctor who diagnoses, laboratory who tests, hospital information, death notifications). Nonetheless, public health contact tracing activities will impact the rate of new infections, their severity and deaths. They will be critical to ascertain vulnerability of settings and the ability to reduce actions limiting socio-economic activities, while maintaining acceptable rates of new infections and deaths. Therefore, proficient public health track and tracking activities will have short-term overall effects on the epidemic evolution, health outcomes and health care needs.
We will characterize tracking and tracing activities in several public health units along time, relating with resources allocated to tracking and tracing activities. We will relate the variability of track and tracing activities with the likelihood for hospital admission, ICU admission and death. This will allow estimating an optimal performance curve, and well as understanding the amount of variability on the performance that is, or is not, explained by data on human resources availability, providing evidence for identifying local good practices. The resources and costs needed for optimizing public health tracking and tracing activities will be calculated, and the projected impact on the rate of new cases, hospital admission, ICU admission and death.

R4COVID.2.395/2020

Assessing the decontamination effectiveness for the safe reuse of filtering facepiece respirators

PRINCIPAL INVESTIGATOR	Marco Paulo Seabra dos Reis
LEADING INSTITUTION	Universidade de Coimbra
FUNDING	€ 31 590

The response to the COVID-19 pandemic generates a shortage of personal protective equipment worldwide, in particular Filtering Facepiece Respirators (FFR) or respiratory masks, which are fundamental to slow down the spread of the virus and guarantee the safety and well-being of professionals and the society in general.
Given the huge demand for FFRs in pandemic periods, producers and existing logistic circuits are incapable to produce and distribute masks to all those in need of them. However, for each new reuse of a mask by the general population and organizations not directly involved in treating COVID-19 patients, a much larger contribution in terms of effective availability of masks is achieved. Therefore, it is important to plan ahead and create, test and validate several protocols that allow for a safe reuse of FFRs, which can be readily activated in situations of extreme shortage of FFRs. These decontamination protocols should be simple to execute and not requiring expensive equipment or the manipulation of hazard substances, in order to make them scalable to the general population and organizations. They should also be effective both from the standpoint of maintaining the structural integrity of the masks and their filtering efficiency, as well as regarding the depletion of microbiological pathogenic agents. This last aspect in particular has been somewhat underappreciated but it will be an integral part of this project. In this project, special focus will be given to decontamination methods that can be adopted by private entities and non-hospital institutions, without access to autoclaves or sterilization by ethylene oxide. The following decontamination protocols will be tested: hydrogen vapor (VHP), steam treatment ("steam bags") and washing with sodium hypochlorite solution and drying (LLS). The types of masks considered are: surgical, FFP1-FFP3 and social masks. Besides developing decontamination protocols for general use that are simple and scalable, evaluating their impact on filtration efficiency over the cycles and their microbiological effectiveness, this project also aims at providing accurate and objective information for the safe reuse of FFRs and develop stratified recommendations for different profiles of users: public, nursing homes, schools, companies, USFs, among others.

R4COVID.2.671/2020

Ser cuidador na pandemia por COVID-19: a massive open online course (MOOC) sobre medidas de prevenção e de autocuidado aos mais vulneráveis

PRINCIPAL INVESTIGATOR	Maria José Silva Lumini Landeiro
LEADING INSTITUTION	Escola Superior de Enfermagem do Porto
FUNDING	€ 21 628

There are an estimated 827,000 informal caregivers in Portugal. Data calculated on the basis of the 2011 Census and research conducted by Costa (2013) and Parente (2015), released in the Relatório da Primavera (2015), point to 110,355 adults dependent in self-care living in their homes, of which 48,454 being totally dependent. Most of these persons depend on the care of family members, who are usually poorly prepared and without regular support from health professionals. There is a gap in providing solutions to inform/empower these caregivers to the new challenges posed by the SARS-CoV-2 pandemic. This project aims to design, develop and validate a MOOC integrating personal hygiene and housing measures to be adopted in self-care activities (eating, basic hygiene care, positioning, transferring, dressing and giving medication) of surveillance and monitoring by caregivers of the most vulnerable dependent people, living in a home setting, with a view to preventing coronavirus infection. The contents of the course will be based on the Plano Nacional de Preparação e Resposta à Doença por novo coronavírus of the Portuguese National Health System and the available scientific evidence. It will be structured in modules: Module I - Presentation of the course; Module II - Prevention measures of COVID-19; Module III - Feeding and hydration; Module IV - Positioning and transfer; Module V - Hygiene care; Module VI - Pressure ulcers and falls prevention; Module VII - Medication. Each module will be supplemented with educational material, videos, discussion forums and questionnaires to assess learning and user satisfaction. The contents of the course will be previously validated by a group of experts external to the project team and the course will be tested in a group of caregivers recruited through a caregiver support association. After the validation phase the course will be made freely available by the NAU platform. This proposal is a sub-project of INTENT-CARE project, a digital platform with guidelines for carers on basic care for dependent persons. This proposal aims to gather and use videos and content from the platform already created to prompt usability, but there is a need to create new educational content.

R4COVID.2.640/2020

Reducing biased information processing to increase compliance with SNS's recommended measures for COVID-19 prevention

PRINCIPAL INVESTIGATOR	Irene Consiglio
LEADING INSTITUTION	Universidade NOVA de Lisboa - Nova School of Business & Economics
FUNDING	€ 7 755

As strict confinement measures are gradually being lifted and people return to their routines, citizens' compliance with the SNS recommended COVID-19 prevention measures becomes critical. We explore how a cognitive bias – called confirmation bias – affects people's decision to follow SNS's recommendations and test a simple cost-effective intervention to improve the rate of compliance. The confirmation bias is a tendency to look mostly for information that supports pre-existing opinions and ignore or downplay the significance of counter information, which leads to errors in decision-making, including health decisions. For instance, it is a cause of biased selection of data concerning vaccinations, which contributes to deciding against them. Confirmation bias is a critical issue in the current context, because information of varying quality reaches people through different channels: a biased selection of information might cause implementing fewer or wrong prevention measures. The objective of this research is to test a previously validated intervention that reduces the confirmation bias. This intervention has already shown good results in the lab, with positive short-term and long-term effects on decision-making quality, but has never been tested in a real-crisis situation. We expect that de-biasing people's selection of COVID-19-related information will improve their autonomous implementation of correct prevention measures.

Diagnostic

R4COVID.1.006/2020

How sick will the coronavirus make you? The answer may be in your plasma IgG glycome signature

PRINCIPAL INVESTIGATOR	Salomé Pinho
LEADING INSTITUTION	IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto
FUNDING	€ 30 000

COVID-19 is a highly selective disease. Only some infected people get sick, and although most of the critically ill are elderly, some of the patients that die are previously healthy and/or relatively young. There is an urgent need to early predict (at diagnosis) who is likely to develop a severe/complicated disease aiming to improve the risk stratification system at diagnosis and discriminate high-risk individuals requiring intensive care resources (as ventilators) from those with low-risk that do not require hospitalization. This will optimize the allocation of health care resources. In the last decade, our research group at i3S/IPATIMUP has been demonstrating that glycans are master regulators of the immune system. The relevance of glycans in COVID-19 is also highlighted by the fact that SARS-CoV-2 and its receptor ACE2 are both highly glycosylated. There is a significant heterogeneity in terms of glycans composition (glycome) in the serum among the population which results in significant inter-individual differences. This glycome variation is translated in differences in the effector functions and potency of neutralizing antibodies. In this project, we AIM to determine whether plasma glycome heterogeneity or switching among SARS-CoV-2 patients can be used as a reliable and minimally invasive biomarker to early identify those individuals at risk of serious illness from those who might be protected. In straight collaboration with Infection Unit of Centro Hospitalar e Universitário do Porto (CHUP) led by Prof. Rui Sarmento e Castro and more recently with the participation of the Infectious Unit of Centro Hospitalar de Vila Nova de Gaia and Hospital Beatriz Ângelo, Loures we are analyzing up to 100 serum samples from SARS-CoV-2 infected individuals at diagnosis and controls. The glycans composition of antibodies in the serum has been done by advanced glycoproteomics approaches and functional studies. Patients will be followed up after diagnosis and the serum glycome signature will be correlated with severity of the disease. In this study we propose to assess how serum glycome profile can be used as a reliable risk stratification system (a blood biomarker) of COVID-19.

R4COVID.1.009/2020

Rapid, low cost and reduced complexity test for SARS-CoV-2 RNA detection

PRINCIPAL INVESTIGATOR	João Manuel Braz Gonçalves
LEADING INSTITUTION	FARM-ID, Associação da Faculdade de Farmácia para a Investigação e Desenvolvimento
FUNDING	€ 30 000

The current diagnosis of COVID-19 combines clinical symptoms and molecular methods. In most molecular diagnostics, RT-qPCR is the most widely used method, but requires expensive and complex instrumentation. In this project, we will implement a diagnostic method for SARS-CoV-2 RNA using loop-mediated isothermal amplification (LAMP) and visualization of amplification by colorimetry. This methodology has already been used on a large scale in the detection of the Zika virus in urine and even detections on the International Space Station.
In this project we are going to test pairs of oligos from the ORF1a and N gene of SARS-CoV-2. The RNA will be converted to cDNA by RT and amplified via LAMP by DNA polymerase. Internal controls (RNA MS2) and extraction controls (amplification of beta-globin) will prevent false negatives. The dye will bind to the amplified DNA strands. We will compare LAMP with RT-qPCR for all conditions of sensitivity and specificity and use swab cell lysate to avoid variability in RNA purification. We will develop a mobile phone application to quantify the color resulting from the amplification. This application will be able to estimate the number of SARS-CoV-2 RNA copies in the sample, enhancing the application of LAMP at the diagnosis site. The results will allow to obtain a fast and reliable method to amplify viral RNA, with a single reaction temperature, avoiding the need for RT-qPCR.
LAMP validation will be performed with 1000 clinical samples from COVID-19 patients that will be obtained at the SARS-CoV-2 screening center at the Faculty of Pharmacy at University of Lisbon. The RNA will be extracted from the swab by column and will be tested by the LAMP colorimetric method and RT-qPCR. The comparison between LAMP and RT-qPCR will validate the agreement on several values. Unpurified RNA samples will be used to test LAMP compliance with purified samples. The results obtained from this project will allow to validate the colorimetric LAMP technique, as a quick technique (1 hour), easy, low cost (<10 euros) and high turnover (100-200 samples, depending on the number of dry baths), without need for expensive equipment and complex techniques.

R4COVID.1.031/2020

Very high throughput low cost test for the massification of SARS-CoV-2 screening

PRINCIPAL INVESTIGATOR	Manuel António da Silva Santos
LEADING INSTITUTION	Universidade de Aveiro
FUNDING	€ 30 000

The diagnosis of SARS-CoV-2 infection is based on the extraction of viral RNA followed by amplification and detection of the viral genome by Real-Time Polymerase Chain Reaction (RT-PCR). The dramatic increase in COVID-19 cases world wide resulted in a strong market shortage of kits for RNA extraction and RT-PCR, creating significant bottlenecks in SARS-CoV-2 testing. As such, high-capacity alternative viral screening methods are urgently needed.
The main objective of our project is to develop and/or implement new SARS-CoV-2 screening methods to overcome the shortage of reagents and other the limitations of existing screening methods. We are optimizing experimental protocols to detect SARS-CoV-2 directly from clinical samples, increasing the availability of viral RNA in the Reverse Transcription Step, thus reducing the costs and processing time for each sample. For this, different incubation times and temperatures are being optimized during cDNA synthesis to determine the best experimental conditions for detecting this coronavirus.
In order to test thousands of samples in parallel and sequence the viral genome in the same reactions we are replacing traditional RT-PCR detection with new next generation sequencing methodologies. This protocol increases samples processing capacity and is expected to reduce testing costs. Another important advantage is the scalability of the method; it can screen as low as 96 samples per hour or as much as 1500 samples per day, increasing dramatically the flexibility of the testing protocol. Its maximum capacity can be scaled up to 5 600 samples, eliminating exiting laboratory sample processing bottlenecks.
We expect to have the new methodologies ready for use during the Fall/Winter 2020 to overcome eventual SARS-CoV-2 screening difficulties arising from a second wave of COVID-19.

R4COVID.1.041/2020

Cdots Biosensing COVID-19

PRINCIPAL INVESTIGATOR	Paula Filomena Martins Lopes
LEADING INSTITUTION	Universidade de Trás-os-Montes e Alto Douro
FUNDING	€ 30 000

"Cdots Biosensing COVID-19" was built based on an international patent belonging to the University of Trás-os-Montes and Alto Douro which was developed on other biological samples. The prototype under development will be used for swabs analysis, without amplification pre-steps, in a fluidic system. This prototype will be a direct alternative to RT-PCR and should provide a result in 10-20 min (that's considerably faster than the 3-6 h protocol using PCR). The device is based on the hybridization between viral RNA and probe, using fluorescence for detection. The overall analysis will also be very cheap and will not require specialized technicians, allowing its application for wide population screening in a cost effective manner. Additionally, this solution can be easily used by countries with lower resources. Wide testing can contain SARS-CoV-2 dissemination, and the technology behind this biosensor is drawn for such purpose. The consortium behind this project is composed of academics, researchers and health professionals, from the following institutions: UTAD (leader); REQUIMTE; Instituto Superior de Engenharia do Porto; Instituto de Saúde Pública e Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto; Centro Hospitalar de Trás-os-Montes e Alto Douro and Centro Hospitalar Universitário Cova da Beira.

IPP4AFA R4COVID.1.104/2020

Apoio ao diagnóstico molecular SARS-CoV-2 no ACES Entre Douro e Vouga I – Feira / Arouca

PRINCIPAL INVESTIGATOR	Ruben Miguel Pereira Fernandes
LEADING INSTITUTION	Instituto Politécnico do Porto
FUNDING	€ 30 000

O ACES FA serve uma população com grande incidência da doença com várias unidades prestadoras de saúde e lares de idosos. No PPORTO será criada uma ADC (Área Dedicada ao COVID) para implementação do laboratório temporário. Metodologia: Diagnóstico molecular mediante qRT-PCR, de acordo com as normas OMS e com a aprovação do CDC (CDC-006-00019, versão 03). Após a prescrição do MGF, serão feitas colheitas com zaragatoa na orofaringe / nasofaringe. No teste, irão ser utilizados controlos positivos do vírus e controlo interno da RNAse P humuna (RP). Quando estiver complemente recomendado pela DGS pretende-se utilizar o método Português (IMM), com os reagentes produzidos em Portugal para fazer face à potencial quebra de stocks dos fornecedores estrangeiros. Neste momento, a equipa possui em stock, kits suficientes para 2500 reações de extração de RNA e conversão para cDNA, e kits para a amplificação por RT-PCR de outros 2500 rxs. Pelo que, esses reagentes não irão faltar proximamente. Falta adquirir os primers e sondas para o SARS-CoV-2, materiais de colheita, EPIs, etc.
Impacto na população: O IPP possui uma unidade de Saúde Móvel que pode ser utilizada para a colheita de amostras. População a incluir: Neste programa de rastreio serão incluídos todos os seguintes os elementos da população que não cumpram os critérios da norma da 004/2020 DGS: a) profissionais de saúde - por rotina, os profissionais de saúde do quadro do ACeS, serão alvo de colheita de zaragatoa nasal e de orofaringe com uma periodicidade de 15 dias; b) os utentes e profissionais de lares de terceira idade na área de influência do AceS; c) os cuidadores de doentes coronavírus positivo; d) todos os cidadãos que, por critério e recomendação escrita e validada pelo seu médico de família se considere útil incluir neste rastreio.
População a excluir: Excluem-se deste rastreio todos aqueles que se enquadrem na norma 004/2020 da DGS para realização de teste, devendo, neste caso dirigir-se aos locais previstos para esse efeito, em funcionamento nas unidades do SNS, nomeadamente ADC-Comunidade, no âmbito dos cuidados de Saúde Primários e ADC-SU, no âmbito dos serviços de urgência dos hospitais.

R4COVID.1.107/2020

Which, when and for who? Serodiagnosis as a tool to complement diagnosis and evaluate population immunity against SARS-CoV-2

PRINCIPAL INVESTIGATOR	Margarida Correia-Neves
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 30 000

Serological testing is crucial to evaluate the immunity of the population, to complement the diagnosing of acute SARS-CoV-2 infection (especially for situations with false negative results obtained with the gold standard RT-qPCR) and for tracing transmission clusters. A few studies described the timing for anti-SARS-CoV-2 antibodies initial detection and progression along COVID-19. Anti-SARS-CoV-2 IgM and IgA are detectable 3-6 days after symptoms onset, while IgG at about 10-18 days. Interestingly, individuals with no symptoms have been reported to become serologic positive; which highlights that productive infection with SARS-CoV-2 might pass unnoticed and be a risk for transmission. As the virus mutates, continuous research on COVID-19 serology is essential. Viral proteins N and S (intact or the S1 and S2 fragments) are currently the most prominent in eliciting a host antibody response and led over 30 companies to release a myriad of serologic tests for COVID-19.
METHODS AND TASKS:

1. Launch a biobank of sera and/or plasma of individuals with past and ongoing SARS-CoV-2 infection (confirmed by RT-qPCR) varying by sex, age, presence or absence of symptoms, comorbidities, severity and disease course. This will originate from the 3 major hospitals of the Minho Region (Braga, Guimarães and Viana do Castelo), and from the Community Health Centers ACES-Braga I). Ethical approval was already obtained from Braga Hospital; collection is ongoing;
2. Test 8 of the most promising commercially available kits (based on clinical evidence), on 350 samples from the biobank (at the time of diagnosis by RT-qPCR, 1-2 weeks afterwards and when considered cured);
3. Create and feed a freely available online platform to aggregate information relevant for COVID-19 serology: i) kinetics of the anti-SARS-CoV-2 Ig (IgA, IgG, IgM); ii) Bioinformatic detection of antigenic variation in the dataset; iii) Supporting clinical evidence.

EXPECTED OUTCOMES:

1. Validate a serologic test for IMMEDIATE use in the current CoVID-19 outbreak;
2. Identify key features of serologic response of individuals at various disease stages, with potential to infer for disease progression/outcome;
3. Create a biobank to be used to evaluate improved versions and new tests; and
4. Create serodiagnostic online platform.

R4COVID.1.109/2020

Development of a fast and cheap SARS-CoV-2 diagnostic tool based on CRISPR-Cas13a

PRINCIPAL INVESTIGATOR	Luísa Pereira
LEADING INSTITUTION	IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto
FUNDING	€ 30 000

As the COVID-19 pandemics continues to affect the globe, it is urgent to invest in the development of fast and cheap diagnostic tools that allow to establish efficient track and trace strategies. We are implementing in our lab the revolutionary CRISPR-Cas13a technique specifically designed to detect two SARS-CoV-2 genes and one human gene. The procedure includes: reverse transcription of the viral RNA, recombinase polymerase amplification, T7 transcription to RNA, Cas13a activation and collateral nuclease action detection through fluorescence. All these reactions occur in the same well in a multi-sample plate placed in a Synergy 2 instrument, at 37ºC, allowing to detect the virus after 45 minutes.
So far, we were successful in designing specific primers and RNA guides, and establishing all steps individually. We are now testing their inclusion in a single tube, and still need to test the direct use of the inactivated virus instead of the extracted viral RNA (as this saves the extraction procedure and time). Along the project, we confirmed that dependency on the only company that sells the recombinase polymerase amplification kit is extremely limiting. So we also tested to produce this kit in our lab, by acquiring the individual proteins, and were successful in doing so. We will probably now produce also these enzymes in our lab, and as we already produce Cas13a, we would become fully independent from the exterior for all enzymes.
This technique has the important advantages of not needing complex instruments (just a fluorescence reader) and specialised technicians (as plates can be provided with all needed reagents, and technician only need to pipet the inactivated virus).

IPP4AVSS R4COVID.1.112/2020

Apoio ao diagnóstico molecular SARS-CoV-2 no ACES Tâmega II Vale do Sousa Sul

PRINCIPAL INVESTIGATOR	Ruben Miguel Pereira Fernandes
LEADING INSTITUTION	Instituto Politécnico do Porto
FUNDING	€ 30 000

O ACES Vale do Sousa Sul serve uma população de mais 170 000 utentes e mais de 210 000 unidades ponderadas. Implementou ADC para onde são derivados com sintomatologia respiratória ou suspeita de COVID.
Metodologia: Diagnóstico molecular mediante qRT-PCR, de acordo com as normas OMS e com a aprovação do CDC (CDC-006-00019, versão 03). Após a prescrição do MGF, serão feitas colheitas com zaragatoa na orofaringe / nasofaringe. No teste, irão ser utilizados controlos positivos do vírus e controlo interno da RNAse P humuna (RP). Quando estiver complemente recomendado pela DGS pretende-se utilizar o método Português (IMM), com os reagentes produzidos em Portugal para fazer face à potencial quebra de stocks dos fornecedores estrangeiros. Neste momento, a equipa possui em stock, kits suficientes para 2500 reações de extração de RNA e conversão para cDNA, e kits para a amplificação por RT-PCR de outros 2500 rxs. Pelo que, esses reagentes não irão faltar proximamente. Falta adquirir os primers e sondas para o SARS-CoV-2, materiais de colheita, EPIs, etc.
Impacto na população: O IPP possui uma unidade de Saúde Móvel que pode ser utilizada para a colheita de amostras.
População a incluir: Neste programa de rastreio serão incluídos todos os seguintes os elementos da população que não cumpram os critérios da norma da 004/2020 DGS: a) profissionais de saúde; b) os utentes e profissionais de lares de terceira idade na área de influência do AceS; c) os cuidadores de doentes coronavírus positivo; d) todos os cidadãos, forças de segurança que, por critério e recomendação escrita e validada pelo seu médico de família se considere útil incluir neste rastreio.
População a excluir: Excluem-se deste rastreio todos aqueles que se enquadrem na norma 004/2020 da DGS para realização de teste, devendo, neste caso dirigir-se aos locais previstos para esse efeito, em funcionamento nas unidades do SNS, nomeadamente ADC-Comunidade, no âmbito dos cuidados de Saúde Primários e ADC-SU, no âmbito dos serviços de urgência dos hospitais.

NAM4Covid19 R4COVID.1.128/2020

Nucleic acid mimic lateral flow assay (NAM-LFA) for the detection of COVID-19

PRINCIPAL INVESTIGATOR	Carina Manuela Fernandes Almeida
LEADING INSTITUTION	Instituto Nacional de Investigação Agrária e Veterinária, I.P.
FUNDING	€ 30 000

The current COVID-19 pandemic has emphasized the need for rapid diagnostic devices. The early diagnosis of infected people with SARS-CoV-2 is crucial to prevent the spread of the virus and provide the best medical treatment at the initial phase of the disease avoiding further social and health complications. With increasingly higher suspected daily cases, the health system is not always able to respond effectively in a timely manner. The official protocol for SARS-CoV-2 detection requires a complex and time-consuming methodology, as well as, specialized technicians and equipment, which are expensive. Consequently, it is not available on most hospitals or other first line health care institutions, delaying the identification of positive cases (the analysis of a suspected case takes at least 24 hours).

NAM4Covid19 aims to develop a simple, fast, and economical point-of-care diagnostic kit for the detection of SARS-CoV-2 that can be used by anyone without the need for specialized equipment. This kit is based on the combination of two methods called lateral nucleic acid flow (LFA) and amplification by recombinase polymerase (RPA). NAM4Covid19 will detect the presence of specific viral genes, providing results in less than 1 hour. It will use a device similar to a pregnancy test as the detection device. The development of this point-of-care test will allow not only to support the health system in the current fight against COVID-19 pandemic, but also in an eventual "second wave" through the rapid identification of infected people without the need for specialized technicians and equipment. NAM4Covid19 can be used in hospitals, health centres and other facilities with high risk of infections, such as airports, schools, day-care centres, as a quick and simple detection test.

NAM4Covid19 development is the result of the combined efforts of 3 teams: Instituto Nacional de Investigação Agrária e Veterinária, LEPABE - Faculdade de Engenharia Universidade do Porto and Instituto Nacional de Saúde Doutor Ricardo Jorge. Based on the knowledge of these research teams, NAM4Covd19 will allow the detection of suspected cases in a simple and fast way, reducing the pressure on the national health system and giving autonomy to other institutions to an early diagnosis of COVID-19.

R4COVID.1.162/2020

Test, Test, Test: Diagnostic of COVID-19

PRINCIPAL INVESTIGATOR	Vanessa Zuzarte Luis
LEADING INSTITUTION	IMM-Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 30 000

When the SARS-CoV-2 pandemic reached Portugal, the available monitoring solutions were clearly insufficient. The limited capacity to test for SARS-CoV-2 incidence in the Portuguese population would not allow for the accurate determination of the infection rate, neither the geographic mapping of infection, both necessary to define effective measures to control the pandemic.

The SARS-CoV-2 testing capacity depends, in part, on the availability of specific reagents, that were in shortage. To surpass this obstacle iMM established a testing protocol using national reagents. The protocol was made available to the entire scientific community allowing for the rapid upscaling of the country's testing capacity. The "Test, Test, Test" project was developed in 3 phases:

1. Turning a Research Institute into a Test Factory: The research laboratories at IMM were converted into a safe and efficient molecular diagnostic laboratory. The safety measures and protection equipment were defined and adopted; the protocol for SARS-CoV-2 detection was rigorously designed and tested. In only two weeks samples, mainly from risk groups, were arriving at iMM to enter the analysis pipeline ensured by a team of 120 volunteers - iMM researchers from all career levels.
2. Molecular Diagnostic kit made in Portugal: The iMM team successfully adapted reagents from the Portuguese company NZYTech to SARS-CoV-2 dignostic: RNA isolation kit and RT-PCR mix. The first step consisted in testing and optimizing the reagents using patient samples in collaboration with the HSM. The protocol was then validated by the national reference laboratory INSA. The iMM team also worked with NZYTech to test new reagent formulations specifically developed for SARS-CoV-2 testing.
3. From iMM to the entire country: Despite the great achievement of optimizing a protocol and setting up a diagnostic lab in 2 weeks, testing at iMM would not be enough to cover the country's needs. iMM wrote and made available a detailed SOP, encompassing all the lab adaptations, safety measures, protocols and procedures put in place so that the model could be replicated by any Institute or University willing to join the fight against COVID-19.

This endeavour, helped the national health authorities to obtain reliable data on the status of infection at a national levels supporting the timely implementation of the protective measures.

R4COVID.1.172/2020

Developing a portable SERS chip for point-of-care analysis of virus-specific nucleic acid

PRINCIPAL INVESTIGATOR	Lei Wu
LEADING INSTITUTION	Laboratório Ibérico Internacional de Nanotecnologias
FUNDING	€ 30 000

Rapid COVID-19 diagnosis at early stage is important to the prevention of disease spreading. To this aim, researchers from Medical Devices Group at INL is working on a project to develop a chip-based medical device for fast screening of SARS-CoV-2 virus-specific nucleic acid, which not only improves the efficiency of detection, but also simplifies the detection for point-of care (POC) diagnosis.
Aimed at increasing the efficiency of COVID-19 diagnosis, this project is expect to reduce the detection time from 1.5-2 hours to 30-40 minutes using the ultrasensitive spectroscopic technique, i.e. surface enhanced Raman spectroscopy (SERS). The SERS sensor is integrated into a microfluidic platform, which can provide a new tool for POC COVID-19 disease diagnosis.
The basic principle of this sensor is to design a hairpin molecular probe to recognize the target sequence and employ SERS technique for detection. The hybridization of the hairpin probe with target nucleic acid would induce the change in SERS intensity. A portable Raman spectrometer is used for in-situ signal readout to facilitate POC diagnosis.
3 viral RNA sequences, which have been commonly used for COVID-19 diagnosis sequences have been selected as the detection targets. Currently, the molecular probes have been designed and integrated into a SERS chip for simultaneous identification of these RNAs. In the latest tests, the SERS chip was capable to differentiate the synthetic target RNA and the nonspecific control. Quantitative detection has also been achieved through Raman measurements. In the next stage, the researchers will forward to test the patient samples from IPO-Porto to validate the performance of this biochip for real sample analysis.

R4COVID.1.226/2020

CoVTec em Saliva - Diagnóstico da COVID-19 em saliva

PRINCIPAL INVESTIGATOR	Nuno Ricardo das Neves Rosa
LEADING INSTITUTION	Universidade Católica Portuguesa
FUNDING	€ 30 000

COVID-19: how can saliva help control the pandemic?
After a few months under a pandemic, what do people want the most? To return to their jobs, their families, their routines. Basically, everyone wants to recover the lives they had before the pandemic, without social distancing, masks, and fear of social contact. So why can´t we do just that? What is still needed for this to happen? SalivaTec from the Universidade Católica Portuguesa is using saliva to develop an easy, fast and accurate SARS-CoV-2 test, to help us to return to "normal" daily life.
Testing capacity is vital to fight the COVID-19 pandemic and it is widely accepted that a return to the new "normal" depends on our ability to contain the spread of the virus and rapidly identify infected and/or immune individuals. A fast, low cost, safe and reliable test, to detect people carrying the virus, as well as those which have been exposed and carry antibodies, is the "holy grail" which could rid us of generalized confinement.
The tests currently used are largely based on oropharynx swabs (for viral detection) and blood (for antibody presence and titer). The collection of swabs and blood is invasive (even painful) and must be done in specific settings and by trained nurses or health technicians, limiting a wider use of the tests. Saliva accumulates SARS-CoV-2 (the virus responsible for COVID-19) since salivary glands are one of the first organs to be infected. This facilitates the identification of people at the beginning of the infection. Furthermore, the use of a single sample for both viral and antibody detection is an advantage. Last, but not least, saliva collection is non-invasive and can be self-administered, potentially expanding test application.
CoVTec in Saliva - Diagnosis of COVID-19 in saliva, a project led by the Universidade Católica Portuguesa (CIIS-SalivaTec) in partnership with the Tondela Viseu Hospital Centre and the Polytechnic Institute of Viseu, aims to establish protocols for the diagnosis of COVID-19 in saliva and assessment of the immune response to SARS-CoV-2. The final goal is to have information to produce a single test for viral and antibody detection from single saliva sample.

R4COVID.1.250/2020

Deep Learning in the diagnosis and therapeutic monitoring of COVID-19 patients

PRINCIPAL INVESTIGATOR	Fernando Manuel Ferreira Lobo Pereira
LEADING INSTITUTION	Faculdade de Economia da Universidade do Porto
FUNDING	€ 30 000

We present a support system for clinical diagnosis, using the Deep Learning (DL) framework to create computational models, based on convolutional neural networks architectures (ResNet, Xception , etc.), for classification of chest radiographic images. Optimize the severity assessment process determined by chest X-ray. In this context, it is possible to highlight the affected zones, through the deep autoencoders and/or the using grap-CAM algorithm on the classifier, which are the standard for anomaly detection. We use an online open data set of X-ray images. The developed APP for the user interface is also described. In the therapeutic field we are developing a process of temporal analysis of biometric data collected from patients to formulate a model to estimate the evolution of the disease in a particular patient. This analysis will be done with models based on recurrent neural networks oriented to the study of multivariable time series: RNN, LSTM with specialized attention mechanisms.
For the process of marking the affected areas in the image i.e. anomaly detection/annotation, we chose a methodology based on the grad-CAM algorithm. This algorithm aims to create visual explanations from deep networks via gradient-based localization.
With this DL based models we develop a web based application that will be available online.

R4COVID.1.269/2020

Validação expedita e Fabrico em larga escala de um dispositivo de sopro para colheita com inativação de amostras para deteção do SARS-CoV-2

PRINCIPAL INVESTIGATOR	Rui Jorge Gonçalves Pereira Nobre
LEADING INSTITUTION	Universidade de Coimbra
FUNDING	€ 30 000

In the fight against COVID-19, testing is a critical tool. However, Portugal has found as a limiting factor the availability of swabs, whose supply does not reach the desired quantities and/or delivery times. On the other hand, the use of traditional swabs does not allow self-collection or the inactivation of viral activity; therefore, the samples need to be collected by health professionals and have a high infectious potential, putting all stakeholders at risk in the process of the screening. This project aims to carry out the validation and large-scale manufacture of an innovative tool to combat the pandemic COVID-19. It is a blowing device that allows both self-collection and inactivation of biological samples for SARS-CoV-2 testing. For this purpose, a device, previously developed by the research team, will be used to collect material from the respiratory tract. In this, the exhaled aerosol material is directed to a filter, which is composed by nucleic acid preserving and microbiological inactivation agents.
As part of the project, a comparative SARS-CoV-2 testing study will be initially carried out in at least 100 cases that perform, in parallel, swab collection (traditional method) and self-collection using the innovative breath test. After its validation and optimization, it will be produced on a large scale.
In the end, the development, validation and manufacture of a blowing device is expected to allow the self-collection of exhaled air for subsequent detection of SARS-CoV-2. The use of it, as a method of self-collection, will simultaneously reduce the risk of contagion and eliminate the need of health professionals for collection. This project will produce 10,000 kits, which will be available to the National Health System (SNS), creating a paradigm shift in mass testing for SARS-CoV-2.

R4COVID.1.283/2020

Ultra-sensitive, specific, scalable, fast and cheap: a colorimetric-assisted single-tube nested conventional PCR to detect the SARS-CoV-2 RNA in nasopharyngeal swabs

PRINCIPAL INVESTIGATOR	Vasco M. Barreto
LEADING INSTITUTION	Universidade Nova de Lisboa - Faculdade de Ciências Médicas
FUNDING	€ 30 000

Most protocols for SARS-CoV-2 RNA detection involve RNA extraction, cDNA synthesis, and qPCR. They take 4-5 hours and require extensive manipulation in BSL2/3 rooms. Alternatives relying on trendy technologies such as CRISPR and LAMP have a sensitivity similar to or worse than the current method, which has an alarming up to 30% frequency of false negatives. Thus, compared to the currently widespread method, a new one should be significantly more sensitive (without compromising specificity), require fewer manipulations, and be based on generic and cheaper reagents, as well as equipment that is more basic. We have designed a protocol that explores long-established procedures, namely the making of viral cDNA without RNA extraction, nested-PCR of the single-tube type, and colorimetric methods for the detection of specific amplicons such as gold nanoparticles and DNAzymes. We emphasize a number of clear advantages: 1) replacing the isolation of RNA using columns by a heating step to release RNA into the solution will simultaneously inactivate the virus at the very first step, simplifying the downstream manipulations; 2) nested PCR remains the most sensitive nucleic acid detection technique and its single-tube variant prevents sample contamination; 3) an optimized combination of colorimetric methods should allow us to multiplex the amplification of a human cDNA and two regions of viral cDNA, thus avoiding the laborious analysis on a gel and achieving in a single tube the same degree of control and redundancy that in some versions of the current protocol require three tubes. By removing the bottlenecks that limit testing, namely RNA isolation and the need for a rare qPCR machine, the method would scale up the installed capacity of the Portuguese research units by at least a factor of six, while lowering the cost price of a single test to about 25% of the cost estimated by the IMM (FMUL) for the current method. To achieve this goal in a time-effective way, the different variations we plan to introduce will be independently implemented by experienced researchers. Then the optimized procedures will be assembled in a workflow that should take under 4 hours to process 90 samples (and six control reactions).

CAIRUS R4COVID.1.156/2020

COVID-19 Artificial Intelligence-based Risk Unified Stratification tool for clinical management

PRINCIPAL INVESTIGATOR	João Tiago Guimarães
LEADING INSTITUTION	Faculdade de Medicina da Universidade do Porto
FUNDING	€ 29 940

COVID-19 may cause mild symptoms or be asymptomatic for days and then progress quickly to severe disease requiring ventilation aid. Additionally, there are patients, which recover in a fast way, while others in a slow manner without a clear explanation of the biological mechanisms that are involved. While prediction of hospital stay/discharge is uncertain, it is vital to manage the demand of limited resources. Enabling the discharge of low-risk patients earlier could reduce the strain on healthcare systems. We propose a low-cost, fast stratification/clinical outcome prediction tool based on blood serum analysis, using a validated photonics Artificial Intelligence (AI) platform.
Within the framework of this project, we are developing a tool capable of predicting the evolution of COVID-19 in a patient-specific basis. This platform is based on an "optical fingerprint" that results from the interaction of near-infrared light with several bionanostructures found dysregulated in the plasma/serum that are associated with the inflammatory response (C-reactive protein, albumin, procalcitonin, ferritin, among others). By comparing the fingerprint with the library of fingerprints previously stored in the data set, it is possible to identify disease fingerprints associated with specific phenotypes/biochemical profiles, in 20 seconds, using a previously validated laser photonics approach – the iLoF (intelligent Lab on Fiber technology). This project is firstly addressed to Centro Hospitalar Universitário de S. João, but in further stages other SNS structures taking care of COVID-19 patients may also benefit.
Expected impact of the developed tool include: improvement in management of hospitalization and intensive care unit occupation by stratifying patients based on risk of COVID-19 associated complications – e.g., prediction of disease evolution based on "mild" and "severe" outputs; and the development of a rapid and low-cost way to routinely check risk patients (surveillance) for the potential to have an accelerated clinical disease progression. CAIRUS platform was able to stratify healthy and infected patients with a sensitivity and specificity of 95% and stratify the ones that evolved for the ICU ("severe state") from the ones who remained hospitalized or with mild symptoms ("mild/light symptoms") with a sensitivity and specificity of 75-86%.

R4COVID.1.208/2020

Develop fast, highly accurate, low-cost PCR-based protocol to test SARS-CoV-2

PRINCIPAL INVESTIGATOR	Maria Isabel Mendes Veiga
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 29 932

The COVID-19 pandemic caused an unprecedented need for rapid and reliable diagnostic of the disease to best guide clinical practice and to contain the risk of infection spreading in the community.
The gold standard diagnostic test consists of detecting SARS-CoV-2 viral nucleic acid (RNA) in nasopharyngeal swab sample. The test consists of two steps, first extraction of the nucleic acids contained in the collected patient sample followed by detection of specific SARS-CoV-2 nucleic acids through a technique based on reverse transcription polymerase chain reaction (RT-PCR). This molecular diagnostic test is presently based on the use of commercial kits (of international origin) and the shortage of these kits, well noticed since the beginning of the pandemic, has resulted in severe bottleneck in testing capacity, contributing for a long delay in accurate COVID-19 diagnosis.
To improve existing molecular methods and circumvent supply chain issues, we are developing alternative strategies to increase the nucleic acid yield present in the swab collected samples and design a new RT-PCR reaction assay, to increase sensitivity, specificity and throughput for SARS-CoV-2 detection.
We have tested and optimized several nucleic acid extraction methods with preliminary results showing yields comparable with most of the commercial extraction kits, revealing an effective alternative to the lack of kits. We are also working on a much simpler, faster and cheaper extraction protocol, pointing for a RT-PCR assay directly from patients' swab, as a future direction. Moreover, taking in consideration the observed evolution of SARS-CoV-2 genomes and its interference with efficient detection through RT-PCR assay, we are re-designing the method to clearly distinguish from other coronaviruses even at low viral infection. To increase throughput, we are further trying to multiplex the assay as it will decrease sample handling and costs.
By the end of this project, we aim to deliver an alternative molecular diagnostic protocol, independent from commercial kits, faster than existing options and with less inconclusive results by accounting for the fast-viral genetic evolution. Results will be vastly disseminated to the public.

R4COVID.1.126/2020

Development of a new assay do detect SARS-CoV-2 directly from clinical samples

PRINCIPAL INVESTIGATOR	Clévio David Rodrigues Nóbrega
LEADING INSTITUTION	Universidade do Algarve
FUNDING	€ 29 720

The golden standard for SARS-CoV-2 detection is currently performed by a technique named RT-qPCR, involving a first step of purification of the genetic material of the virus and after the RT-qPCR itself to detect the presence (or not) of the virus. This results in a time-consuming procedure, with high cost per sample. Considering the need for massive testing and rapid results, with this project we aim to develop a direct detection of SARS-CoV-2 from clinical samples using an express RT-qPCR (Xpress-qPCR), without the genetic material extraction step. This will significantly reduce both time and cost of current assays and will minimize the risk of human error and accidental exposure associated with viral genetic material purification.
From the general proposed goal, several others were outlined during the project development: i) to optimize a collection medium that inactivates the virus and allows a direct detection through RT-qPCR with increased security levels, ii) to analyze the sensitivity of our detection process using different collection methods of the samples (e.g. saliva), and iii) to compare the sensitivity of our process with the gold standard protocol for SARS-CoV-2 detection.
Altogether, we expect that this project will allow the development of a new process for SARS-CoV-2 detection that will be easier, cheaper, quicker, and safer.

R4COVID.1.231/2020

Generating SARS-CoV-2 seroconversion assay

PRINCIPAL INVESTIGATOR	Marc Veldhoen
LEADING INSTITUTION	IMM-Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 29 692

Nucleic acid-based tests detect acute infections. However, their use is limited to those actively infected. Serological assays are needed and the capacity for their large-scale use created. These assays detect the immune response against SARS-CoV-2, resulting in the production of antibodies. The determination of seroconversion allows the accurate assessment of infection and fatality rates, epidemiologic flow and is key in the definition of the inoculation strategy of a future vaccine.
Importantly, these tests characterize the immune response to the virus in a detailed qualitative and quantitative manner, allow longitudinal studies, monitor the continued immune protection and accurately identify those already exposed to the virus. The latter may form a buffer between the virus and the vulnerable, and can safely return to front line services (e.g. health professionals). Although commercial kits are developed, their validation and distribution were limited and in insufficient numbers with high costs. Furthermore, the in-house capacity to setup rapidly these assays and to validate these with a detailed SOP will ensure national capability building and readiness for any future pandemics.
Using known negative sera (iMM Biobank; 180 samples) and positive sera (HSM patients >250 samples), we robustly tested for reproducibility, accuracy and sensitivity. We have optimised and run serum tests for the Hospital Santa Maria (>250 samples), IPST (>400 donors) and the university of Lisbon (>2570 staff screened), thereby improving and expanding national testing capability. We will contribute to the national screening efforts in September 2020. The assays have been use to validate iMM Biobank samples, generating a valuable resource for future studies, and to help clinicians for accurate assessment of their patients. In addition, our assay has been used in a clinical case study (under review), clinical special cohort-of-interest studies (in progress) and the results of the screening, especially the longitudinal follow up, is being prepared for publication.

CXR_AI4Covid-19 R4COVID.1.071/2020

Chest Radiography-based AI for Supporting Clinical Decision on COVID-19

PRINCIPAL INVESTIGATOR	Aurélio Joaquim de Castro Campilho
LEADING INSTITUTION	INESC TEC - Instituto de Engenharia de Sistemas e Computadores, Tecnologia e Ciência
FUNDING	€ 29 379

Chest radiography (CXR) can play an important role in the decision-making process for COVID-19 detection and management, given the low sensitivity (60-70%) and significant turnaround time of the reference standard method in COVID-19 diagnosis, the Reverse Transcription Polymerase Chain Reaction (RT-PCR).
As the visual analysis of CXR is experience-dependent and many CXRs are read by clinicians with limited experience, Artificial Intelligence (AI) can help identifying images with features indicative of the disease, thus acting as a second opinion to support the clinician in the triage of COVID-19 patients. This can contribute to a better confidence in clinical decisions, and help in the reduction of false negatives, a major drawback of the relatively low-sensitivity of RT-PCR.
The project CXR-AI4COVID-19 aims at developing a computer-aided diagnosis system to identify COVID-19 radiological features. The development of these algorithms is headed by INESC TEC, in cooperation with ARSN. In the first phase of the project, CXRs from public datasets were collected, including COVID-19 positive patients as well as normal subjects and other pathological cases. Each CXR was labelled independently by two radiologists as “normal”, “not normal”, “COVID-19”, “undetermined” or “compromised”, using a tool developed by INESC TEC. Using the collected data and annotations, an AI algorithm was developed, based on state-of-the-art methods, which informs the clinician whether the CXR contains features compatible with COVID-19, with another pathology or is a normal case. An explanation of the decision is also provided through indication of the regions of the CXR which led to the decision, together with the probability associated with each one of the three classes.
The results obtained so far are promising, achieving performances comparable to that of experienced radiologists. The AI algorithm will be further evaluated on data provided by Centro Hospitalar Vila Nova de Gaia e Espinho (CHVNGE). The developed system will be deployed at CHVNGE and other health units for both prospective and retrospective analysis of CXR data.

R4COVID.1.165/2020

LAMP-Light in the diagnosis of COVID-19

PRINCIPAL INVESTIGATOR	Alejandro Garrido-Maestu
LEADING INSTITUTION	Laboratório Ibérico Internacional de Nanotecnologias
FUNDING	€ 29 268

COVID-19 is a viral disease that rapidly spread worldwide, and at present has infected more than 12 million people. The standard to detect this virus relies on molecular technique which first converts the RNA of the virus into DNA, and then performs its amplification to detect it through sequential cycles of temperature, this technique is called RT-qPCR. Even though it is highly sensitive and reliable, it also presents some drawbacks such as the need for expensive equipment and highly trained personnel, additionally, the global need for reagents and kits for RT-qPCR tests has caused supply problems in certain countries. In this project we will develop a SARS-CoV-2 detection methodology based on RT-LAMP. This technique can be performed at a single temperature, thus it does not need specialized equipment (can even be run in a hot water bath), it has a fast turnaround time, and detection can be performed by naked-eye by simple color change or appearance of turbidity in positive samples; all this also allows a reduction of the cost of the assays, and the investment needed in infrastructure to perform this method. Thus this novel method has great potential to enhance diagnostics throughput, reduce time of analysis, and improve implementation of appropriate isolation, and control measures of diseased people.

R4COVID.1.149/2020

Track and trace COVID-19

PRINCIPAL INVESTIGATOR	Carla Patrícia Alves Freire Madeira da Cruz
LEADING INSTITUTION	Universidade da Beira Interior
FUNDING	€ 28 700

"Track and Trace COVID-19" team is multidisciplinary and composed of researchers from CICS-UBI, clinicians and pathologists from hospitals in Beira Interior, municipalities of Covilhã and Fundão and ACeS Cova da Beira agency. As the director of WHO said, "we cannot fight a fire blindfolded", "Track and Trace COVID-19" intends to implement a new, faster and lower-cost diagnostic method to detect SARS-CoV-2. This method is based on the detection and quantification of guanine-rich sequences in the SARS-CoV-2 viral RNA, by hybridization with sensors that will fluoresce in the presence of the virus's RNA and will be quantified in a fluorescence plate reader. SARS-CoV-2 genome has guanine-rich sequences that can form G-quadruplex structures, which are more stable and can be used as sensors. Recently, C. Cruz research team identified two G4-specific sequences of SARS-CoV-2 that are not found in other coronaviruses and influenza virus in the Nsp2 and 3 ORF1ab and spike glycoprotein regions of the virus. The sensors only produce fluorescence in the presence of viral RNA.
The proposed diagnostic test will identify COVID-19 "outbreaks" who return to workplaces, people living in institutions (elderly, detainees), who are more vulnerable to infection and, isolating them, either in a health unit or at home, according to the symptoms presented. It is necessary to do well the aftermath of this "fire" to avoid a second wave of infection that will be unpredictable at this moment and if it will exist as it will be. The massive increase in the national testing and tracking program is essential to control the unpredictability of SARS-CoV-2. "Track and Trace COVID-19" is ongoing, the sensors have already been produced and optimized in a pull of RNA sequences of the virus to check specificity and COVID-19 samples versus negative controls are being collected from Beira Interior health institutions to be tested.

R4COVID.1.029/2020

Implementation of rapid endpoint PCR systems for SARS-CoV-2 detection in conventional molecular biology laboratories

PRINCIPAL INVESTIGATOR	Filipe Adão Macedo Pereira
LEADING INSTITUTION	Universidade de Coimbra
FUNDING	€ 17 500

The World Health Organization (WHO) has called on countries to 'test, test, test' for COVID-19. The ability to detect the SARS-CoV-2 in a pandemic is crucial for screening of symptomatic and asymptomatic carriers and for the success of quarantine efforts. Laboratories face two major challenges when doing SARS-CoV-2 diagnosis. First, the magnitude of tests necessary and the global constraints in the supply of reagents has bring diagnostic laboratories to their limits and some laboratories lack the necessary equipment to perform conventional testing. Second, commercial kits may produce false negative results due to new mutations on circulating SARS-CoV-2 lineages. RNA viruses are known for their high genetic diversity, which poses a major challenge for the design of efficient testing assays.
Our project aims to develop a rapid and reliable endpoint PCR protocol for SARS-CoV-2 testing to be used in laboratories without qPCR systems. The project will increase the testing capacity of national laboratories without the need to purchase new equipment. The new SARS-CoV-2 detection kit will detect different lineages of the virus avoiding false negative results. Moreover, we are also developing a free database named CoV2ID (http://covid.portugene.com/) to facilitate the evaluation of molecular methods for detection of SARS-CoV-2 and treatment of COVID-19. The database evaluates all available diagnostic and therapeutic protocols according to the virus genetic diversity, allowing the detection of mutations that may lead to false negative results. Updated datasets are used to constantly verify the theoretical efficiency of available methods. Researchers can find the best oligonucleotides to design their own protocols. Detailed information on available protocols are also available to help laboratories implementing SARS-CoV-2 testing and COVID-19 treatment.
Overall, this project will contribute to increase the testing capacity of Portuguese laboratories and also to reduce diagnostic errors of available methods due to false negatives. A better and more widespread SARS-CoV-2 testing allows the identification and consequently the isolation of more infected individuals, reducing the pandemic progression.

R4COVID.1.101/2020

Impact of chest ultrasound in SARS-CoV-2 pneumonia patients

PRINCIPAL INVESTIGATOR	João Leote
LEADING INSTITUTION	Hospital Garcia de Orta EPE
FUNDING	€ 17 024

Pandemic virus from the corona family (CoV 2) is responsible for the severe acute respiratory syndrome (SARS) in humans and spreads rapidly by droplets. Patients suffering from SARS-CoV-2 pneumonia present a variety of severity degrees. After initial symptoms, development occurs rapidly and chest X-ray remains the standard option to diagnose pulmonary involvement or improvement during hospital stance. However, due to high person to person spreading, personal protective equipment is used in each patient contact. Additional to ionization energy, the clinical value of serial chest X-rays still remains to be studied.
Our group, prospectively recruited patients with SARS-CoV-2 pneumonia admitted either to the Intensive Care Unit or to conventional stance. They performed serial chest X-rays, inflammatory blood markers, and chest ultrasound (US). Our aim was to evaluate if chest US in comparison with chest X-ray, is able to influence clinical decision-making by showing pulmonary disease progression. From June to 24th July, 34 patients were recruited and preliminary results show that chest US is able to show diffuse and characteristic pulmonary findings. In addition, the chest US was made by patient medical doctor avoiding the use of additional personal protective equipment and further staff exposition to SARS-CoV-2.
At this moment, a high number of patients are needed to define chest US patterns compatible with pneumonia resolution of improvement. Preliminary comparisons between chest X-ray and US results remain to be studied. However, pregnant patients with SARS-CoV-2 pneumonia may already be evaluated using our preliminary US findings.

SARSChip R4COVID.2.414/2020

On-chip testing of SARS-CoV-2

PRINCIPAL INVESTIGATOR	Verónica Cristina Baião Martins Romão
LEADING INSTITUTION	INESC Microsistemas e Nanotecnologias
FUNDING	€ 40 000

In a viral pandemic panorama, the ability to test the population is key to control the disease. However, the tools and methods available often present limitations, either at the level of performance (sensitivity, specificity, quantifiability) or operationally (require dedicated labs). On one hand, very specific and sensitive molecular tests demand complex sample preparation procedures and expensive equipment operated by experts. On the other hand, simple and rapid serologic tests often present poor performance. Moreover, molecular tests (PCR-based) are only effective in the initial period of the infection, while serologic tests are only useful on a later stage, when anti-virus antibodies are produced. In this context, the combination of tests in a practical diagnostic tool is the solution to widen testing capacity while increasing diagnostic confidence.
The SARSChip project, coordinated by INESC – Microsystems and Nanotechnologies, proposes the applicability of an easy to use diagnostic tool to facilitate the screening of COVID-19 patients. The proposed technology is based on a hand-held electronic reader and disposable biochip cartridges. The biochips, based on proprietary technology, are composed of multiple magnetic sensors able to perform in parallel the detection of viral RNA (molecular test) and quantitative antibody analysis (serologic test).
The proposed technology has been validated for clinical applications. Namely, in the detection of viral genes (Zika, Dengue and Chikungunya virus), bacterial genes (milk-borne pathogens), and serum biomarkers in stroke patients.
The aim of the project is to transform the viral testing concept by combining in a sensible solution the latest advances in serologic and molecular tests. The offered tool will speed up patient screening by enabling the decentralization of COVID-19 testing, freeing up healthcare personnel and lab resources while allowing auxiliary staff to run the tests and read out results on site.
The project is being developed in collaboration with STABVIDA, UTAD (Department of Genetics and Biotechnology), INESC ID, INL and the clinical pathology services of Centro Hospitalar de Trás os Montes e Alto Douro (CHTMAD) and Centro Hospitalar Cova da Beira (CHUCB).

R4COVID.2.429/2020

Genome wide association study to evaluate human genetic susceptibility to SARS-CoV-2 infection: towards a polygenic risk score

PRINCIPAL INVESTIGATOR	Luísa Pereira
LEADING INSTITUTION	IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto
FUNDING	€ 40 000

We will conduct a genome wide association study (GWAS) in 1000 cases X 1000 controls in North Portuguese, selected from samples molecularly tested for SARS-CoV-2 infection, based on the characterization of an array containing 1 million variants. This study aims at identifying the genetic markers significantly associated with susceptibility/resistance to SARS-CoV-2 infection in the Portuguese population (most will be shared with Eurasian ancestry, but founder effects are important). First, this project will be an opportunity for local GPs to contact their patients and gather more precise information about the dynamics of SARS-CoV-2 infection in North Portugal. This part is essential and worth per se but is substantially empowered by the ascertainment of the genetic susceptibility/resistance to COVID-19 in a representative pool of this community. The selection of cases and controls based on diagnosis and close GP-patient contact increases the GWAS statistical power. In fact, the inclusion of cohabiting non-relatives (like couples), one symptomatic and positive and the other asymptomatic and negative, increases the probability of finding the associated variants.
The Identified markers will contribute to the knowledge of the biology of SARS-CoV-2 infection and guide drug repurposing. But we also want to implement a predictor tool made of an array for genotyping ~20 associated markers and bioinformatics polygenic risk score for COVID-19. The capacity to identify individuals at unusually high or low risk of infection is essential for a proper management of the disease in the future.
Since the beginning of the project in the 1st of July 2020, we adapted the protocol of preparation of samples for the array in order to use directly the remains of the extracted sample where the diagnosis was made. This saves a huge amount of time. We are now selecting and contacting the individuals to include in the study, and gathering socio, epidemiological and COVID-19 associated clinical data.

R4COVID.2.480/2020

CRISPR technology against the COVID-19 pandemic. The detector of SARS-CoV-2

PRINCIPAL INVESTIGATOR	Alejandro Garrido-Maestu
LEADING INSTITUTION	Laboratório Ibérico Internacional de Nanotecnologias
FUNDING	€ 40 000

COVID-19 is a viral disease that rapidly spread worldwide, and at present has infected more than 12 million people. The standard to detect this virus relies on molecular technique which first converts the RNA of the virus into DNA, and then performs its amplification to detect it through sequential cycles of temperature, this technique is called RT-qPCR. Even though it is highly sensitive and reliable, it also presents some drawbacks such as the need for expensive equipment and highly trained personnel and long turnaround time, additionally, the global need for reagents and kits for RT-qPCR tests has caused supply problems in certain countries. Thus, there is a need for methods equally sensitive and specific. DETECTR technology, takes advantage of the most recent developments in molecular biology by using CRISPR sequences, commonly used for genome editing, to very specifically target the virus, which is later detected through the activity of the Cas12a protein. This CRISPR-Cas system is combined with isothermal RNA amplification to improve the sensitivity of the method. In the current project the isothermal technique of choice will be one recently developed named RPA, which can be easily run at 36-42ºC in only 20-30 minutes. The implementation of an isothermal nucleic acid amplification technique allows to reduce the cost of infrastructure (all microbiology laboratories have incubators set between 36-42ºC which may be used for the amplification step). We will target 2 viral genes for higher specificity, and to avoid problems related with viral mutation which may hinder the detection of certain targets. The amplified nucleic acids are treated by the CRISPR-Cas system, and then loaded in a lateral flow strip, similar to a pregnancy test, where the results can be easily seen and interpreted by naked-eye observation. The overall assay is expected to be performed in less than 1 hour compared to 3-4 that an RT-qPCR may take.

fta4COVID19 R4COVID.2.598/2020

Use of FTA cards for low-budget collection and transport of sputum samples for molecular detection of SARS-CoV-2

PRINCIPAL INVESTIGATOR	Irina Amorim
LEADING INSTITUTION	Instituto de Ciências Biomédicas Abel Salazar - Universidade do Porto
FUNDING	€ 40 000

Obstacles to expanding sampling in the SARS-CoV-2 pandemic include the cold chain requirements for sample transport (4 to 8°C and stored at -70°C; WHO, 2020, https://apps.who.int/iris/handle/10665/331501). Moreover, logistic occupancy of devoted sampling areas in hospitals, the occupation of healthcare workers to nasal swab sampling and the need for patient transport to these sampling areas drains important financial resources and increases the movement of high-risk individuals. In other epidemics, alternative sampling methods have been applied (WHO, 2008. https://apps.who.int/iris/handle/10665/241169). Flinders Technology Associates (FTA) cards consist of filter paper impregnated with reagents that lyse cells, denature proteins, and immobilize nucleic acids in the fibers of the matrix. After transfer to FTA cards, samples can be shipped at ambient temperature as non-infectious material and the cards have been used successfully to transport RNA-based enveloped viruses such as SARS-CoV-2. Fta4COVID19 will evaluate the efficacy of using FTA cards for self-sampling of sputum, a WHO validated matrix, eliminating the need for visits to healthcare facilities (sputum could be collected from home and sent by postal mail to the clinical laboratories), reducing the logistic occupancy of devoted sampling areas and the occupation of healthcare workers for nasal swab sampling, and eliminating the need for use of the cold-chain in sample transport.
SARS-CoV-2 patients from Hospital Geral Santo António (HGSA) (N=200) will be asked to provide a sputum sample onto a Whatman FTA cards (Sigma-Aldrich, USA) at the moment of nasopharyngeal swabbing for COVID-19 testing. Viral RNA will be extracted and extracts will be screened using the same real-time RT-PCR assay as in HGSA. Quantified SARS-CoV-2 RNA will be compared to the quantification provided at HGSA using the nasopharyngeal swab sampling. To ascertain the genomic stability and evaluate possible downstream genomic applications of this sampling method, a set of 20 FTA card-samples will be further tested for full genome characterization by nanopore sequencing technology.

SenseBreath R4COVID.2.618/2020

Masks for Monitoring Breathing Rhythm

PRINCIPAL INVESTIGATOR	Joana Diniz da Fonseca
LEADING INSTITUTION	CENTITVC - Centro de Nanotecnologia e Materiais Técnicos, Funcionais e Inteligentes
FUNDING	€ 40 000

CeNTI, Center for Nanotechnology and Smart Materials, is developing a sensor that, incorporated in the protection mask, will monitor the user's breathing rhythm and identify possible changes and deviations from standard patterns. With this information, in case of contamination by the SARS-CoV-2 coronavirus, it will be possible to act earlier and minimize the impact in the patient. The development of the device is another of CeNTI's initiatives to help society reduce the spread of the disease.

The innovation involves the development and integration, in the mask, of a disposable sensor, in which the user's respiratory rhythm will be monitored. The disposable sensor consists of a capacitive sensor using paper as a substrate and silver ink as the electrodes. The data collected by this sensor will be sent to a mobile application that can detect any deviations in the results. The user can then send the data to be analyzed by health professionals.

The sensor, which is being developed by CeNTI, will be incorporated in masks that are being produced by OldTrading. The company is a collaborating partner of the project and a specialist in research in the textile sector. Academic Clinical Center - 2CA-Braga is also a partner of the project and is responsible for carrying out tests to evaluate the performance and usability of the technological solution.

Some of the main results that have been achieved are the development of several designs for the sensors, the fabrication of a 3-D printed electrical connector, to allow the plug-and-play feature of the sensors, and the testing of the system on a development board.

QuiCoviDe R4COVID.2.662/2020

Quick COVID-19 Detection

PRINCIPAL INVESTIGATOR	Maria Gabriela Machado de Almeida
LEADING INSTITUTION	Egas Moniz - Cooperativa de Ensino Superior, CRL
FUNDING	€ 39 788

Fast and extensive testing SARS-CoV-2 is fundamental to understand and prevent the COVID-19 pandemics Being at the first line of defence, it allows prescribing early therapies, preventing silent infections by isolating asymptomatic viral carriers and avoiding needless quarantines. Having quick, accurate, and deployable SARS-CoV-2 tests is thus pivotal for the disease's control. However, currently available tests have many limitations and none of them enables the massive, rapid diagnosis of COVID-19. The golden standard diagnostic tests are based on the amplification of viral RNA extracted from nasopharyngeal swabs. These molecular tests are time-consuming, require trained technicians, and specialized laboratory equipment. Immunological assays are another category of tests that detect the presence of antibodies produced in blood/serum following exposure to SARS-CoV-2 (early IgM and late IgG). Despite being much faster and simpler, they often lead to false negatives and are only effective after 8-10 days of infection. For these reasons, the WHO is encouraging the development of a new class of rapid diagnostic tests, which detect viral surface proteins - the antigens - in respiratory samples (e.g. sputum, throat swab), instead of RNA or antibodies against the new corona virus.

This project aims at developing a simple, quick and cost-effective test for SARS-CoV-2, the QuiCoviDe, which falls within this new category of antigen detecting tests. In particular, monoclonal antibodies targeting viral surface proteins will be firstly conjugated with nanostructured materials and then coupled to transparent sensor chips. When in contact with samples from infected people, SARS-CoV-2 antigens will be captured by the immobilized antibodies, thereby inducing small changes in the surface environment (refractive index) that are easily detected by a localized surface plasmon resonance-based optic fiber reader. This ultrasensitive immunosensor will be able to spot COVID-19 at an early stage, with no need of cumbersome viral RNA preparation. Noteworthy, the QuiCoviDe reader is deployable and can be used by non-trained personnel, enabling the disease's control at the point-of-care (e.g. hospitals, clinics) and outbreak control spots, such as schools, airports, and nursing homes. The QuiCoviDe project benefits from a highly interdisciplinary team having complementary expertise in Biosensors, Optoelectronics, Nanotechnology, Virology, Molecular diagnostics and Infecciology.

R4COVID.2.393/2020

Rapid assessment on COVID-19 disease severity and SARS-CoV-2 immunity by infrared spectroscopy

PRINCIPAL INVESTIGATOR	João Pedro Martins de Almeida Lopes
LEADING INSTITUTION	FARM-ID, Associação da Faculdade de Farmácia para a Investigação e Desenvolvimento
FUNDING	€ 35 500

The procedures for treating COVID-19 patients, caused by the SARS-CoV-2 virus, depend to a large extent on the clinical history as well as on the severity and extent of the infection. For adequate treatment, it is essential a deep knowledge of the extent of the infection and its potential severity in the short term. Currently, the biochemical assessment of the viral infection severity requires typically 6 to 8 hours and important resources, both material and human. Faster methods, not dependent on expensive reagents that may suffer from market shortage, is absolutely essential for clinicians timely decision on the procedures for each patient. Infrared radiation is used in many fields, with applications ranging from astronomy (e.g., composition of a planet atmosphere) to medical diagnosis (e.g., cancer diagnosis or bacteria identification). The ability to interpret the complex structure of matter interaction with infrared radiation requires complex mathematical methods, though.
This project proposes the use of infrared radiation for quickly assessing COVID-19 patients infection severity. The proposed methodology requires only blood collection, extraction of blood plasma, and within 30 minutes, it reports the severity of the infection as well as important immunity system biochemical indicators. This will allow doctors to be more effective in the treatments to be adopted and to assess their urgency. The method is safe for analysts, inexpensive (does not use any chemical reagents) and can be performed easily by hospital staff.
The methodology is based on the analysis of plasma by infrared radiation (instrument accessible to any health unit) coupled with an algorithm based on artificial intelligence that will diagnose the extension and severity of infection and many biochemical indicators produced during the immune response to the SARS-CoV-2 infection. The algorithm development requires a database of COVID-19 patients, other viral infections patients as well as healthy people plasma. Its development will require approximately 3 to 4 months until a prototype is ready for validation in the hospital environment. In routine, the method will produce between 40 to 60 analyses per equipment, being especially suitable for high frequency monitoring of inpatients.

DETECT R4COVID.2.433/2020

Development of an Easy, fast-Track and Economical Colorimetric Test for autonomous national diagnosis of COVID-19

PRINCIPAL INVESTIGATOR	Catarina Pimentel
LEADING INSTITUTION	ITQB NOVA - Instituto de Tecnologia Química e Biológica António Xavier
FUNDING	€ 35 000

After several weeks of lockdown, people are returning to their workplaces and resuming their routines. Now, more than before, there is a need to substantially increase our testing capacity and implement a robust contact tracing scheme.
The current testing strategy for SARS-CoV-2 detection relies on quantitative RT-PCR (qRT-PCR) - a complex, slow, expensive, but very reliable test. Its worldwide use has however caused a shortage of reagents and therefore driven an unprecedented global demand for accurate, easy and inexpensive alternative diagnostics.
DETECT brings together a team with complementary skills and expertise, with members from ITQB NOVA, Academia Militar and Hospital das Forças Armadas to develop a colorimetric molecular test designed to simplify and accelerate COVID-19 diagnosis.
The test, developed with the intent of being fast, inexpensive and independent of imported reagents, has the potential to increase Portugal's testing capacity and autonomy. This type of testing is crucial to prevent the spread of the disease and future waves of infection.

Therapeutics

R4COVID.1.133/2020

An open labeled randomized controlled pragmatic trial to evaluate the efficacy and safety of Montelukast as add on treatment to the novel coronavirus pneumonia (COVID-19)

PRINCIPAL INVESTIGATOR	André Moreira
LEADING INSTITUTION	Instituto de Saúde Pública da Universidade do Porto
FUNDING	€ 30 000

Considering the urgent clinical demand, clinical trials on testing adjuvant treatments for the novel coronavirus HCoV-19 (also known as SARS-CoV-2) infection have risen. There is no specific drug treatment against this infection. Hence, identification of readily available drugs for repurpose in HCoV-19 therapy are a rapid option to be studied to improve clinical treatment and prognosis. Montelukast, a safe drug widely use in asthmatic patients, may be an adjuvant in the treatment of HCoV-19 infected patients, either by improving lung injury and inflammation, or by acting as an anti-viral drug. Hence, we aimed to assess the efficacy and safety of Montelukast as add-on treatment to the novel coronavirus pneumonia (NCP).
We propose a randomized, controlled, parallel, open-label trial involving 160 hospitalized adult patients with confirmed COVID-19. Patients will be randomly assigned in a 1:1 ratio to receive either montelukast 10mg, once a day for 14 days, in addition to standard care, or standard care alone. Standard care comprises, as necessary, supplemental oxygen, non-invasive and invasive ventilation, antibiotic agents, vasopressor support, renal-replacement therapy, and extracorporeal membrane oxygenation. The primary outcome will include improvement of disease status, defined by the percentage of subjects reporting each severity, rating on an 8-point ordinal scale. Secondary endpoints will include time to clinical improvement, changes in hemogram and in biochemical parameters, hospitalisation data, and adverse events. This phase IV clinical trial will take place at the University Hospital of São João, Porto. EudraCT number: 2020-001747-21. Currently has been approved by the Portuguese National Drug Agency and provisionally by the National Ethics Committee for Clinical Research.
We intend to generate scientific evidence on efficacy and safety of montelukast administration as add-on treatment to NCP. The results will be essential to improve clinical outcomes related to COVID-19 infection, which remains to be determined. The success of this study may contribute to a better prognosis of patients, improvement of lung injury and respiratory symptoms, and decrease in the duration of hospitalisations.

GLYCOVID-19 R4COVID.1.140/2020

Testing existing glycan-based drugs to neutralize SARS-CoV-2

PRINCIPAL INVESTIGATOR	Paula Alexandra Quintela Videira
LEADING INSTITUTION	Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa
FUNDING	€ 30 000

The goal of GLYCOVID-19 project is to test drugs that neutralize the entry of SARS-CoV-2 into host cells, preventing infection. The project is based on the concept that SARS-CoV-2 binds to host cells through its S glycoprotein which is extensively decorated with glycans. Glycans are a set of sugars that decorate all of our cells and proteins, and that can affect their function or assign them new ones. Viruses that have an envelope, such as SARS-CoV-2, infect the cell, and when released by the host cells they carry molecules from the cell that they infected, including glycans. This mechanism allows the virus to escape detection by the host immune system. In the past, we have investigated how tumor cells use glycans to progress and escape the immune response and developed strategies that could target these glycans. Interestingly, both cancer cells and SARS-CoV-2 infected cells shared the same glycan decorations. So we hypothesized that compounds that could block these glycans would have a potential application to neutralize the entry of SARS-CoV-2 during infection. At the moment, Paula Videira and her team are testing different compounds, namely anti-glycan antibodies, but also glycans, for their potential to neutralize SARS-CoV-2 entry into cells during infection. The tests are underway and we are expecting to have results very soon. We are also revising all the available literature and clinical trials regarding the use of plasma from convalescent patients. We aim to gather information regarding their efficacy and safety, so that we can, in the future, compare it with our approaches. GLYCOVID-19 project will provide preliminary efficacy results for new molecules that may be further developed as antiviral drugs or coadjuvants. Neutralizing strategies are of the utmost importance for individuals who are already infected, often at an advanced stage of the disease, for whom the vaccine would no longer be effective. New therapies will reduce the pressure at public hospitals, avoiding long hospitalization periods of the infected patients while relieving the economic and management burden on the health system. In addition, understanding the relevance of glycans in SARS-CoV-2 will help the design of other therapies.

R4COVID.1.187.2020

Accurate tidal volume monitoring to optimize safe non-invasive ventilation settings in patients with SARS-CoV-2

PRINCIPAL INVESTIGATOR	Miguel Ramalho do Souto Gonçalves
LEADING INSTITUTION	Faculdade de Medicina da Universidade do Porto
FUNDING	€ 30 000

Respiratory failure is a major complication and the first cause of death in patients with severe acute respiratory syndrome coronavirus-2. For mechanical ventilatory support, early invasive ventilatory support (IVS) with an artificial airway has been preferred over non-invasive ventilation (NIV) with a facial mask, mainly because the risk of droplets and the difficulty of patient adaptation (reported failure ranging from 50 to 60%). Such difficulty is due to the anxiety, significant increase in respiratory rate with high ventilatory drives contributing to the rapid development of a lung injury self-inflicted by the patient (P-SILI) leading to a further oxygenation impairment and increase of respiratory severity.
NIV can be valuable strategy to avoid the complications of IVS, however one of the main difficulties in managing NIV settings is accurate noninvasive monitoring of ventilatory parameters such as tidal volume (TV) and minute ventilation (VE). We hypothesized that P-SILI during NIV in patients with SARS-CoV-2 is partly attributed to anxiety and excessive pressure settings with high inspired volumes. Thus, with accurate TV monitoring, we propose an individualized adjustment of continuous positive airway pressure (CPAP) through a oronasal mask in complement with a sedation protocol in order to reduce NIV failure in an intensive care protective environment.
In this study we will use an impedance-based monitor device which has the great advantage of continuously monitoring such parameters without the need to access patients' airways. This accurate monitoring can also work as feedback for the sedation/anxiolysis control protocol.
In conclusion, this study has the goal to implement a protocol to adjust safe and more efficient settings of NIV with continuous monitoring of accurate tidal volume (TV), respiratory rate (RR), minute ventilation (VE) and routine vital signs in patients admitted to intensive care unit with severe acute respiratory syndrome coronavirus 2. Accurate and real time TV monitoring may permit to early detect NIV failure and implement a more secure continuous intravenous anesthetic/sedation plan. Thus, we expect to reduce NIV failure rate thus reducing necessity of intubation and invasive mechanical ventilation support and therefore optimize intensive care recourses.

R4COVID.1.268/2020

Gut microbiota, "Spark and Flame" of COVID-19 disease

PRINCIPAL INVESTIGATOR	Maria da Conceição Costa Pinho Calhau
LEADING INSTITUTION	Universidade Nova de Lisboa - Faculdade de Ciências Médicas
FUNDING	€ 30 000

The novel coronavirus, 2019-nCoV, spread rapidly across China and the whole world. The World Health Organization (WHO) named the disease COVID-19 on 11 February 2020, characterizing it as predominantly a severe acute respiratory syndrome, and declared it a pandemic on 12 March.
Although the COVID-19 risk groups were quickly identified as the elderly, and hypertensive, diabetic and cardiovascular patients, the reason for this remained unknown. Gut flora (microbiota), i.e. all microorganisms (bacteria, yeasts, fungi, virus) living in the gut environment, play a critical role in health, notably in the immune system. Gut flora composition could affect vulnerability and disease outcomes. Microbial fingerprinting among SARS-CoV-2-infected patients will provide a predictive value for disease severity, serving as a target for disease management – to look in the gut for the potential mitigation of SARS-CoV-2 infection. Thus, on 7 April 2020, we hypothesized that gut microbiota could play a pivotal role in the pathophysiological pathway of the SARS-CoV-2 infection and, importantly, in the severity of its clinical progression. Confirming this assumption will open the way for potential therapeutic targets for these patients. We therefore analysed around one hundred SARS-CoV-2-infected patients with [1] mild disease (self-isolation at home), [2] severe disease (room isolation in hospital) and [3] critical patients (hospital ICU). The presence of the virus in the faecal samples of these patients was also analysed. After 3 months of research, we concluded that our hypothesis was confirmed. Significant differences were found in microbiota of these patients, according to the level of disease severity. Our results could lead to novel therapeutic strategies based on gut microbiota modifications. These results could be crucial to highlight the need of implementing lifestyle modifications that influence gut microbiota composition and function as well as immune response. This advantageous approach could be taken before a vaccine is available and, surprisingly, could have a key role on host response and immunity and consequently, on vaccine efficacy.

PNEUMA R4COVID.1.082/2020

Sistema de ventilação com recurso a um balão auto-insuflável

PRINCIPAL INVESTIGATOR	António Paulo Gomes Mendes Moreira
LEADING INSTITUTION	INESC TEC - Instituto de Engenharia de Sistemas e Computadores, Tecnologia e Ciência
FUNDING	€ 29 965

It is a recognized challenge the global lack of ventilators needed to face COVID-19. Although ventilators are sparse, bag-valve devices are available in all hospital services, providing a rapid response to respiratory depression. Bag-valve devices consist of a bag (self-inflating) and a valve (nonrebreathing). They can be used with a mask, a tracheal tube, or other alternative airway adjuncts (e.g. supraglottic airway device). These devices imply the presence of a healthcare professional. This project envisions the development of a system to automate the use of a bag-valve device.
This system does not intent to be a substitute for a ventilator. The system is designed to be a temporary solution for emergency use, allowing positive pressure ventilation though a standard self-inflating manual resuscitator, without the need of healthcare personal manually operating the resuscitator. The system is designed to be used in sedated patients with neuromuscular relaxation (without autonomic breathing) and airway secured through endotracheal intubation (or a supraglottic airway device).
The present proposal is based on the clinical requirements established for a similar system under-development by the MIT (USA), on current guidelines for patient ventilation, on the recommendations for COVID-19 patients' ventilation management, on the Disease commodity package - Novel Coronavirus (nCoV) from WHO, and on the Rapidly Manufactured Ventilator System specifications from MHRA.
In compliance with the recommendations for testing of the Rapidly Manufactured Ventilator System specifications from MHRA, a 2-phase testing protocol will be implemented and coordinated by FMUP – Biomedical Simulation Center.

MINIVENT R4COVID.1.096/2020

Pressure-controlled emergency mechanical ventilator for COVID-19

PRINCIPAL INVESTIGATOR	António Grilo
LEADING INSTITUTION	Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa
FUNDING	€ 28 512

Patients that are infected with COVID-19 may develop severe SARS-CoV-2 pneumonia and require early mechanical ventilation. The number of patients needing invasive mechanical ventilation has surpassed in several countries the installed capacity and the existing manufacturers are having difficulties to address this increased demand. Medical mechanical ventilators are normally sophisticated machines for general use, although this level of sophistication is not needed to save lives.
The MINIVENT team of medical doctors and engineers present a simple mechanical ventilator implementing the pressure controlled continuous mandatory ventilation mode (PC-CMV) with settable breathing rates, inspiration/expiration time ratios, intended as a last resort to ventilate COVID-19 patients. Although very safe by design, we try to minimize the use of technical components and those used are common in industry or easily printed in 3D Printers, so its construction may be possible in times of logistical disruption or in areas with reduced access to technical materials and at a moderate cost, affordable to lower income countries. Most of the device can be manufactured by modest technical means and construction plans are openly provided, with the final cost being lower than 1.000 euros per unit.
Following our proof-of-concept, this project has developed 20 viable prototypes, with different configurations, that implement the following main characteristics: Positive Inspiratory Pressure (PIP) adjustable in the range 20 to 40 cmH2O; Positive End Expiratory Pressure (PEEP) adjustable in the range 0 to 20 cmH2O; Safety pressure relief valve in the inspiration tube adjustable in the range 0 to 45 cmH2O; Breathing rate adjustable in the range 12 to 25 breaths per minute (bpm); Inspiration/expiration time ratio (I/E) adjustable in the range 1:2 to 1:3; and Low and high PIP and PEEP alarms
The prototypes have two different baseline configurations. Medical doctors from intensive care have been involved to provide feedback and the team is closing the final testing with life animals. We aim to submit the prototype for approval by the Portuguese regulatory body for medical devices INFARMED, in the context of the COVID emergency.

R4COVID.2.402.2020

Purinome-rejuvenated autologous STEM cells against COVID-19. Who's gonna win the ageing battle?

PRINCIPAL INVESTIGATOR	Paulo Correia-de-Sá
LEADING INSTITUTION	Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto
FUNDING	€ 40 000

Epidemiological data demonstrate that SARS-CoV-2 pneumonia is difficult to treat and has a worse prognosis in elderly patients. The lack of specific drugs and/or effective vaccines against COVID-19 prompted researchers and clinicians to look at STEM cells transplantation as last resource to treat SARS (severe acute respiratory syndrome) in critically ill inpatients in intensive care units (ICU). However, upon aging STEM cells lose their differentiation multipotency, immunosuppressive and antimicrobial properties. Scarcity of young donors and difficulties in processing and/or transportation of STEM cells during pandemic hamper a more widespread use of allogenic STEM cells for SARS-CoV-2 pneumonia.
These limitations led our group to think about laboratory rejuvenation strategies of bone-marrow derived STEM cells for auto-transplantation in elderly patients. This truly innovative concept is based on our previous expertise in manipulating the purinergic signalling cascade for cells rejuvenation in other diseases (e.g. osteoporosis), now adapted to COVID-19.
Purinome-based rejuvenation may be achieved (i) using pharmacological modulators (drugs/antibodies) or (ii) under drug-free safer conditions (e.g. cells stretch, low O2). Notably, (1) injected bone-marrow derived STEM cells become hosted in the alveolar microcirculation, and, (2) are relatively protected against SARS-CoV-2 invasion as they lack the obligatory human angiotensin-converting enzyme 2 (ACE2) receptor, contrary to their pulmonary siblings. Thus, based on preliminary data, we trust that prevention of the "cytokine storm" aggravating SARS by transplanted STEM cells may be due, in part, to endogenous formation of adenosine (local immunosuppressant) from the nucleotidase breakdown of ATP (danger molecule) released by injured cells, providing that purinome-rejuvenated STEM cells are present in the lung microcirculation.

COVID2ndID R4COVID.2.425/2020

Improved detection of COVID-19 secondary bacterial infections for efficient therapy

PRINCIPAL INVESTIGATOR	Sílvio Roberto Branco dos Santos
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 40 000

Respiratory viral infections increase the risk to secondary bacterial infections (SBI), consequently increasing the disease severity. It was shown that SBI were responsible for "the vast majority" of deaths in the 1918 influenza outbreak and for the negative impact of the H1N1 influenza pandemic in 2009. COVID-19 is not an exception. It was shown that in Wuhan hospitals, half of the deaths of COVID-19 patients were caused by SBI. The risk of COVID-19 patients to SBI is also evident by the high percentage (>90%) of antibiotics administered to those patients.
The problem is that these antibiotics are used not to treat diagnosed bacterial infections but as a preventive measure of COVID-19 patients, selecting for resistant bacteria and leading to untreatable SBI with dramatic consequences. Thus, there is an URGENT NEED for a fast and accurate identification of SBI that allows for the application of the proper antimicrobial therapy ASAP, reducing the infection severity and associated costs.
The current conventional culture methods have a slow turnover and the immune and molecular assays, which are much faster, still present many limitations.
Thus, we propose here an innovative technology based on the receptor binding proteins (RBPs) of bacteriophages to improve and develop cheaper, faster and more accurate diagnostic methods with a low limit of detection overcoming thus the limitations of the current ones. Bacteriophages are the viruses of bacteria, presenting a high specificity to their hosts and are innocuous to humans, animal and plants. RBPs are responsible for the high specificity and affinity of bacteriophages and are thus powerful biorecognition elements. We have been studying these proteins and already identified and produced RBPs specific for P. aeruginosa and S. aureus, two of the most important bacteria in pneumonia infections and which will be the target of this project. These RBPs will be used to create new chimeras able to specifically bind to bacteria isolated from COVID-19 patients and to produce a signal that can be easily detected through different routine lab equipment.
This new technology based on bacteriophage RBPs will allow for an improved (and cheaper) detection of the BSIs and consequently the sooner application of the proper therapy, reducing the severity and deaths related to COVID-19, as well as the costs associated.

R4COVID.2.470.2020

RIGHT-NOW-RIGHT-HERE: Evidence-based off-label application of porphyrin-based medicines to fight SARS-CoV-2.

PRINCIPAL INVESTIGATOR	Miguel A. R. B. Castanho
LEADING INSTITUTION	Instituto de Ciências Biomédicas Abel Salazar da universidade do Porto
FUNDING	€ 40 000

NOVIRUSES2BRAIN is a H2020-funded project with 4M€ to develop antiviral drugs able to reach the brain and inactivate enveloped viruses such as SARS-CoV-2, HIV or Dengue Virus (www.noviruses2brain.pt). The antivirals under development are conjugates of a porphyrin with peptides that translocate the Blood-brain barrier.
The present project is a specific add on to NOVIRUSES2BRAIN as it will consist in finding porphyrin medicines that can be repurposed as antivirals.

R4COVID.2.582/2020

Repurposed antimalarial and anti-Ebola drugs as Organic Salts and Ionic Liquids to prevent and fight COVID-19

PRINCIPAL INVESTIGATOR	Miguel Santos
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 40 000

The project "ILs4Treatment - Repurposed antimalarial and anti-Ebola drugs as Organic Salts and Ionic Liquids to prevent and fight COVID-19" focuses on developing novel ionic formulations of drugs with known activity against SARS-CoV-2 that provide decreased toxicity as well as enhanced bioavailability and activity against this coronavirus. The approach will consist on the preparation of novel organic salts and ionic liquids based on drugs such as Hydroxychloroquine and Remdesivir, taking advantage of their chemical properties. The synthesis and physicochemical characterization of these new salts will be conducted at the CHARM – Cultural Heritage and Responsive Materials – group of Faculdade de Ciências e Tecnologia da Universidade NOVA de Lisboa, by the researchers Miguel M. Santos (Project Leader), Luís C. Branco and Željko Petrovski. The in vitro toxicity and antiviral activity studies will be performed by the researchers Helena Rebelo-de-Andrade and Vanessa Correia of the Instituto Nacional de Saúde Dr. Ricardo Jorge and iMed.ULisboa – Faculdade de Farmácia da Universidade de Lisboa. Future in vitro and in vivo studies, including clinical trials, will be outlined together with INFARMED for the most promising formulation, aiming at a fast development of a safe and effective tool for prevention and treatment of COVID-19 for the entire population.

Viral Vectors for discovery of COVID-19 pathogenesis, treatment and vaccination

PRINCIPAL INVESTIGATOR	Luís Pereira de Almeida
LEADING INSTITUTION	Centro de Neurociências e Biologia Celular - Universidade de Coimbra
FUNDING	€ 40 000

In the absence of vaccines or drugs to combat the new SARS-CoV-2 coronavirus, a rapid concerted effort is needed to clarify the pathogenesis of the disease, identify therapies and develop vaccines. In this context, one of the great difficulties of research in this area is that COVID-19 is a highly infectious pathogenic agent, whose manipulation has non-negligible biosafety risks requiring the use of specialized facilities, not available in most hospitals, laboratories or even research centers.

To address this issue we will engineer viral vectors to exhibit at its surface the SARS-CoV-2 spike protein S, which guides the virus to attach to the host cell receptor - the Angiotensin Converting Enzyme 2 (ACE2) to initiate cellular entry, but that will be devoid of other sequences that confer replication capacity and pathogenicity to SARS-CoV-2. The vectors will encode reporter genes, green fluorescent protein and luciferase that will allow precise quantitative analysis of the infection/transduction process.

These vectors will allow the following activities to be developed:

1. Studying the infection process in vitro and in vivo by monitoring fluorescence/luminescence;
2. Identifying drugs that inhibit this interaction and have potential to be used as therapies;
3. Vaccinating animals and humans, as well as testing the effectiveness of other vaccination methods.

The project will be developed at the ViraVector - gene transfer unit of the national scientific and technological infrastructure roadmap https://www.uc.pt/ucbusiness/pts/viravector, involved in testing Covid19 at the Univ Coimbra in collaboration with CHUC & ARS.

High-throughput SARS-CoV-2 neutralising antibodies assessment

PRINCIPAL INVESTIGATOR	Marc Veldhoen
LEADING INSTITUTION	IMM-Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 39 800

Serology tests can detect anti-SARS-CoV-2 antibodies, but neutralization assays are required to identify if these are protective. We establish a safe, high throughput screening method to rapidly detect neutralizing antibodies (NAb).

The high-throughput assay established for detection of NAb is based on modified vesicular stomatitis virus pseudotyped particles (VSVpp). The VSV used (VSVΔG) is infection defective due to the deletion of its envelope gene (G), which we coat with SARS-CoV-2 Spike, thus creating a one cycle infection competent pseudo particle for a safe NAb screening method. Cellular entry mediated by the envelope protein is detected with a reporter gene inserted in the VSV genome, replacing the G gene. This rVSVΔG system carries the Renilla luciferase (Rluc) gene. Thus, rVSVΔG:Rluc can be pseudotyped with SARS-CoV-2 Spike proteins and pseudotyped VSV infections can be detected via luminometry.

We collected large cohorts of pre-COVID-19 and COVID-19 positive sera at the iMM Biobank, to our FCT funded seroconversion assay (231_596873172, Generating SARS-CoV-2 seroconversion assay), and the Portuguese blood bank (IPST) has recruited >400 possible donors.

We have setup of the neutralisation assay at iMM using SARS-CoV-2[Rluc]pp using known negative and positive sera. We have setup the capacity to generate and quality control SARS-CoV-2[Rluc]pp. To validate the test, we use conventional methods of screening for NAb, using SARS-CoV-2 virus isolated at iMM and the iMM BSL3 facility, Pedro Simas-lab.

We are in the process of screening donors in collaboration with IPST. High-throughput screening of serum takes place by in-house ELISA to first identify those donors with high anti-SARS-CoV-2 IgG antibody titres, with total Ig, IgM and IgA levels assessed in addition. Subsequently, selected sera will be assayed for neutralisation activity.

We are in the process to complete a high-throughput assay that is able to identify donors with high titres of neutralising anti-SARS-CoV-2 antibodies. Identified donors' plasma is currently collected and stored by the blood bank (IPST), preserving these antibodies for lifesaving therapy of those severely affected by COVID-19, now and in the future. We have obtained and preserved the knowledge to rapidly setup and adapt this assay to any future pandemics.

Ion channel blockers mechanism of action against SARS-CoV-2/ COVID-19: a fast-track ex-vivo study to complement the current on-going clinical trials

PRINCIPAL INVESTIGATOR	Miguel Viveiros Bettencourt
LEADING INSTITUTION	Universidade NOVA de Lisboa
FUNDING	€ 39 749

There is no known effective pharmacological treatment for COVID-19 and the current treatment of severe cases includes the use of antiviral drugs (lopinavir / ritonavir and remdesivir), eventually in conjunction with the immunomodulating antiparasitic - hydroxychloroquine - proposed as an inhibitor of in vitro replication of SARS-CoV and MERS-CoV. The efficacy and safety of chloroquine (which interferes with endosome acidification and viral decapsidation) for the treatment of SARS-CoV-2 pneumonia is not consensual. In pioneering studies with other coronaviruses, other safe and effective drugs were chlorpromazine CPZ [Largactil ©] and Verapamil VP [Isoptin ©] - currently in clinical trials in France and Poland [NCT04366739; NCT04351763]. CPZ is an inhibitor of clathrin binding in the plasma membrane that prevents viruses from entering host cells and, similarly, SARS-CoV also uses clathrin-mediated endocytosis to enter target cells followed by endosomatic penetration. These processes are inhibited by CPZ and VP. IHMT / NOVA has more than 20 years of experience in the study of the enhancement of microbial death by alveolar macrophages using Ca2 + channels blockers, such as CPZ and VP, using them to treat antibiotic-resistant bacterial infections. We recently described its mechanism of action, via cellular and endosomal Ca2 + channels and pH change. In this project we will evaluate these drugs and this mechanism of action against SARS-CoV-2, trying to describe how these drugs inhibit the internalization of the virus by endocytosis mediated by Ca2 + channels, limiting intracellular traffic and pH of the endosomes, blocking the decapsidation of the virus. We hope to explain how and to what extent ion channel blockers can inhibit SARS-CoV-2 infection in safe doses and potentially become an effective therapeutic option against COVID-19. The project started in July 2020 and in silico simulations and in vitro viral infection inhibition tests are already underway, confirming the effectiveness of these compounds in vitro. The laboratory strategy for testing the optimal dose for the inhibitory effect is being implemented.

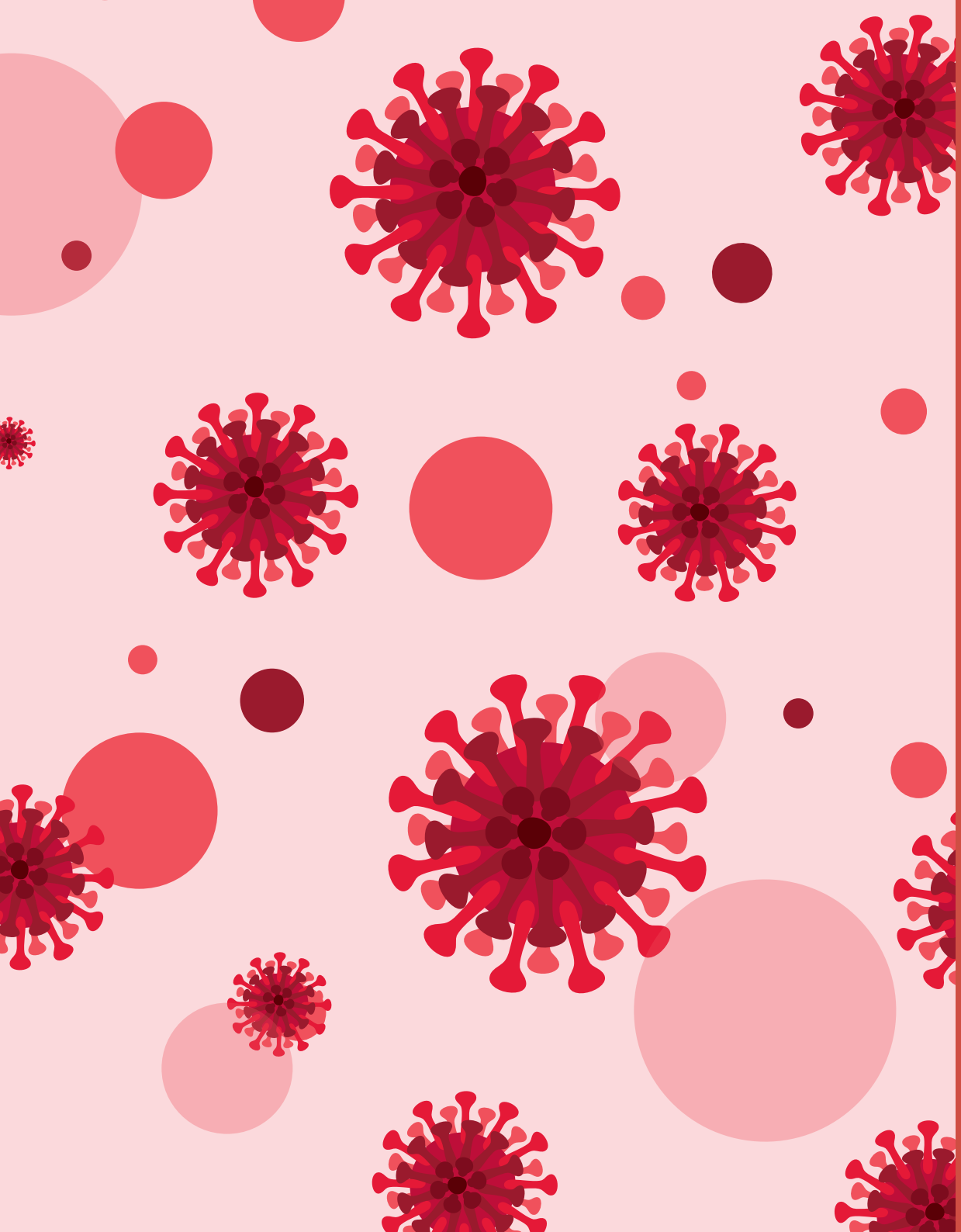
Agilização da colheita de plasma convalescente

PRINCIPAL INVESTIGATOR	Sofia Cruz Gomes
LEADING INSTITUTION	INESC TEC - Instituto de Engenharia de Sistemas e Computadores, Tecnologia e Ciência
FUNDING	€ 39 135

Convalescent Plasma (CP) can offer the first and only therapeutic strategy in the context of emerging infectious threats, while specific vaccines or drugs are not available. In the current setting of the COVID-19 pandemic, CP appears to be a promising therapeutic option. Despite the public interest and the existence of the infrastructures required for the collection and storage of CP, this therapy is not yet available in Portugal. Some challenges, concerning donor eligibility, donor recruitment and CP processing can compromise their effective harvest.
The project team, through its long experience in immunohemotherapy, identified some problems that could compromise the ability to harvest CP and respond to the growing demand.
The PLASMA4COVID project aims to answer these challenges, streamlining the CP harvest at a national level. For that purpose, three key activities will be performed:

1. Validate the use of automated serological tests for anti-SARS-CoV-2 IgG (in place of viral neutralization tests) for the evaluation of CP donors;
2. Validate the pathogenic reduction methods that are available in Portugal for inactivation of Convalescent Plasma;
3. Develop a simple and accessible approach for screening potential donors of convalescent plasma among the existing donor population.

By finding solutions to the identified difficulties, it will be possible, on the one hand, to ensure the quality of CP as a therapeutic product to be used by hospitals and, on the other hand, to speed up the procedure for recruiting and selecting CP donors, significantly increasing the capacity to respond to harvest Convalescent Plasma.
In the short run, this project will allow anticipating the beginning of CP harvests in other NHS hospitals which are struggling with the same issues. In the long term, the tools developed can be used, and the methods can be replicated to create a Convalescent Plasma harvest plan more readily in a new epidemic scenario due to an emerging pathogen.



Clinical and Epidemiological Studies

R4COVID.1.081/2020

Repository of single cell transcriptomes of COVID-19 immune cell subsets

PRINCIPAL INVESTIGATOR	Luís Graça
LEADING INSTITUTION	IMM- Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 30 000

A significant part of the COVID-19 research effort has relied on broad immune cell phenotyping. This project will complement those efforts by acquiring information from defined cell subsets at single-cell resolution. We will provide a detailed analysis of the transcriptome of three critical immune subsets, that will be available to researchers to complement and enhance their studies. By providing detailed information on gene expression of multiple cell populations, we will improve the impact of clinical studies developed across the country. We will establish a repository of 12 datasets.
We will rely on the transcriptomics capacity of GenomePT, and our experience with the collection and analysis of single-cell RNA sequencing datasets from human immune samples. Defined immune populations will be isolated from the blood of COVID-19 patients with mild disease (hospitalized but not requiring intensive care) and with severe disease (patients at the intensive care unit). Importantly, the approach was designed to avoid duplication of efforts with other international single-cell transcriptomics efforts. Information regarding the single-cell transcriptomics of global populations will become rapidly available elsewhere. However, those global datasets will lack the required resolution to address small populations within the sequenced cells. We will focus on small, albeit important, immune subsets in order to generate valuable datasets that will complement global datasets. This way, rather than analyzing global immune populations we will focus on specific immune subsets hypothesized to play an important role in immune responses to SARS-CoV-2. This project will start with a selection of subsets of special interest to the Portuguese research community. We aim to expand the collection to additional immune cell populations.
Through this strategy, we will provide detailed information about the characteristics of key immune cell populations important for COVID-19. These data will complement and improve ongoing studies based on immunophenotyping.

R4COVID.1.125/2020

COVID-19 pneumonia outcome: an immunological approach

PRINCIPAL INVESTIGATOR	Susana M Fernandes
LEADING INSTITUTION	IMM- Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 30 000

COVID-19 evolution towards severe pneumonia requiring invasive lung support is thought to rely on individual immune responses to SARS-CoV-2 virus, although the main immune determinants of severity and lung repair are yet to be found. We had an ongoing project in our lab addressing lung repair in the context of Acute Respiratory Distress (ARDS), a very severe form of acute lung injury that is also the most severe consequence of COVID-19 pneumonia. We adjusted this study protocol, approved by the CHULN ethical board, to face the SARS-CoV-2 pandemic, and started a study based on blood samples to understand how immune responses determine COVID-19 pneumonia severity as well as lung repair. We included patients admitted to the hospital with COVID-19 pneumonia requiring few litters of oxygen and follow them during their disease course, sub-dividing into two groups: 1) requiring mechanical ventilation and 2) not requiring mechanical ventilation. At each time-point (hospital admission, during mechanical ventilation, and then at time of recovery) clinical data and blood samples were collected, and a detailed immunological profile was studied using 3 high-dimensional flow cytometry tubes, addressing the phenotype of the main immune cell populations. In parallel, we have gathered samples of these patients to further study possible serological or transcriptional markers of disease severity.
This project will give valuable hints into the evolution of immune phenotype of the main cells involved in adaptative immune responses to infectious diseases as well of the innate immune response landscape profile, the first line of defence against a virus, like SARS-CoV-2 virus.
The analysis of these results in relation to detailed clinical/virology data, is expected to clarify crucial aspects related to pathogenesis, particularly the role of immunomodulators, and to identify new targets to treat and prevent COVID-19.

R4COVID.1.170/2020

Myocardial Injury in COVID-19: a Prospective Clinical and Mechanistic Study

PRINCIPAL INVESTIGATOR	Roberto Roncon-Albuquerque Jr.
LEADING INSTITUTION	Faculdade de Medicina da Universidade do Porto
FUNDING	€ 30 000

Myocardial injury is detected in a significant percentage of COVID-19 patients, even in the absence of previous cardiovascular disease. Despite its prognostic relevance, the underlying pathophysiological mechanisms, diagnostic approach and therapeutic management are largely unknown. To address this gap, the project consists in a comprehensive clinical, analytical, imaging and genetic evaluation of COVID-19 patients admitted to the ICU, together with mechanistic studies using post-mortem myocardial samples. Statistical-learning models will then be built to capture relevant clinical, analytical, histological and molecular features associated with myocardial injury in COVID-19.
The project combines an experienced team in clinical and translational cardiovascular research, particularly in the field of inflammatory cardiomyopathies, working in a unique hospital that aggregates a large ICU capacity for COVID-19 (~100 ventilated beds) and an autopsy room with the required biosafety level.
With this comprehensive bedside-to-bench approach, ranging from a purely clinical evaluation to the analysis of myocardial transcriptome, the project proposes to describe novel, clinically relevant and therapeutically exploitable mechanisms of myocardial injury and dysfunction in COVID-19.

R4COVID.1.198/2020

Enriching epidemiologic information on SARS-CoV-2 transmission through complete viral sequencing

PRINCIPAL INVESTIGATOR	Veronica Fernandes
LEADING INSTITUTION	IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto
FUNDING	€ 30 000

The first COVID-19 cases in Portugal were introduced in the Northern region at early March 2020. In the first couple of weeks, it was possible to relate the cases with the transmission chains and conduct careful epidemiologic questionnaires. Some of these chains are large and have several rounds of transmission or "generations". In this project, we aimed to characterise through next-generation sequencing the viral genome isolated from ~250 North Portuguese infected individuals, using this molecular information to enrich the epidemiologic knowledge on the dynamics of SARS-CoV-2 transmission. For comparison purposes, besides including samples from the large transmission chains, we also gathered samples when the transmission was already in the community, at different time-points (April, when transmission levels were peaking; May and early June when transmission was occurring in localized outbreaks).
By the end of July, we have the fully annotated SARS-CoV-2 genomes isolated from 260 individuals. The strains/clades are already identified. We observed: 2 of clade 19A; 2 of clade 19B; 83 of clade 20A; and 173 of clade 20B. Clade B increased in frequency along time: 60% in March, 70% in April; 86% in May and 83% in June. The median number of mutations per month was: 7 in March; 8 in April; 8 in May; and 9 in June. These values match the described mutation rate for SARS-CoV-2. We are still processing the epidemiological and clinical information, in order to be able to relate the strains with clinical data, and infer its impact in virulence and efficiency of transmission.

Contribution to the National Preparedness and Response Plan to new coronavirus disease: evaluation, through the ECOS panel, of the impact of the pandemic on the Portuguese population with chronic diseases and mental health unmet needs identification, characterization of changes in lifestyle and new social and family dynamics.

PRINCIPAL INVESTIGATOR	Mariana Augusta Neto
LEADING INSTITUTION	Instituto Nacional de Saúde Dr. Ricardo Jorge
FUNDING	€ 29 500

This study aims to answer a set of questions raised by the National Plan for Preparedness and Response to COVID-19 and to support public health decision making and the development of interventions aimed at minimizing the impact of the COVID-19 pandemic in the Portuguese population, besides meeting the R&D priorities identified by the WHO. It intends to carry out 3 waves of the ECOS (Em Casa Observamos Saúde) telephone panel survey, which is a representative sample of the Portuguese population. Major depression, sleep disturbances, health needs in chronic diseases, nutrition and food insecurity, alcohol and tobacco consumption, practice of physical exercise, effects on the work and family dynamics induced by the pandemic and use of social networks to maintain health will be surveyed.
ECOS consists of a random sample of household units (HU) with landline or mobile phones, stratified by the seven administrative regions, with a homogeneous and representative allocation of the Portuguese population. Panel participants remain for 3 years. The current panel was created in 2018 and contains 1549 HU. In each HU, only one individual (respondent), 18 years of age or older at the time of telephone contact, will be asked to provide information about himself and the rest of his household (proxy). Data collection will be carried out through the application of structured questionnaires by computer-assisted telephone interview (CATI) and computer-assisted web interview (CAWI). Results of the first wave, conducted during the final phase of the confinement period, showed, when compared with 2018 results, that the self-perceived general health has improved but general daily activity limitation, depressive disorder and difficulty on falling asleep have aggravated. Concerning healthcare needs, one fifth of the surveyed individuals needed a medical appointment during the confinement period due to the COVID-19 pandemic, while one seventh needed medical exams and one thirteenth medical treatments. Almost half of the individuals referred the need to buy prescription drugs.

CheckImmune

PRINCIPAL INVESTIGATOR	Miguel Castelo Branco
LEADING INSTITUTION	Universidade da Beira Interior
FUNDING	€ 28 750

SARS leads to the production of IgM (recent infection - 3-6 days) and IgG (past infection - 8 days). Will the same profile be presented in the infection with SARS-CoV-2?. Like other European countries, Portugal intends to study the population's immunity. In this cross-sectional study, a representative sample of the population (95% confidence interval) of 384 individuals (excluding cases + PCR SARS-CoV-2) was calculated, distributed among the following groups: previously tested by PCR with result -; not tested and with no history of symptoms; untested and with a past history of mild symptoms (asymptomatic ≥ 3 weeks). We will also study the immunity from people that had PCR +, these and - cases will be from the database of the 3 health units. Asymptomatic or mild symptomatic individuals will be selected from the general population.
Task 1 - Development of a survey to assess current symptomatic status, history of symptoms when applicable, co-morbidities, data for inclusion in groups, demographic, socio-cultural data, and others considered relevant (concluded).
Task 2 - The project documents (plan, survey and informed consent) will be submitted to the Ethics Committee of the University of Beira Interior for evaluation and issuing an opinion. (concluded, positive opinion obtained)
Task 3 - Recruitment of volunteers will be carried out according to the defined groups, considering the individuals tested for virus research and civil society (from both districts). Everyone will be given free and informed consent and the survey developed for the study. (concluded)
Task 4 - Collection of biological samples (serum) and application of ELISA assay: EUROIMMUN kit for IgA and IgG - CE marking, Ag domain of the specific S1 protein SARS-CoV-2 and EDI® kit for IgM research) and immunochromatographic assay (SureScreen Diagnostics - DM IVD registered, IgG and IgM search). (Concluded)
Task 5 - Analysis of results: immunity will be assessed within the defined groups, considering the biomarkers defined separately and in groups. The results obtained with the 2 methods will be compared in order to conclude on the application of the most efficient (considering the properties of the diagnostic tests and also the relationship of these parameters with the cost and ease of use). The results will be analyzed using statistical methods.

R4COVID.1.079/2020

COVID-19: Effects of social isolation in the mental health of adults and older adults

PRINCIPAL INVESTIGATOR	Sandra Cristina Lopes Freitas
LEADING INSTITUTION	Universidade de Coimbra
FUNDING	€ 27 000

In the face of the current health and social crisis caused by COVID-19, the research project "COVID-19: Effects of social isolation in the mental health of adults and older adults" was developed with the aim of assessing, in a multidimensional fashion, the effects of social isolation derived from the implemented lockdown measures, in the mental health of adults and older adults in the Portuguese population.
Gathering both scientific interest and expertise in neuropsychological assessment and aging, a team of experienced neuropsychologists assessed 250 community-dwelling adults and elders from mainland Portugal and Azores, in order to fully assess the emotional, functional and cognitive effects of the COVID-19 pandemic. All subjects included in this study have had a prior one-year old neuropsychological assessment carried out, within the scope of the ESCUDO project (Aging and Cognitive Decline in the Portuguese Population: Incidence, profiles, risk and protective factors – FCT/IF/01325/2015). This longitudinal frame enabled a comparative analysis between the results obtained in the post-confinement period and the data collected prior to the COVID-19 pandemic, thus allowing the fully understanding of the real impact of social isolation in the physical, psychological and social well-being of adults and older adults.
Simultaneously to this work package, a website named CuidaIdosaMente was created in order to offer to the general population a more immediate product of the research project. CuidaIdosaMente is aimed towards the increase of mental health literacy and the accessibility to preventive strategies. It is designed to be a pleasant and interactive website that counts with weekly updates.
This project was welcomed by the Center for Research in Neuropsychology and Cognitive and Behavioral Intervention (CINEICC) of the University of Coimbra. The research team is composed by Professor Mário R. Simões (CINEICC), Professor Manuela Vilar (CINEICC), Doctor Ana Rita Silva (CINEICC, CNC), Doctor Marina Cabral Pinto (GEOBIOTEC), PhD student Joana Nogueira (CINEICC), PhD student Bianca Gerardo (CINEICC), and PhD student Paula Pinto (CINEICC), and is oriented by the Principal Investigator Professor Sandra Freitas (CINEICC).

R4COVID.1.174/2020

The impact of the COVID-19 pandemic on the diagnosis and treatment of cancer patients in Northern Portugal

PRINCIPAL INVESTIGATOR	Nuno Lunet
LEADING INSTITUTION	Instituto de Saúde Pública da Universidade do Porto
FUNDING	€ 22 020

The COVID-19 pandemic has affected the availability of healthcare resources, and has required adjustments to cancer care considering the risk of morbidity by COVID-19 and cancer progression. The proposed project aims to quantify the impact of the pandemic on cancer patients by comparing a period of four months since the outbreak began (March 2, 2020) with an equal period from 2019.
All cancer cases of the esophagus, stomach, colon and rectum, pancreas, lung, skin-melanoma, breast, cervix, prostate, lymphomas and leukemia diagnosed at the Portuguese Institute of Oncology of Porto (IPO-Porto) from March 2 to July 1 of 2019 (before COVID-19) and of 2020 (after COVID-19) will be identified. Patients receiving a first treatment outside IPO-Porto will be excluded from the analyses to ensure the comparability between the two periods, as cases diagnosed in 2019 and treated elsewhere are more likely to have potentially received additional care at IPO-Porto until the present than those diagnosed in 2020. Information regarding sociodemographic characteristics, cancer diagnosis, treatment and complications, date of symptom onset, first medical exam, first appointment, multidisciplinary tumor board meeting and first treatment, and COVID-19 diagnosis will be collected from clinical files. Vital status will be assessed to July 31 of the respective years. The number of cancer cases will be compared considering sociodemographic, clinical and treatment characteristics. The time from symptom onset, first medical exam and first appointment to diagnosis, and from diagnosis to first appointment, multidisciplinary tumor board meeting, first treatment and death will be compared between patients diagnosed before and after COVID-19.
The project has been approved by the Ethics Committee of IPO-Porto (CES IPO: 164/020) and by the Data Protection Officers of the participating institutions.
The project´s results will describe the effect of the COVID-19 pandemic on the care of patients at IPO-Porto, while identifying the needs to be considered in healthcare planning in the coming months. When normal service resumes at a population and healthcare level, there will likely be a backlog of cancer patients needing healthcare as well as a surge in new cancer cases.

R4COVID.1.229/2020

Caracterização das manifestações neurológicas em doentes com COVID-19

PRINCIPAL INVESTIGATOR	Manuel Correia
LEADING INSTITUTION	Centro Hospitalar Universitário do Porto
FUNDING	€ 21 946

Neurological involvement in COVID-19 patients (NeuroCovid) has been consistently described in hospital-based retrospective studies, affecting nearly 30% of hospitalized patients. However, population-based studies were still lacking. In this project we generated a multicentric COVID-19 epidemiological registry in the north of Portugal targeting neurological phenotypes. For that purpose, we developed a prospective registry with data collection in a centralized web platform of hospitalized NeuroCovid patients requiring a Neurologist evaluation. This registry includes patients from Centro Hospitalar Universitário do Porto (CHUP), Centro Hospital Universitário São João (CHUSJ), Hospital de Braga, Unidade Local de Saúde do Alto-Minho, Centro Hospitalar Vila Nova de Gaia/ Espinho, Centro Hospitalar Entre-Douro e Vouga (CHEDV), Unidade Local de Saúde de Matosinhos (ULSM), Centro Hospitalar Trás-os-Montes e Alto Douro (CHTMAD) and Centro Hospitalar Tâmega e Sousa. A total of 65 patients has been consecutively recruited and is under prospective follow-up since April 2020. Strikingly, we identified both central and peripheral nervous system phenotypes such as encephalopathy, stroke, Guillain-Barré syndrome and posterior reversible encephalopathy syndrome, among others.

In addition, we conducted a retrospective registry of all hospitalized COVID-19 patients, admitted in CHUP, CHUSJ, CHEDV, ULSM and CHTMAD since March 2020. In the hospitalized patient's cohort in CHUP, 35.6% presented neurological involvement. The most frequently described neurological symptom was headache in 66.7%, with anosmia and hypogeusia identified in 32.2% and 21.1% respectively. Delirium, decreased consciousness, and sleep disturbances were also consistently reported. In the ambulatory patient cohort, the most commonly reported neurological manifestations were headache (73.5%), anosmia (68.7%) and/or dysgeusia (70.1%). Sleep pattern alterations, vertigo, cognitive complains (mainly memory and dysexecutive symptoms) and visual and sensitive alterations have also been identified.

Overall, our comprehensive dataset supports that NeuroCovid is a highly prevalent condition in COVID-19 patients. NeuroCovid is not necessarily related to the severity of the systemic infection. NeuroCovid phenotypes are diverse and both host and agent factors may play a role in its emergence and characteristics.

R4COVID.1.263/2020

COVID-19 in Pregnancy: Obstetric and Neonatal Outcomes

PRINCIPAL INVESTIGATOR	Carina Rodrigues
LEADING INSTITUTION	Instituto de Saúde Pública da Universidade do Porto
FUNDING	€ 15 135

There is currently no evidence that the risk of having COVID-19 is greater among pregnant women than in the general population. However, COVID-19 during pregnancy implies an increased risk, as any other viral respiratory infection. Information is still limited as to the effect of infection by the new coronavirus (SARS-CoV-2) on pregnancy. One of the main concerns is the possible transmission of the virus from the mother to the fetus. Although most of the cases described in published scientific studies point to the absence of transmission of the virus during the intrauterine period, there are already cases of infants infected in the first days of life. Since knowledge about the effect of SARS-CoV-2 infection on pregnant women and newborns is also limited, it is important to produce scientific evidence that allows the identification of priority areas to prevent and treat COVID-19 in this population.

This study aims to determine the adverse effects of COVID-19 on pregnant women and newborns, as well as to identify the practices adopted by healthcare units in managing the disease during pregnancy, childbirth, and the puerperium, relating them to health outcomes.

Thus, we are recruiting pregnant women infected with SARS-CoV-2 during any trimester of pregnancy from the public obstetrics units belonging to the geographical areas of the Regional Health Administrations of the North, and Lisbon and Tagus Valley (25 units).

We are collecting data on sociodemographic and medical information about pregnancy, delivery, and newborn. Clinical information is also gathered regarding SARS-CoV-2 infection and the practices adopted by the hospital (mother-newborn separation, breastfeeding). Moreover, we are collecting biological samples (placenta, amniotic fluid, umbilical cord blood, and breast milk) to analyze the possibility of SARS-CoV-2 infection. About a month following delivery, we are contacting the participants to answer a questionnaire, to assess their physical and mental health, and the health of their babies. The information provided will be used to produce scientific knowledge, through the production of reports addressed to the health authorities and hospitals.

The Institute of Public Health of the University of Porto is responsible for the study, in partnership with the Obstetrics and Neonatology Services of the participating hospitals.

R4COVID.1.015/2020

Early recognition of cardiac injury associated with COVID-19 and clinical outcomes

PRINCIPAL INVESTIGATOR	Filipe Gonzalez
LEADING INSTITUTION	Hospital Garcia de Orta EPE
FUNDING	€ 14 436

SARS-CoV-2 is a virus from the corona family and is responsible for the severe acute respiratory syndrome (SARS) in humans, among other less severe symptoms, which is known as Corona Virus disease 2019 (COVID-19). SARS-CoV-2 can also cause damage to the heart, presenting as direct damage to the myocardium, recognized as an elevation in a myocardial specific protein called high sensitive troponin (Ths). Patients with underlying cardiovascular disease and SARS-CoV-2 infection have an adverse prognosis. Therefore, particular attention should be given to cardiovascular protection during treatment for COVID-19. Cardiac injury in COVID-19 is associated with ICU (Intensive Care Unit) admission, respiratory failure, renal failure, and increased mortality.
So, we started a study in the ICU patients to detect early cardiac injury in severe COVID-19, which could change the clinical management of these patients and consequently, less organ dysfunction and mortality. For early recognition of cardiac injury, we measure cardiac-specific markers, such as Ths and NT-proBNP (an indicator of cardiac overload), markers of inflammation, such as CRP (C reactive protein), PCT (procalcitonin) and ADM (adrenomedullin), and immunologic markers, such as interleukins 1 and 6 (IL-1 and IL-6) and differential lymphocyte analyses (flow cytometry). These measurements are repeated along the time in the ICU, together with advanced echocardiography (with strain technology), to register the evolution of these markers during the worst phase of the disease, until patients are transferred to a lower care level.
From 12th June to 24th July, we recruited 15 patients, median of age 62,5 years, 40% were male, troponin elevation occurred in at least 62.5% of the patients, associated with some dysfunction in echocardiography.
Recruitment is still ongoing and we hope to show you some results soon.

R4COVID.2.369/2020

Immune senescence in COVID-19

PRINCIPAL INVESTIGATOR	Luis Graça
LEADING INSTITUTION	IMM-Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 40 000

In COVID-19, age and comorbidities have a strong correlation with lethality. Both aging and chronic diseases are linked to persistent immune activation (often termed "inflammaging"). Therefore, the assessment of the immune-senescence of COVID-19 patients can provide key information to explain the vulnerability of the elderly and those with co-morbidities. Moreover, protective antibody production declines with age, namely in influenza, leading to a progressive reduction of vaccination efficacy. The reduced antibody production of the elderly has been linked to defects in T cell subsets, named follicular T cells, that are critical for the formation of germinal centers (GC) – structures where the B cells improve their affinity to viral antigens leading to high-affinity neutralizing antibodies. Therefore, our immune-senescence studies will contribute to define the vulnerability to severe COVID-19 and to plan future vaccination strategies.
"Inflammaging" is an immune state characterized by persistent low-grade activation that has been described in the elderly and in chronic diseases such as atherosclerosis and linked to risk of death.
In this study, we will collect samples from COVID-19 patients at the time of hospital admission and examine the immune cells from those patients. With time, the majority of those patients will get better while a minority will develop complications requiring admission to the Intensive Care Unit. We will then compare the characteristics of the immune cells at the time of admission with the evolution of the disease, in order to identify cell characteristics that predict disease severity.
In addition, we will collect blood from patients after COVID-19 recovery to quantify the production of antibodies specific to SARS-CoV-2. We will then compare the characteristics of the follicular T cells concerning the antibody production.
Our overall objective is to demonstrate that immune-senescence may be the common feature linking aging and co-morbidities with an enhanced inflammatory state ("inflammaging") that explains COVID-19 severity and high lethality among the known vulnerable groups. Our secondary objective is to assess whether there is a declining ability of old individuals to produce protective antibodies targeting SARS-CoV-2, with implications for successful vaccination campaigns.

VITACOV R4COVID.2.388/2020

Vitamin D-related polymorphisms and vitamin D levels as risk biomarkers of COVID-19 infection severity

PRINCIPAL INVESTIGATOR	Fausto José Conceição Alexandre Pinto
LEADING INSTITUTION	Centro Cardiovascular da Universidade de Lisboa - Faculdade de Medicina da Universidade de Lisboa
FUNDING	€ 40 000

Hospitalized COVID-19 patients have a very high prevalence of hypovitaminosis D, suggesting a strong association between severe vitamin D deficiency and mortality rates. Additionally, large-scale studies suggest the serum 25(OH) D-level to be inversely correlated to the prevalence of hypertension and other cardiovascular diseases, major risk factors in the COVID-19. Vitamin D is a fundamental regulator of host defenses by activating genes related to innate and adaptive immunity. Observational studies report that vitamin D induces protection against respiratory pathogens.
It is known that, in a normal scenario, vitamin D deficiency is common in Europe and the Middle East. It occurs in <20% of the population in Northern Europe, in 30–60% in Western, Southern and Eastern Europe and up to 80% in Middle Eastern countries. Data from Portugal show that 66% of adults present vitamin D insufficiency/deficiency.
VITACOV is built on: i) published data showing that vitamin D deficiency has been linked to hypertension, autoimmune, infectious and cardiovascular diseases, all risk factors in the current COVID-19; ii) COVID-19 patients have a very high prevalence of hypovitaminosis D; iii) genetic factors can influence the disease severity. The main goal of VITACOV is to understand if an association exists between vitamin D levels and polymorphisms in vitamin D-related genes and disease severity.
To achieve our goal, genetic variants in vitamin D-related genes and vitamin D levels in hospitalized patients will be assessed and an association of these data with the progression of the disease (mild to severe and critical disease) will be highlighted. VITACOV will contribute to find biomarkers with a major impact on identifying patients that will develop the most severe forms of disease, opening new perspectives to help minimizing the pandemic severity. This could be very relevant mainly for patients with cardiovascular risk factors including male gender, advanced age, diabetes, hypertension and obesity, as well as patients with established cardiovascular disease, as they were identified as particularly vulnerable populations, with increased morbidity and mortality when suffering from COVID-19.

iHIPI R4COVID.2.418/2020

Hiperinflamation and immunological profile of patients with COVID-19 from Centro Hospitalar de Vila Nova de Gaia/Espinho

PRINCIPAL INVESTIGATOR	Matilde Monteiro-Soares
LEADING INSTITUTION	Universidade do Porto - Faculdade de Medicina da Universidade do Porto
FUNDING	€ 40 000

"iHIPI: Hiperinflamation and immunological profile of patients with COVID-19 from Centro Hospitalar de Vila Nova de Gaia/Espinho" is a collaborative project including a core team of five researchers affiliated to Faculty of Medicine from Porto University, PORTIC, Centro Hospitalar de Vila Nova de Gaia and I3S.
The infection by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) may lead to devastating clinical consequences such as acute respiratory distress syndrome or even death. However, it is still not well known why some people remain asymptomatic or with light symptoms while other develop severe complications. One of the hypotheses that has been raised is that this discrepancy may be linked with the patients' immune system, particularly with an event designated as "cytokine storm".
This "cytokine storm" defines an exaggerated and uncontrolled response from the immune system and creates an anomalous inflammatory response that is deleterious to the organism. This event causes high fever, blood vessels leaking, blood clotting, extreme reduction of blood pressure, lack of oxygen, blood acidification and accumulation of fluids in the lungs. However, it is crucial to clearly distinct between this phenomenon and the needed and adequate immune response.
So, we aim to characterize the immune profile of patients with COVID from Centro Hospitalar de Vila Nova de Gaia/Espinho, their caregivers and health professionals, by mainly collecting blood samples and quantifying several biomarkers, focusing on cytokines level, and to understand if they are associated with the presence of symptoms, COVID-19 related complications and death. By achieving this goal, we could help identify faster individuals requiring specialized care and develop appropriate treatment strategies.

R4COVID.2.441/2020

Phenotypes of infection by SARS-CoV-2: an integrative longitudinal analysis to create predictive prognostic models

PRINCIPAL INVESTIGATOR	Pedro Miguel Guimarães Marques da Cunha
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 40 000

The main goal of this project is to unveil early features of the infection by SARS-CoV-2 that allow to pinpoint those subjects that will most likely evolve to severe and complicated forms of the disease. To achieve such goal, a research Consortium has been established including Minho University (through its School of Medicine, Life and Health Research Institute and Centre for Digital Medicine), Hospital Senhora da Oliveira (Guimarães), and the Karolinska Institute (through the SciLife Insititute, Stockholm, Sweden). The researchers in these institutions will apply artificial intelligence tools to a set of thoroughly documented clinical, radiologic and laboratory information of 150 patients admitted with COVID-19, with the ultimate objective of building models that can predict those complications and allow for a more precise approach of medical care and resource allocation. To insure that the models built using artificial intelligence are robust, the consortium will also analyse 92 molecules associated with inflammation and infection, from blood samples of the infected patients collected in different and sequential days of their disease evolution. Some studies with similar goals have looked into the initial features of infected patient to understand how some of them would influence the evolution of disease.
In this project the researchers will also look at the dynamic, longitudinal evolution of those characteristics during the infection period, to understand how shifts in several biologic markers may signal the development of severe forms of disease. We still do not know why some patients with the same apparent clinical features have a different clinical evolution and need for distinct medical interventions. The outlook provided by the incisive analysis of such a clinical cohort as the one we have described above, will hopefully provide more answers and contribute to a better comprehension of the disease and more targeted treatment of those in need.

R4COVID.2.519/2020

Unresolved inflammation and endothelitis in severe COVID-19 patients: identification of risk stratification biomarkers and therapeutic targets

PRINCIPAL INVESTIGATOR	António Albino Coelho Marques Abrantes Teixeira
LEADING INSTITUTION	Faculdade de Medicina da Universidade do Porto
FUNDING	€ 40 000

Cytokine storm, an important contributor to the development of acute respiratory distress syndrome (ARDS), multiorgan failure and death in severe COVID-19 patients, may occur due to a failure in resolution of inflammation. This process is responsible for limiting inflammation and promoting tissue regeneration, being mediated by specialized proresolving mediators, such as lipoxins and resolvins, which exert potent immunoresolvent effects in the lung. Both inflammation and oxidative stress contribute to endothelial dysfunction, which in turn is involved in ARDS pathophysiology and organ failure. Reports of COVID-19 patients suggest the existence of widespread endothelial activation leading to microvascular dysfunction, tissue ischemia, edema and a procoagulant state. Since angiotensin-converting enzyme-2 (ACE-2) is the receptor for SARS-CoV-2 entry in human cells, including endothelial cells, virus binding might decrease ACE-2 catalytic activity, lowering angiotensin II metabolism. Furthermore, pulmonary endothelial activation and angiotensin-converting enzyme (ACE) shedding may also contribute to the rise of angiotensin II, enhancing inflammation, coagulation, and vascular dysfunction.
Our research team will focus on the evaluation of the resolution of inflammation status and endothelial injury, along with the assessment of oxidative stress, coagulation and reninangiotensin system (RAAS) biomarkers, in patients with severe COVID-19, patients with moderate COVID-19 and controls. We expect to contribute to the improvement of risk stratification in COVID-19 patients, allowing the early diagnosis and management of the most vulnerable individuals, and to identify putative therapeutic targets and the treatments most effective at counteracting morbidity and mortality in COVID-19 patients. This project takes advantage of the team expertise in the fields of resolution of inflammation, endothelial dysfunction and oxidative stress, critical care, infectious diseases, RAAS and oxidative DNA damage.

R4COVID.2.617/2020

From SARS-CoV-2 infection to COVID-19. A study of viral kinetics and immune response to understand contagion and clinical progression.

PRINCIPAL INVESTIGATOR	Margarida Tavares
LEADING INSTITUTION	Instituto de Saúde Pública da Universidade do Porto
FUNDING	€ 40 000

A longitudinal study was designed to address the natural history of SARS-CoV-2 infection, researching: a) the period of viral transmission - from exposure to disease convalescence; b) the association between viral detection using molecular biology techniques (i.e. able to detect certain viral genetic components) and viral culture (i.e. able to ascertain viral ability to replicate, and thus infectivity), and its relationship with antibody production and titre levels; c) different immunological trends and their respective longitudinal relationship with disease presentation, evolution and outcomes, virus kinetics and viability.
The study will follow 4 groups of participants: 1) 60 asymptomatic individuals with high-risk exposure identified by means of contact tracing; 2) 10 SARS-CoV-2 infected but asymptomatic patients with a positive molecular biology test (i.e. RT-PCR) identified after contact and risk groups screening; 3) 20 outpatient individuals with mild COVID-19; 4) 30 in patients with severe COVID-19. Throughout disease evolution, samples from the respiratory tract will be taken to assess SARS-CoV-2 viral load by qRT-PCR and its viability as determined by culture. Furthermore, blood samples will be collected to assess the individual inflammatory and immune response evolution (i.e. inflammatory markers, immunoglobulin and complement assays, blood flow cytometry for characterization of peripheral lymphocyte subsets, specific IgM and IgG antibodies).
The duration and modes of transmission of the SARS-CoV-2 are unknown. This study will fill that gap by identifying viable viruses in culture, possibly even before symptom onset, and determining the duration of their persistence in patients. By determining SARS-CoV-2 replication and viability, and identifying its clinical and immunological determinants, this study will influence public health measures and treatment individualization adjusted to the spectrum of infection severity (asymptomatic, pauci-symptomatic, mild, severe with respiratory and/or critical end-organ failure). It will provide original contributions to address the potential for contagiousness in asymptomatic, pre-symptomatic and convalescent individuals, fundamental for contact tracing policies and isolation measures.

R4COVID.2.625/2020

Is thyroid gland a target of SARS-CoV-2 infection? Early identification and follow-up of thyroid dysfunction in COVID-19 patients

PRINCIPAL INVESTIGATOR	Ana Paula Soares Dias Ferreira
LEADING INSTITUTION	IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto
FUNDING	€ 40 000

In the 2002 outbreak of severe acute respiratory syndrome (SARS) a substantial number of patients presented abnormalities in the thyroid functioning which affected the (neuro)endocrine and calcium homeostasis. Several patients presented in the follow-up decreased levels of thyroid hormones (triiodothyronine (T3), thyroxine (T4), thyroid stimulating hormone (TSH)). It was detected in autopsies from SARS-CoV patients that the thyroid gland was significantly affected by the disease, with extensive injury and death of follicular and parafollicular cells. More recently, it was shown that thyroid presents one of the highest expression of angiotensin-converting enzyme 2 (ACE2), a cell membrane receptor considered as a candidate for infection with SARS-CoV-2 and related lesions
In the project we aim to establish if thyroid can be directly infected by the SARS-CoV-2 and what are the consequences of this infection in the development of thyroid dysfunction in COVID-19 patients. We will monitor recovered patients at Centro Hospitalar Universitário de S. João and Centro Hospitalar Lisboa-Norte, for the levels of T3, T4 and TSH, to determine if there is any indication of thyroid dysfunction, namely hypothyroidism.
In collaboration with Hospital Universitário de São Paulo, Brazil and Centro Hospitalar Universitário de S. João, we will have access to autopsy thyroid samples and clinical data from patients infected with SARS-CoV-2. We will evaluate the expression, in the autopsy thyroid samples and in a series of other thyroid lesions (normal, thyroiditis and tumours), of the ACE2, the host receptor for SARS-CoV-2 already shown to be highly expressed in thyroid cells. We will analyze the autopsy thyroid samples for the presence of viral particles, and together, these results will establish if: the thyroid cells are directly infected by the virus; and, if the ACE2 expression is enabling the infection. The autopsy thyroid samples will be studied regarding other parameters: histological features, apoptosis, and proliferation. We will also perform the immune cell characterization in the autopsy thyroid samples. We expect to disclose the effects of SARS-CoV-2 infection in thyroid by characterizing the effects in thyroid cells, by establishing the effects in the immune response and the consequences in thyroid function of recovered COVID-19 patients.

R4COVID.2.644/2020

Predicting SARS-CoV-2 susceptibility by tracking the genetic variability of the ACE2 receptor

PRINCIPAL INVESTIGATOR	Ricardo B. Leite
LEADING INSTITUTION	Fundação Calouste Gulbenkian- Instituto Gulbenkian de Ciência
FUNDING	€ 40 000

This pandemic is unusual in the way that the degree of severity and lethality is determined by preexistent morbidities among other factors. Whether genetic predisposition explains this heterogeneity remains to be assessed. The SARS-CoV-2 binds human ACE2 which acts as an anchor for the virus on host cells. ACE2 is polymorphic, and it is the prime candidate gene to explain the heterogeneity of susceptibility to SARS-CoV-2 infection and disease severity.
To address this, we are aiming to test 1000 health professionals for genetic variants, taking advantage of established collaboration of IGC with 3 hospitals in the Lisbon area. One of the benefits of enrolling healthcare professionals is the detailed information about symptoms and self-evaluation of the severity of the infection. Crossing information of genetic variation, symptoms, with information from parallel initiatives for viral charge determination/sequencing and SARS-CoV-2 immunity will allow to correlate genetic risk factors with a susceptibility to infection and disease in high risk environments. A preliminary study was conducted to verify polymorphisms in a pre-pandemic set. ACE2 sequencing will be used to predict the effect of amino acids substitutions on the protein 3D structure and its complex with the SARS-CoV-2 S protein RBD, by modelling the consequences of residue substitutions on protein functionality. Simulations will be carried over on wt and variant ACE2 transcripts to define structural stability aiming to identify substitution critical for the susceptibility, symptoms, and outcomes.
The feasibility of the project is ensured by our data indicating that both host genomic DNA and host RNA can be recovered from the standard RT-PCR diagnostic swabs. Nevertheless, blood will be collected. The recovered material was already successfully tested using an in house developed protocol for parallel sequencing of both the virome and ACE2 gene. Data from the sequencing of ACE2 in our cohort will be confronted with viral load/antibodies, and symptoms and integrated into a dataset. A genotype/phenotype/symptomatology db will be made publicly available according to FAIR principles. We have all the genomic and bioinformatic skills, the appropriate computing and sequencing platforms to conduct this work and make results available in a short time. Personal clinical data will be anonymized according to national requirements and consent forms will be clear on data usage and disclosure.

R4COVID.2.803/2020

COVID-19 prognosis: innate immune determinants

PRINCIPAL INVESTIGATOR	Amelia Chiara Trombetta
LEADING INSTITUTION	IMM-Instituto de Medicina Molecular João Lobo Antunes
FUNDING	€ 40 000

A worse prognosis, in 5% of COVID-19 patients, is known to be determined by contrasting immune system responses combining hyper-activation and immune-paralysis, similarly to what is described for severe inflammatory reactions like sepsis.
The first response to a pathogen is mounted by innate immune system, and among the main actors, monocytes and macrophages and the molecules they secrete can determine the resolution of the acute infection already in the lung. In contrast, if this mechanism is failing, an uncontrolled systemic immune response spreads to the whole human organism.
Our preliminary data such as those from other research centres worldwide, show that specific monocyte/macrophage and innate immune system characteristics, including a mix of immune-regulatory or suppressive features, might be associated with SARS-CoV-2 infection.
To better comprehend the pathogenic process and develop a useful guide for possible future therapies, our project aims to investigate monocyte and macrophage system characteristics associated with worsening of clinical conditions or higher mortality during the clinical follow up of COVID-19 patients.
To this purpose, we will collect detailed clinical and immunologic data of a cohort of COVID-19 patients,
Several techniques will be used for the wide structural and functional monocyte/macrophage system description, from multi-parameter flow cytometry, to investigate the structures expressed from the cells, to large cytokine arrays to evaluate the inflammatory molecules secreted in blood. Other important variables that may impact in the monocyte function, like the possible presence of antibodies against the virus will be detected by ELISA and viral genome in swabs and plasma, will be determined targeting 2 different virus gene regions.
The study will allow the comprehensive clinical patient stratification, at baseline and during the follow up, contributing to the description of the early features of cell activation that might be related to development of protective/harmful innate and adaptive immune responses and possibly finding patterns of activation that might be objective for specific immune modulating therapies.

R4COVID.2.510/2020

Impact of COVID-19 on the treatment of cancer patients

PRINCIPAL INVESTIGATOR	Fernando Carlos de Lander Schmitt
LEADING INSTITUTION	IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto
FUNDING	€ 38 600

The ongoing pandemic caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a huge impact on medical care, particularly in cancer patients. However, information on the effect of COVID-19 on cancer cells is unknown. SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) receptor for host cell entry and has protean clinical manifestations attributable to distribution of ACE2 in multiple organs in addition to lungs. Also, ACE2 is highly expressed in cancers. The coronavirus spike protein used to enter human cells is heavily glycosylated, with N- and O-glycosylation sites, and that certainly impacts on that SARS-CoV-2 binds to ACE2 with a 10-20 increased efficiency compared to SARS-CoV. Previous studies demonstrate that ACE2 inhibits the growth of lung and prostate cancer and overexpression reduced angiogenesis and invasion and cancer patients receiving ACE inhibitors had a longer survival. Recently, it was demonstrated that SARS-CoV-2 needs furin to cleave the viral spike protein, similarly to HIV, influenza, dengue, and Ebola, and enter cells. This increases the interest of evaluating SARS-CoV-2 interaction with furin, abundantly expressed in cancer, since it was recently demonstrated that furin plays a role in ERK-MAPK activation. Understanding how virus infection affects cancer cells, by interaction with ACE2, will clarify their involvement in carcinogenesis and therapeutic strategies. We aim to analyze the expression of ACE2 alongside the presence of SARS-CoV-2, in cancer samples obtained from patients with past or current SARS-CoV-2 infection. We want to explore the interference of the virus in cell processes as necrosis, apoptosis, proliferation, and immune response across cancer types to establish the impact of SARS-CoV-2 on cancer patients and its effect on therapeutics. Lastly, we want to evaluate whether cancer cells may be a reservoir for reinfection.

R4COVID.2.460/2020

Combining serology and virus specific cytokine profiling for evaluation of SARS-CoV-2 exposure

PRINCIPAL INVESTIGATOR	Anabela Cordeiro da Silva
LEADING INSTITUTION	Instituto de Biologia Molecular e Celular da Universidade do Porto
FUNDING	€ 37 500

SARS-CoV-2 is a highly contagious virus causing the ongoing COVID-19 pandemic. While reliable nucleic acid tests to detect acute infection are available, real epidemiological burden evaluation, in particular asymptomatic infections rate is challenging. Serological studies to detect SARS-CoV-2 specific antibodies are essential tools to estimate the real number of infections and the possibility of immunity. Notably, our preliminary data comparing 3 commercial assays for detecting IgG in COVID-19 patients (>15 days post-diagnosis; n=202) support only fair-moderate agreement (Cohen's Kappa statistics between 0.241-0.511), revealing high variability and low clinical validity. Recent scientific advances support the use of viral antigens produced in eukaryotic cells for SARS-CoV-2 exposure evaluation by ELISA. Thus, we propose the same technical approach using 3 viral proteins to conduct a serological screening on blood bank donors from Centro Hospitalar Vila Nova de Gaia/Espinho. Additionally, inconclusive serology will be complemented by quantitative multiplex cytokine profile from whole blood stimulation assay with a SARS-CoV-2 spike glycoprotein peptide pool. This project is held at IBMC/i3S from the University of Porto in collaboration with Centro Hospitalar e Universitário de Coimbra, Centro Hospitalar Vila Nova de Gaia/Espinho and Instituto de Saúde Pública from the University of Porto.
With this project we will contribute to defining the epidemiological burden of SARS-CoV-2 in a geographic area highly afflicted by COVID-19. Provide new biomarkers of exposure to SARS-CoV-2 that may improve assessment of the epidemiological burden in an asymptomatic population. This survey can also help estimate the overall exposure of a defined population enabling informed decision-making concerning, risk of exposure, asymptomatic prevalence, and infection dynamics in exposed populations.

ONCOVID.PT R4COVID.2.634/2020

Registo nacional de doentes ONcológicos com Coronavirus disease 2019 (COVID-19)

PRINCIPAL INVESTIGATOR	Júlio Oliveira
LEADING INSTITUTION	Sociedade Portuguesa de Oncologia
FUNDING	€ 35 658

COVID-19 pandemic dramatically impacted oncology care. Cancer patients are more susceptible to infections due to their malignancy-related immunosuppressive state and to the disease-oriented treatments (chemotherapy, radiotherapy, and surgery). Evidence suggests that, in cancer patients, COVID-19 infection rates and risk of severe complications are significantly higher. However, it remains unclear if the higher COVID-19 mortality in cancer patients is driven by the anticancer therapy per se, rather than by other clinical characteristics (sex, age, frailty, and co-morbidities), and in which proportion. It is therefore imperative to collect real-world evidence about the impact of COVID-19 pandemic on cancer patients and cancer care to promptly inform clinical decisions and health policies. ONCOVID.PT is a multicentre registry created to overcome the knowledge void in cancer care produced by COVID-19. ONCOVID.PT is led by Sociedade Portuguesa de Oncologia and comprises a national multicentre registry that will be developed in 3 phases. In the 1st phase, a retrospective-prospective cohort will enrol cancer patients (any age, sex, histology, stage, in active treatment as well as in clinical follow-up) which developed COVID-19 infection. In the 2nd phase, data from cancer patients diagnosed/treated during COVID-19 pandemic without COVID-19 infection will be gathered. In the 3rd phase, efficacy and cancer care related outcomes from the 2 cohorts will be compared with historical controls provided by Registo Oncológico Nacional. This design will allow us to understand how COVID-19 infection behaves and impacts efficacy related-outcomes in cancer patients and how an unprecedented global health crisis like the COVID-19 outbreak increased stress over the health-care systems worldwide and impacted proper cancer care (aim of the 1st and 2nd phase). We assembled a group of participating institutions comprising Portuguese public cancer centres, public general hospitals providing cancer care and private institutions. ONCOVID.PT registry will provide data regarding COVID-19 impact on cancer patients outcomes, treatments and care enabling the assessment of current cancer care status Data will support evidence-based clinical decisions and public health policies that can and will contribute to the re-organization and planning of SNS during COVID-19 and future pandemic times.

R4COVID.2.657/2020

Monitoring the integrity and genetic evolution of SARS-CoV-2 during infection, to support clinical and public health decision

PRINCIPAL INVESTIGATOR	João Paulo Gomes
LEADING INSTITUTION	Instituto Nacional de Saúde Dr. Ricardo Jorge
FUNDING	€ 34 000

The Portuguese National Institute of Health (INSA) is conducting a project that aims to monitor the integrity and genetic evolution of SARS-CoV-2 during infection, to support clinical and public health decision. In fact, the existence of many cases of unusually long infections (> 1 month), identified in the laboratory by the persistence of positive results, is a concern of health entities due to the need to maintain a long confinement of the infected person in the hospital or at home. By using whole-genome sequencing approaches and culture on multiple positive samples from each infected person, it may be possible to disclose it:

i). the last positive samples for patients with abnormally long infection are simply random fragments of non-viable viruses;

ii). or, if it is a process of evolution of the virus. We hypothesize that, for example, mutations that occur in the protein Spike (the main antigen, also involved in binding to the host cell) may be the basis of an adaptive process of the virus, leading to the maintenance of the period of persistence in the organism.

Given that the maintenance of positive results after a long period of COVID-19 prevents hospital discharge (for hospitalized patients) or the end of social isolation (for patients isolated at home), this study: i) will allow to accelerate these processes if it is concluded that the latest positive samples for these patients reflect only fragments of non-viable viruses not yet eliminated; or ii) suggest the maintenance of such measures if a process of adaptive evolution of the virus is observed.

This project has started on 1st July and will last for about 6 months. Nevertheless, the results will be periodically reported to the scientific community and public as long as important observations to the Public Health are obtained during the study period.

Ironing COVID-19 R4COVID.2.569/2020

Finding in the host iron status the signature to predict the severity of the disease

PRINCIPAL INVESTIGATOR	Maria Salomé Gomes
LEADING INSTITUTION	IBMC-Instituto de Biologia Molecular e Celular
FUNDING	€ 30 000

Iron is a key element for almost all forms of life. Infectious agents such as fungi, bacteria and viruses need iron for their proliferation and for the establishment of disease. Our team and others have shown that alterations of iron distribution and availability are an important part of the host defense strategies against infection. Significant correlations were found between iron-related molecules and the outcome of infectious diseases, such as sepsis, tuberculosis, hepatitis C or HIV/AIDS. We thus anticipate that iron may also play an important role in infection by SARS-CoV-2.
The severity of COVID-19 is highly variable and clearly related to the previous health status of the patient. This project intends to use the team's expertise in the fields of iron and infection, to solve the clinical problem of predicting and preventing the severe forms of SARS-CoV-2 infection.
Blood is being collected at Centro Hospitalar Universitário de S. João (CHUSJ), from 3 groups of individuals: healthy non-infected controls; asymptomatic SARS-CoV-2-positive individuals; patients newly diagnosed with COVID-19. Patients in the latter group are followed for clinical status, including severity of the disease, need for ventilation and intensive care and time to recovery. A second blood sample will be collected after full clinical recovery. At CHUSJ, routine clinical laboratory determinations will be performed in these blood samples. Additionally, specific iron-related determinations will be performed at CHUSJ and at IBMC. Finally, statistical analysis will be performed to find correlations between each of the iron-related parameters and the clinical indicators of disease severity. Altogether, the data obtained during this project will allow to characterize the relationship between host's iron status and the progress of COVID-19. As an immediate outcome, the project will give the clinicians important tools for a correct prognosis of the course of disease in a given individual, based on the early identification of iron related blood signatures. In a longer term perspective, the project will contribute to reveal cause-effect relationships between iron-related factors and disease severity. This will potentially allow the identification of molecular targets which can be pharmacologically modulated to treat COVID-19, as part of a host-directed therapeutic strategy against this disease.

COVID-19 in-CTRL R4COVID.2.692/2020

Projeção do Impacte das medidas Não-farmacológicas de Controlo e mitigação da epidemia de COVID-19 em Tempo ReaL

PRINCIPAL INVESTIGATOR	Baltazar Emanuel Guerreiro Nunes Bravo Nunes
LEADING INSTITUTION	Instituto Nacional de Saúde Dr. Ricardo Jorge
FUNDING	€ 16 164

A equipa que propõe este projeto tem elaborado diariamente desde Março relatórios sobre a evolução da epidemia de COVID-19 em Portugal, com o objetivo de monitorizar a transmissibilidade da epidemia e desenvolver cenários de impacto das medidas de saúde pública. O trabalho consistiu na implementação de um modelo de dinâmica de transmissão de doenças infeciosas, estruturado por idade e que incorpora os comportamentos sociais dos Portugueses através de matrizes de contatos entre os indivíduos em casa, no trabalho, na escola e na comunidade em período pré-epidémico. O modelo permite prever a evolução dos indivíduos suscetíveis, expostos (infetados), infeciosos (sintomáticos, assintomáticos, internados, em cuidados intensivos) e recuperados por grupos etários. Consegue ainda avaliar o impacto das medidas de contenção e supressão dos contactos sociais, e a sua suspensão total ou gradual, combinadas com o isolamento de casos e rastreio de contactos medindo assim a probabilidade de contenção da epidemia, ou de uma possível recorrência da mesma. O objetivo é desenvolver uma ferramenta de modelação e cenarização da epidemia de COVID-19 em Portugal, e do impacto das medidas de saúde pública, que possa ser disponibilizada para serviços de saúde pública.
Tarefas do projeto: T1: desenvolvimento matemático e implementação computacional do modelo. T2: obter estimativas para os parâmetros do modelo e para o efeito que as medidas de saúde pública terão no tempo de infecciosidade e na taxa de contactos. T3: Informação sobre a evolução dos contactos da população e a sua adesão às medidas de confinamento ou desconfinamento será medida recorrendo a informação colhida no projeto Epipose e CoMIX do qual a equipa ficará ligada como "linked third party". T4: serão desenvolvidos cenários com diferentes pacotes de medidas de saúde pública nacionais e locais.
O resultado final será uma ferramenta computacional em Shiny R para simulação do impacto de medidas de controlo da epidemia de COVID-19, a usar pelo INSA para apoio à decisão das autoridades de saúde nacionais e locais.

R4COVID.2.467/2020

Identification and genetic characterization of early COVID-19 positive cases in Portugal

PRINCIPAL INVESTIGATOR	Vera Maria Rêgo Durão
LEADING INSTITUTION	Fundação Calouste Gulbenkian - Instituto Gulbenkian de Ciência
FUNDING	€ 6 500

COVID-19 was first reported in December 2019, China, and quickly spread around the globe. On January 30th, 2020, the World Health Organization declared SARS-CoV-2 infection a public health emergency of international concern. It has already affected over 14 million people worldwide and killed more than 600,000 until July 21th, 2020.

Portugal reported the first two cases of SARS-CoV-2 infection only on March 2nd, 2020, which was considerably later than Italy, Spain, France and other European countries.

A novel retrospective report from France showed a positive COVID-19 patient, with no known relation with China, a month before the first official case in that country, suggesting that the virus was already spreading in the community previously than expected. Since it is estimated that the majority of COVID-19 patients have mild disease and do not require hospitalization we prompted the question whether Portugal had already undetected infection cases before March 2020.

In order to achieve this aim, Centro Hospitalar de Setúbal (CHS) and Instituto Gulbenkian de Ciência (IGC) teamed up to perform certified RNA COVID-19 tests using lower airway samples obtained by bronchoscopy at the Interventional Pulmonology Unit of Hospital São Bernardo, Setúbal, in the months preceding March 2020. The examined samples will be from patients not diagnosed, at that time, with COVID-19. This hospital is close to Lisbon and serves thousands of people, making it a strategic target to search for previously unknown cases. The IGC is currently performing these tests on a regular basis and they have been certified by Instituto Nacional de Saúde Doutor Ricardo Jorge.

Positive cases will be further characterized by whole genome sequencing of the virus allowing the evaluation of its genetic diversity. We will also look for an association between the positive cases and the clinical features of these patients. Our results will be made freely available through an open access paper as soon as possible, contributing to the global knowledge of SARS-CoV-2 virus. We hope our results will contribute critically to inform epidemiological models and determine future scenarios. As a consequence, it ought to improve accurate decisions on its control.

Remaining Areas

R4COVID.1.234.2020

Genetic diversity of the novel coronavirus SARS-CoV-2 (COVID-19) in Portugal

PRINCIPAL INVESTIGATOR	João Paulo Gomes
LEADING INSTITUTION	Instituto Nacional de Saúde Dr. Ricardo Jorge
FUNDING	€ 30 000

The Portuguese National Institute of Health (INSA) is coordinating a national project that aims to monitor the genetic diversity of the novel coronavirus SARS-CoV-2 (COVID-19) in Portugal, using whole-genome sequencing (WGS) data.
The major goals of this project are:

- Determination of SARS-CoV-2 mutational profiles for identification and monitoring of transmission chains, as well as identification of novel introduction in Portugal;
- Predict the start of transmission in the community and measure the impact of the containment efforts on transmission chain outcomes;
- Determination of the genetic variability of antigens and targets of antiviral drugs, with impact on the development / effectiveness of prophylactic (vaccines) and therapeutic measures; and
- Determination of the possible association between specific mutations / genetic profiles (SARS-CoV-2) with clinical outcomes (e.g., disease severity of COVID-19).

This project enrolls the collaboration with more than 50 laboratories/hospitals spread throughout the country (samples providers), with Instituto Gulbenkian de Ciência (collaborator in the experimental procedures) and has already allowed sequencing about 1 700 SARS-CoV-2 (updated on July 2020), representing infections from more than 130 counties.
A scientific report is regularly sent to all collaborating Labs whenever more sequences are added and new conclusions are achieved. In addition, a site has been created (https://insaflu.insa.pt/covid19/) where the results are updated regularly and are freely available to the scientific community and the public.
On behalf of this, multiple collaborations with local health authorities have been established in order to better understand the scenario of the transmission chains and new introductions in specific areas.
The major results of this project are now under analysis and will be released to the scientific community and health authorities within weeks.

e-CoVig R4COVID.1.255.2020

Automated System for Remote Vigilance of Symptoms and Vital Signs on COVID-19 Patients

PRINCIPAL INVESTIGATOR	João Miguel Raposo Sanches
LEADING INSTITUTION	Instituto de Sistemas e Robótica - ISR / IST-ID
FUNDING	€ 30 000

This project is aimed to design and develop a low-cost eHealth platform for monitoring symptoms and vital signals of COVID-19, using smartphones as the primary interface. The target is the group of patients, symptomatic or asymptomatic, in mandatory home quarantine. The core of the system is a mobile application (app), which integrates a COVID-19 electronic diary (e-CoVig). The app enables the acquisition of physiological data related with COVID-19 symptoms such as temperature, respiration, heart rate, and oxygen saturation (SpO2). It is also able to collect behavioral activity (actigraphy), subjective symptomatology (screening questions), and psychological (questionnaires, tests, and visual scales) information. Collecting physiological data is the main goal of this system. For that reason several strategies were designed and implemented at the platform: patients can manual introduce measurements in the e-CoVig diary, perform automated measurements using the embedded sensors of the smartphone, reading automatically from purpose-built device or using an incorporated Optical Character Recognition (OCR) to automate readings from displays of standard household devices, namely thermometer, blood pressure monitor, and/or oxygen saturation level (SpO2) meter. The camera can also be used for in-app Photoplethysmography (PPG) data acquisition, from which heart rate and heart rate variability indicators can be derived. The microphone is used to record audio snippets, with the purpose of detecting cough and periodically monitoring respiratory activity. One of the main features of the system is the ability to perform dense recording of temperature, heart rate, and SpO2, through a specialized external sensor (e-CoVig device). The mobile application sends all the collected data to a remote server where the medical staff is able to follow several subjects without need of direct interaction. In particular, the data of each patient is centralized on the BrainAnswer eHealth cloud-based platform, where it is stored, organized and visualized by the medical team, whom in this way can follow a high number of patients almost in real time, without the need for telephone or face-to-face interaction. The main goal of this system is to help the medical authorities in following these patients, improve the accuracy of the diagnosis and ultimately freeing them from house confinement in which they find themselves, as quickly as possible without risking contamination by third parties.

AppCovidMadeira

PRINCIPAL INVESTIGATOR	Bruna Ornelas de Gouveia
LEADING INSTITUTION	Agência Regional para o Desenvolvimento da Investigação Tecnologia e Inovação - Associação
FUNDING	€ 29 944

The spread of the SARS-CoV-2 virus demonstrates its pandemic potential and the severe epidemiological impact worldwide stances a great challenge to health care systems and public health organizations. While most COVID-19 patients are confined at home until recovery, monitoring of their symptoms and health status by public health authorities is needed. Surveillance is also important for those who have been in contact with a COVID-19 patient or have been in areas where community transmission is established.
Considering the ongoing epidemiological surveillance in a "test, track and trace strategy", it is urgent to have fast and effective means of communication between professional and citizens.
Focused mainly on communication and the monitoring of symptoms and health status, the AppCovidMadeira project aims to develop an application to support the work of public health authorities, looking for greater efficiency in the management of patients, contacts and travelers.
In this context, ITI / LARSyS researchers, in partnership with IASAÚDE, IP-RAM (Regional Health Authority), are developing a web and Android / iOS application, that allows the voluntary registry of people that may be at risk of developing COVID-19, with 3 areas of interaction for the user: 1 - Daily self-assessment of symptoms, psychological and global health status; 2 - Search of activities and places and information on its safety and availability; and 3 - Receive recommendations and information about emergency procedures and patient support line (including a link to the emergency line SRS24). The application ensures an immediate access and individualized feedback by the local public health professional, as well as, the storage of data for longitudinal analyzes and epidemiological projections.
The MadeiraSafeToDiscover system is the preliminary solution already developed in the AppCovidMadeira project and its implementation is ongoing since the 1st of July, in all points of entry of the Autonomous Region of Madeira. The system allows the voluntary registry of travelers entering the region and ensures their active or passive surveillance by the health authorities. On the 31st of July, 41 511 people were registered in the system; 13 646 of those were under surveillance of the health authorities, and 5 926 are automatically contacted and receive reminders and other information about the topic.

Produção e financiamento hospitalar no período pós-pandemia

PRINCIPAL INVESTIGATOR	Rui Manuel Candeias Santana
LEADING INSTITUTION	Universidade Nova de Lisboa
FUNDING	€ 29 858

O contexto pós-pandemia irá caracterizar-se pela perda dos níveis de riqueza atuais e previsivelmente por uma inferior capacidade orçamental para o sector público da saúde (SNS). A este cenário junta-se a evidência de estudos anteriores e a evolução do primeiro mês em Portugal da COVID-19, onde se identificam reduções substanciais dos níveis de produção dos hospitais e ULS. A desmarcação da atividade programada (consulta e cirurgia), o adiamento dos episódios durante este período, o aumento da procura não expressa, o acréscimo dos doentes infetados pela COVID-19 que continuarão a necessitar de resposta e os próprios efeitos que decorrerão da atual situação provocarão um aumento cumulativo de necessidades em saúde por responder que importa conhecer e planificar a sua resposta. Aos problemas da procura e oferta de cuidados de saúde, acresce uma incerteza sobre a evolução da própria pandemia: duração, proliferação, disseminação global, possíveis novas vagas, ou tratamentos efetivos.
Pretende-se desenvolver um projeto que complemente este e que tem como objetivos: estimar a produção e financiamento hospitalar no SNS e; criar cenários que permitam responder de forma planificada nos próximos 18 meses.
Para o efeito serão utilizados modelos interrupted time series para estimar os valores futuros acrescidos da procura não expressa e adicional. Os cenários serão construídos com base nos pressupostos e restrições existentes (recursos), a definir pela ACSS e mediante a situação existente no momento da sua elaboração.
Os resultados esperados são: a determinação da procura que se encontrará por resolver em cada hospital e ULS e respetiva alocação financeira que garanta as atividades de resposta no período pós-pandémico. Pretende-se apresentar os resultados a ACSS, ARS, aos hospitais e ULS, em forma de relatório e na página a desenvolver para o efeito. Como outputs científicos é esperada a produção de dois artigos.

R4COVID.1.110.2020

Promoting Mental Health During Pandemic - a digital platform for monitoring and intervention

PRINCIPAL INVESTIGATOR	Pedro Ricardo Luís Morgado
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 29 500

This project aims to understand in which way the COVID-19 pandemic influences mental health in the general Portuguese adult population. This information enabled the development of a digital platform for adequate mental health care and guidance to the ones in need during the pandemic. We intend to identify protective and risk factors for mental health during pandemic. To explore this, over 2000 participants have provided data regarding their home environment, employment status, sociodemographic variables and personality differences. Moreover, they filled weekly online questionnaires (during the time-period when the confinement measures were stricter) measuring anxiety, depression, stress, and obsessive-compulsive symptoms.
In a preliminary data evaluation, we found some protective factors for mental health such as gender, working, physical exercise and fewer exposition to media contents related to the pandemic. In individuals with previous psychiatric disorders, we found the negative effects of the discontinuation of therapeutic processes on measures of acute symptomatology1. These preliminary results are promising, and are currently being completed with a longitudinal analysis of the data to test the predictive value of the different variables2. Since adequate e-health technologies are needed to cope with situations such as the COVID-19 pandemic, one of the tasks of this project was to design a mental health web app (saudemental.p5.pt). The main goals are to assess psychological distress and to help people manage their symptoms and emotional difficulties. Concerning the psychological assessment, people will be able to assess symptoms of anxiety, depression, stress and obsessive-compulsive related. According to the main symptomatology presented, individuals will be given different psychotherapeutic techniques. We followed a cognitive behavioural therapy approach by providing tools such as psychoeducation, cognitive restructuring, grounding exercises, relaxation and mindfulness techniques, insomnia management and self-care activities. Users are also offered to engage IFDepression, a program to monitor and treat anxiety and depressive symptoms. Information about public mental health services and psychological help lines will also be provided for those who present moderate to severe symptomatology.

CertCOV R4COVID.1.186.2020

Certificate of Immunity for Healthcare workers through the serology study of SARS-CoV-2 infection

PRINCIPAL INVESTIGATOR	João Tiago Guimarães
LEADING INSTITUTION	Centro Hospitalar de São João, EPE
FUNDING	€ 29 500

SARS-CoV-2 serological surveys are the best tool to determine the spread of the disease, accessing who, when and for how long produce antibodies and what types of antibodies are involved in the immune response during the different stages of the disease.
To this end, we are focused on determining the SARS-CoV-2 seroprevalence in a set of healthcare workers from the Centro Hospitalar Universitário de São João (CHUSJ), one of the reference hospitals for COVID-19 and in determining the serological curve of the different antibodies that contribute to the immune response against COVID-19.
For that, it became essential to do a preliminary evaluation of a set of commercial serological tests whose validation in clinical samples was lacking. Thus, we are currently validating eleven serological tests, based on different methodologies and with potentially different applications, using around 400 serum samples from patients with COVID-19. We are able at the moment to report high specificities for seven of these tests, which range from 98.4 to 100% for the determination of IgM, IgG and total antibodies.
Regarding the seroprevalence in health professionals we are already able to report a SARS-CoV-2 seroprevalence of 1.5% in the laboratory healthcare workers group of CHUSJ. Although this group of laboratory professionals work in the Portuguese hospital that performed the largest number of tests between March 27 and May 8 (39.293 tests) we didn't find any case of infection in these professionals as a result of the delivery of healthcare. This can be explained by the successful protection of these professionals, namely from measures applied by the CHUSJ, some of them anticipating those that would later become national guidelines.
The impact of the knowledge coming from this study will allow us to: (1) more accurately determine the number of people infected or who have been exposed to the virus; (2) determine the potentially immune population and the duration of that immunity; (3) define more sensitive, faster and flexible diagnostic algorithms and (4) evaluate the efficiency of future vaccines.

Digital Platform for Supporting Chronic Patients and COVID-19 consultations and Monitoring in Primary Care

PRINCIPAL INVESTIGATOR	Luís Velez Lapão
LEADING INSTITUTION	Universidade Nova de Lisboa - Instituto de Higiene e Medicina Tropical
FUNDING	€ 27 000

The "PrimaryCare@COVID-19" team created a digital platform for primary healthcare to support and monitor chronically ill patients during the COVID-19 pandemic. This digital platform allows people with chronic diseases to have teleconsultations as an alternative to face-to-face consultations. This allows physicians and nurses to monitor chronically ill patients from a distance. This project is part of the digital health context, being an opportunity to manage people with chronic illness during epidemics, preventing their illnesses from getting out of control and avoiding unnecessary trips to healthcare and emergency services. This digital platform has "smart" components, such as algorithms that allow a set of alerts for doctors and nurses. The system's demonstration involved several physicians and nurses in three USF of the ARS Lisbon and Tagus Valley: USF das Conchas, USF Jardim dos Plátanos and USF Ribeirinha, and may be adopted by any other healthcare unit in Portugal. The R&D Team has 5 doctors (Bruno Heleno, Jorge Seixas, Jorge Correia, David Rodrigues and Margarida Conde) and 1 nurse (Vasco Pedrosa) and several digital health specialists (Miguel Mira da Silva, Mélanie Maia, Mariana Santos and João Gregório) in the team coordinated by Luís Lapão. Chronically ill people are particularly vulnerable to COVID complications. This platform is expected to improve the access of people with chronic illness to healthcare at a time of great burden on health systems. In addition, health professionals will be able to consult safely and rigorously, preventing those most vulnerable to complications from having to go to waiting rooms with many people. Finally, it will allow to reserve the spaces of the health units for those in which face-to-face observation by a nurse or physician is essential, reducing the risk of contagion within the health units. With this digital platform, health professionals will be able to safely consult and monitor adherence to medications, as well as inform them about COVID-19 measures.

A digital platform of activities for seniors in social isolation

PRINCIPAL INVESTIGATOR	Nadine Correia Santos
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 20 880

Social isolation is the primary preventive mechanism for COVID-19, but poses enormous societal challenges that affect the senior population. In addition to the distancing of family and friends, there is also a relevant impact regarding the suspension of organized social activities, whether recreational or physical, that are crucial in promoting functional capacity and quality of life. Resulting from a partnership of the Medical School at University of Minho, with the "Tempo Livre" and the P5 Digital Health Center associations, the senior population-directed "GIRO Project" offers content, advice and tips, via digital channels, for daily physical, cognitive stimulation, nutritional, cultural and recreational activities. It is a free platform that encompasses Facebook, YouTube, Instagram and WhatsApp channels. The latter particularly permits for personalized activities and one-on-one communication. Contents are generated, and/or selected, by the team with combined expertise in neuroscience, nutrition, physical therapy, psychology and public health. Summarily, in the 3 months of the project, the platform has averaged >1000 unique monthly interactions, reaching >700 established followers, particularly in Portugal and Brazil. Since the project inception, a total of 210 unique posts and/or content have been created and disseminated, comprising over 40 videos. The project acts on the health axis and has an important socio-cultural component, contributing to the promotion of a more resilient society in a time of need and in the absence of an habitual social structure. To this end, digital contents have also been adapted to a printed version already distributed to >600 seniors without ease of access to digital channels. The GIRO team is currently filming exclusive videos, covering physical activity and cognitive domains, that will be disseminated in the upcoming months. This strategy will be paired with social-inclusion workshops so to promote digital literacy in senior population. This type of support continues to be crucial even in a post-confinement phase, when social groupings and activities continue to be limited.

R4COVID.1.131/2020

Making the way out: model-based evaluation of exit strategies from the COVID-19 lock-down in Portugal

PRINCIPAL INVESTIGATOR	Ganna Rozhnova
LEADING INSTITUTION	FCiências.ID - Associação para a Investigação e Desenvolvimento de Ciências
FUNDING	€ 17 490

Government-imposed social distancing was implemented to reduce transmission of SARS-CoV-2 in Portugal. Our project aims to provide guidance on the implementation of exit strategies from the COVID-19 lockdown and preventing a potential second epidemic wave. Through mathematical modelling, we evaluate the expected impact of a suite of prevention interventions on the course of the epidemic to design effective strategies for COVID-19 control. The interventions include government-imposed social distancing also known as lockdown, self-imposed individual measures, different contact tracing and testing strategies. As part of this project, we recently demonstrated that information dissemination about COVID-19, which causes individual adoption of handwashing, mask-wearing, and social distancing, can be an effective strategy to mitigate and delay the epidemic. We stress the importance of disease awareness in controlling the ongoing epidemic and recommend that, in addition to policies on social distancing, governments and public health institutions mobilize people to adopt self-imposed measures with proven efficacy in order to successfully tackle COVID-19. We also demonstrated that a contact tracing strategy will only contribute to the containment of COVID-19 if it can be organised such that delays in the process from symptom onset to isolation of the index case and their contacts are very short. The process of conventional contact tracing should be reviewed and streamlined, while mobile app technology might offer a tool for speeding up the process. Reducing delay in testing individuals for SARS-CoV-2 should be a key objective of a contact tracing strategy. This work has been featured in various international and national media, including CNN, NBC, O Público, etc..

COVerskIn-D R4COVID.1.150.2020

A hydrogel patch to prevent skin lesions caused by personal protective equipment due to COVID-19

PRINCIPAL INVESTIGATOR	Joana Marques Marto
LEADING INSTITUTION	FARM-ID, Associação da Faculdade de Farmácia para a Investigação e Desenvolvimento
FUNDING	€ 9 750

The COVID-19 pandemic caused by the SARS-CoV-2 enforced the use of personal protective equipment (PPE), such as masks and visors, especially by healthcare professionals (HCPs). However, the prolonged and continuous use of PPEs are responsible for the constant frictional and pressure forces on the tissues, causing skin lesions. Some devices such as semipermeable skin protectors or dressing, padded dressings and hydrocolloid dressings, are already used to prevent skin lesions such as pressure ulcers. However, there are still uncertainties pertaining the protective effect of these devices and the costs of their use in health institutions is high. This project proposes an alternative strategy: a new prevention therapy to avoid cutaneous lesions as a result of PPEs use, by developing an individualized, low-cost, comfortable, biocompatible hydrogel patch with non-occlusive properties to be placed between the skin and the PPE. As a way to prevent such lesions, without changing the safety ability of the PPE, we developed an innovative, low-cost, comfortable, biocompatible hydrogel-patches, consisting on a thin hydrogel-patch with suitable properties for topical application, to introduce in the routine of HCPs can drastically increase their skin health and personal wellbeing without compromising the protective function of PPEs and therefore improve their caregiving duties, not only during the pandemic but also whenever the use of PPEs is mandatory.
A stable formulation of hydrogel-patch was obtained, presenting suitable pharmaceutical characteristics, such as high elasticity, adhesion to skin, a pH value compatible with the skin, and exhibited cutaneous compatibility and acceptability, being suitable for topical application. The hydrogel-patch can be easily compounded with standard hospital pharmacy equipment.
In a near future, the hydrogel-patch will be subjected to clinical investigations and evaluation simulating possible scenarios with HCPs to evaluate its performance and conformity.
Scale-up studies will also be performed to ensure that this product will be available to everyone, especially to HCPs.
Testimony from a hospital pharmacist "This hydrogel patches have been an amazing tool to protect my skin. Comfortable, adaptable, and easy to use on a daily bases.".

Optimal Control and Mathematical Modeling of the COVID-19 Pandemic: contributions to a systemic strategy for community health intervention

PRINCIPAL INVESTIGATOR	Cristiana João Soares da Silva
LEADING INSTITUTION	Universidade de Aveiro
FUNDING	€ 7 981

This project is a partnership between the research unit Center for Research & Development in Mathematics and Applications (CIDMA), hosted at the Department of Mathematics of the University of Aveiro, with the Public Health Unit from ACES Pinhal Litoral - ARS Centro, School of Health Sciences - Polytechnic of Leiria, CINTESIS/ESEP (CINTESIS – Center for Health Technology and Services Research, University of Porto), Department of Applied Mathematics II of the University of Vigo, Department of Statistics, Mathematical Analysis and Optimization, Department of Particle Physics and Department of Applied Physics of the University of Santiago de Compostela, in Spain.
Based on the construction of adequate mathematical models, one of the objectives of the project is to prevent and estimate the spread of the SARS-CoV-2 virus and to develop strategies to control and mitigate COVID-19. The assumptions of the models are based on epidemiological, socioeconomic, cultural and educational publicly available data. Our models fit the Portuguese COVID-19 spread evolution, at national and regional level. More than fitting the reality, we aim to find optimal strategies for the minimization of the number of active infected individuals with less social and economical cost, by applying the mathematical optimal control theory to the epidemic models. For example, optimal deconfinement strategies are proposed, ensuring that the Health System capacity is never overloaded. We also analyze the state of the public opinion and incorporate it into the model. In this way, we can consider and measure the willingness of the population to adhere to public policies relating to confinement or deconfinement strategies.
The project is based on the sharing of knowledge and experience of the teams that integrate it. The articulation with Public Health Services, is crucial so that the mathematical models and the optimal control solutions found can predict the necessary resources (example the number of individuals in intensive care units) in the short and medium term. To this end, computational tools are used and developed, monitoring the resolution process and early identifying new infection cycles.

COnhecer Mais PaRa Intervir melhor no contexto da MObilidade

PRINCIPAL INVESTIGATOR	Nuno Marques da Costa
LEADING INSTITUTION	Instituto de Geografia e Ordenamento do Território da Universidade de Lisboa
FUNDING	€ 40 000

COMPRI_MOV, is a project approved under the second phase of the call "Innovative solutions for quick implementation – COVID-19 (six months). This project intends to characterize the population daily mobility and associate it with epidemic process to assess the epidemic spread risk namely associated to commuting mobility in the territories, namely in large functional urban areas.
The project follows the work developed under project COMPRIME (approved in the first phase of the call), where the relationships between socio-economic and epidemic dynamics were studied.
After the emergency state and social confinement decreed, mobility intensity greatly dropped, in special those related to motorized trips. This project aims to answer to 3 main questions: How the pandemic changes the modal split to daily trips and is relation to geographic, demographics and socio-economic differences? How it changed the mobility behavior related to risk perception? And, after the slow return to a normal activity, the flows attend the same intensity and the same characteristics of the pre-pandemic period?
The project will integrate 3 levels of information: mobility data, linked to demographic, socioeconomic statistical information; tracing data; and a survey to evaluate the population daily mobility pattern and perception in an epidemic environment.
Preliminary results make evident the importance of daily trips between municipalities that traduces larger physical commuting flows, where public transportation assume a crucial role, namely in metropolitan areas.
As results, the project will identify risk areas and social economic vulnerable groups, contributing to a more effective spread simulation model, where mobility will be a central driver, contributing for monitoring and an effective policy definition.

R4COVID.2.608/2020

COVID-19 Barometer: Social Opinion – Knowing, Deciding, Acting. The Portuguese population, COVID-19 and the National Health Service Responses

PRINCIPAL INVESTIGATOR	Sónia Dias
LEADING INSTITUTION	Universidade NOVA de Lisboa - Escola Nacional de Saúde Pública
FUNDING	€ 38 500

In the absence of official information on how citizens are experiencing the pandemic and its effects, the COVID-19 Barometer Social Opinion, developed by NOVA National School of Public Health and currently with 180 thousand responses from citizens, monitors real time perceptions and behaviors, as well as socioeconomic, health indicators and effects of the measures to combat the pandemic. This monitoring is made through an online survey initiated in March 2020. The COVID-19 Barometer Social Opinion allows to quickly analyze the current situation and identify trends throughout the deconfinement stages and the dynamic evolution of COVID-19. The knowledge produced will be a basis of evidence useful for political and technical decision, for healthcare management, optimizing the response of the National Health Service during and after the pandemic, as well as for citizens through identification of health and literacy needs and vulnerabilities. Moreover, the project pursues the translation of evidence into effective practices to mitigate social and health inequalities, to ensure adequate and equitable access to health services and to improve health literacy. A multidisciplinary panel of experts gathering physicians, healthcare managers, epidemiologists, political decision-makers, public health and health promotion experts, as well as professional and patient associations will design practical strategies to minimize the impact of COVID-19, with a focus on the most affected vulnerable groups, but also contributing to improve the use of healthcare services and "to reconnect citizens" to healthcare. Networking is foreseen, namely through COVID-19 Barometer Social Opinion in Brazil and partnerships in other areas (e.g. mental health, violence and high-risk diseases).

R4COVID.2.504/2020

Effects of COVID-19 pandemic on psychological status and cognitive function of senior adults: follow-up of an established aging cohort

PRINCIPAL INVESTIGATOR	Teresa de Jesus da Costa Castanho
LEADING INSTITUTION	Universidade do Minho
FUNDING	€ 37 018

COVID-19 pandemic has brought unprecedented challenges to older adults' health. Seniors are at higher risk for serious illness and are also particularly vulnerable to mental issues associated with the pandemic. As the acute and long-term consequences of the pandemic on seniors' mental health are currently unknown, there is a need to gather high-quality data to ascertain its effects in order to develop intervention strategies. Thus, this project aims to investigate the COVID-19 impact on the psychological status and cognitive function in senior adults of Northern Portugal characterized by our team in previous aging studies before the pandemic. This study results from a collaboration between the ICVS, School of Medicine - UMinho and the Association P5 Digital Medical Centre. Using a telephone-based method, psychologists are collecting data on psychological morbidity, coping strategies, social support and cognitive function, which will be compared with the pre-COVID-19 findings. Information on COVID-19 infection preventive behaviors, lifestyle habits and daily routines during the state of emergency and after lockdown is also being gathered. To determine the long-term impact of this public health crisis, participants will be evaluated again 5 months after the first telephone evaluation. To complement this data, in the last month of the project, blood samples will be collected by a nursing team at participants' location to verify whether psychological alterations are associated with physiological parameters.
With this project we expect to obtain an accurate understanding of the neuropsychological consequences of the pandemic on older adults. Our results will be important to delineate strategies to mitigate and manage mental health risks on this vulnerable group.

R4COVID.2.694/2020

Mind The Mom: an online intervention for perinatal mental health in times of pandemic

PRINCIPAL INVESTIGATOR	Anabela Fernandes Araújo Pedrosa
LEADING INSTITUTION	Universidade de Coimbra
FUNDING	€ 27 500

"Mind The Mom: an online intervention for perinatal mental health in times of pandemic", proposed by CINEICC – University of Coimbra in collaboration with the Obstetrics Service of Maternity Daniel de Matos and the Clinical Psychology Unit of Centro Hospitalar e UNiversitário de Coimbra was approved in the 2nd edition of "RESEARCH 4 COVID-19" by Fundação da Ciência e a Tecnologia.
This project aims to (1) develop and test the preliminary effectiveness of a brief psychological intervention, in the form of a mobile application called Mind the Mom, containing information, exercises and cognitive-behavioural therapeutic strategies with proven evidence of promoting perinatal mental health; those strategies are adapted to the pandemic context and may be used in other similar risk situations; and (2) train health professionals in the use of universal preventive strategies indicated to promote maternal mental health, following a stepped-care model, including the integration of the Mind the Mom application in their clinical practice.
By fulfilling these main objectives this project aims to contribute to the minimization of the specific contingencies imposed by the pandemic on the perinatal population, which represent increased risks for women's mental health and for other maternal-infant's health outcomes. It also expects to help diminish the burden felt by health services, whose search increases when emotional disturbance or psychopathology develops.
The project arose from the experience with the Facebook page Mind the Mom (https://www.facebook.com/mindthemom) created in March make preventive strategies available to the perinatal population; the page will remain active and will serve to advertise initiatives and the disclosure of the project's results.
The building of the mobile application through which the psychological intervention will be delivered is on the way, and the necessary authorizations (namely the approval by the Ethics Committee) have been obtained.

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