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MEMBERS NEWS
Keeping you updated!

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Special issue on COVID-19

Since the start of the COVID-19 pandemic in February 2020 the GABRIEL network has been mobilized to meet the growing need for COVID 19 diagnostics, and to implement research projects on SARS-CoV2 in different fields, such as diagnostic, genomics, viral transmission routes, clinical trials…

This special edition of the GABRIEL newsletter highlights the activities of the GABRIEL network through the testimony of its members.

We would like to thank bioMérieux, which has provided a strong support with its reagent donation program for the diagnosis of COVID-19.

COVID-19 activities of the Charles Mérieux Center for Infectious Disease in Antananarivo, Madagascar

The COVID-19 pandemic began in Madagascar on March 23, 2020. Very quickly, it became essential to increase the number of PCRs to be carried out each day. The Malagasy government requisitioned the Charles Mérieux Center for Infectious Disease together with the Laboratory Rodolphe Mérieux at the University of Antananarivo to provide support to the Pasteur Institute of Madagascar. From April 23, 2020, the date the first tests were carried out at the CICM, until September 11, 2020, more than 6,000 PCRs were performed with the Chinese-built DAAN kit donated to the Malagasy government.

At the beginning, the test positivity rate ranged between 9% and 10%, and in mid-July it was between 50% and 55%. However, we must bear in mind that, initially, all contacts of confirmed cases were tested, whereas in mid-July it was mainly symptomatic patients. Samples were collected from

Contents

a nasopharyngeal, nasal, or oropharyngeal swab. Currently, four laboratories are officially operational for SARS-Cov-2 PCR testing in Madagascar, but 12 other laboratories in the provinces are able to carry out tests with GenExpert especially designed for the Covid-19 at a lower scale in terms of number of tests.

On September 11, 2020, 63,222 PCR tests have been carried out in Madagascar. Meetings for the sharing of experience are organized regularly by the Ministry of Public Health to identify all the problems encountered by laboratories, so that they can work together to find adequate solutions. In July, the CICM also received various consumables and reagents from the Mérieux Foundation. The CICM has planned to use these donations for research and for more widespread PCR testing in Madagascar. It is important to mention that CICM is conducting research on the nosocomial transmission of SARS-Cov-2 with three certified hospitals dedicated to Covid-19 infections in Antananarivo. The aim is to enroll and study 250 cases per hospital, a total of 750 enrollments in one year.

Luc Samison, Charles Mérieux Center for Infectious Disease in Antananarivo, Madagascar

Testimonial from Mame Diarra Bousso Ndiaye, a first-year PhD student in Madagascar

As a student at the University of Paris Versailles, I have been working on my thesis at the Institut Pasteur de Madagascar (IPM) since January 2020, thanks to a doctoral grant from the GABRIEL network. The subject of my thesis is the optimization of the management of tuberculosis (TB) and latent TB through the evaluation of diagnostic and prognostic tools using immunological biomarkers.

My thesis is a part of the APRECIT project, whose objective is to improve the management of latent tuberculosis in Madagascar and Cameroon, in cooperation with the Pasteur Institutes and the Mérieux Foundation.

The fight against the COVID-19 pandemic in Madagascar has mobilized all healthcare institutions and has strongly affected research activities, and this has therefore affected my work for my thesis. As a result, I have volunteered to provide support to research teams working on the molecular diagnosis of the SARS-CoV2 coronavirus with traditional qPCR and by GeneXpert

(Cepheid). I have been doing this work in the virology unit for over 12 weeks, where I have carried out viral RNA extractions from nasopharyngeal samples received mainly from hospitals.

Since June, I have been working on GeneXpert SARS-COV2 tests. It is a rapid, automated qPCR that delivers results within one hour. We use the GeneXpert as a matter of priority to urgently test samples from patients who are hospitalized or who have a severe form of the disease.

IPM is highly involved in the response against COVID-19 and has carried out more than 28,000 diagnostic tests since the onset of the pandemic. For this reason, a COVID-19 component was added to the APRECIT project. This new component measures the impact of COVID-19 on a specific patient population of people with tuberculosis and their household contacts.

Little is known about TB/COVID-19 co-infections. We hope to find answers to the following questions:

- What is the risk of an aggravated COVID-19 infection in tuberculosis patients?
- In the study population, what is the risk of triggering a latent tuberculosis infection into active tuberculosis in a patient who has contracted COVID-19?

Now that the peak of the epidemic in Antananarivo is behind us, and that research activities have gradually resumed at the IPM, I should be able to go back to my own research activities.

COVID-19 activities of Rodolphe Mérieux Laboratory in Lebanon

In the context of the global COVID-19 pandemic, and with the support of the Mérieux Foundation and the network of Rodolphe Mérieux laboratories worldwide, and at the request of the Ministry of Public Health (MOPH) of the Lebanese Republic, the Rodolphe Mérieux Laboratory of Lebanon was the second laboratory to perform SARS CoV-2 molecular diagnosis in Lebanon to support the laboratory of Rafic Hariri University governmental hospital.

To date the LRM has performed more than 12000 RT-PCR for the diagnosis of COVID19 in patients from different hospitals and primary health care centers and from community clusters in refugee camps and migrant workers shelters in collaboration with MOPH, Hotel Dieu de France hospital in Beirut, different private hospitals, the Amel association and other NGOs, IOM (International Organization for Migration), with the financial and technical support of the Mérieux Foundation.

For several months, the LRM has been actively engaged in the response to and in the fight against this pandemic, bringing together the skills of all health professionals: doctors, pharmacists, medical biologists, laboratory technicians, epidemiologists, and researchers.

Different research projects were initiated to study nosocomial transmission, the correlation between clinical and biological determinants, sequencing and genotyping of strains in collaboration with LBTM

(Laboratory of Biochemistry and Molecular Therapy at the School of Pharmacy at USJ) and the sero-prevalence study in the Lebanese population will be started soon.

Marianne Abi Fadel, Rodolphe Mérieux Laboratory, Lebanon & Josette Najar, Mérieux Foundation

Integrative computational platform for characterization of viral and host determinants in COVID-19 using OMICS approaches

The recent coronavirus (SARS-CoV-2) outbreak, which started in China in 2019, has raised an awareness for the need to understand the genetic and molecular mechanisms associated with the pathogenesis of COVID-19, as well as the severe clinical manifestations of the disease. The declarations of national emergencies reflect the urgency for acting in coordination to identify new cases when performing viral and host sequencing for the genomic characterization of the disease's clinical manifestations.

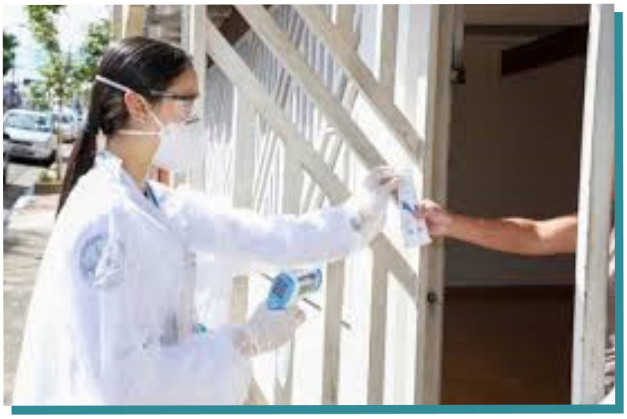
We thus aim to identify and characterize viral and host genomic factors that are involved in the pathogenesis of COVID-19, and associated with the clinical manifestations of the disease through the use of omics data (viral genomics, metagenomics, WES, and transcriptomics) and methodologies for Artificial Intelligence. Viral genomic data will be used in genomic surveillance studies through phylogenetic and phylogeographic reconstructions to assess epidemic dispersion and identify a transmission cluster. Exome and RNA-Seq data will be analyzed to identify prognostic markers and possible therapeutic targets, and to understand the genetic and molecular mechanisms of the disease to support diagnosis.

Our findings will be extremely important not only to elucidate the risk factors associated with cases in our Brazil, but also to understand the biology, pathology, viral immune response, and COVID-19-related aspects that can serve as predictive factors in the clinical follow-up of infected patients. This interdisciplinary project* involves researchers specialized in different areas (bioinformatics, biostatistics, mathematics, medicine, virology, genetics, cell biology) coming from different institutions in Rio de Janeiro and across the country, and seeks to identify the predictive factors that may explain the reasons for the susceptibility of a proportionally small population affected by COVID-19 to develop severe and fatal clinical manifestations.

**http://www.corona-omica.br-mctic.lncc.br, http://www.corona-omica.rj.lncc.br*

Ana Tereza Ribeiro de Vasconcelos, Laboratório de Bioinformática - Laboratório Nacional de Computação Científica (LNCC/MCTI), Brazil.

Laboratory of Medical Investigation of the Tropical Medicine Institute, São Paulo University



In Brazil, the first cases of COVID-19 were detected in February 2020.

Since the beginning of the epidemic, the Virology Laboratory of the Institute of Tropical Medicine has implemented various actions against the epidemic.

These consist in assisting COVID-19 patients and supporting different lines of COVID-19 research to be developed by the laboratory team.

In terms of assistance, the support for carrying out all diagnostic tests using the RT-PCR technique for the municipality of São Caetano do Sul (Corona São Caetano program) is noteworthy.

The Corona São Caetano program is a primary care initiative offering COVID-19 care to all residents of São Caetano do Sul, Brazil.

It provides universal detection and management of symptomatic cases and their contacts. This platform was developed in partnership with two local universities – the Municipal University of São Caetano do Sul (USCS) and the University of Sao Paulo (USP), also called “Corona São Caetano”.

Nasopharyngeal swabs (NPS – both nostrils and throat) were collected at the patients’ homes under the supervision of trained healthcare personnel. A link to a video (https://youtu.be/rWZzV2ZP7KY) was sent to the patients, before the home visit, to provide guidance on self-collection procedures. Healthcare personnel were instructed to maintain two meters from the patient and to wear personal protective equipment. Samples were immediately placed in a cold container at a temperature of between 2-8°C and stored at 4°C in a refrigerator until shipped to our laboratory within 24 hours.

During the period between March and August 2020, approximately 10,000 tests were performed.

Some of the lines of research developed by the laboratory team are in the following areas:

- Development of serological diagnostic tests - ELISA test and neutralization: The ELISA test has already been validated and is being used in some patient communities. The neutralization test is in an advanced stage of development.
- Performance evaluation of self-collection of saliva for diagnosis of SARS-CoV infection
- Standardization of a direct fluorescence assay for detection of SARS CoV-2 antigens in cell culture and in clinical samples

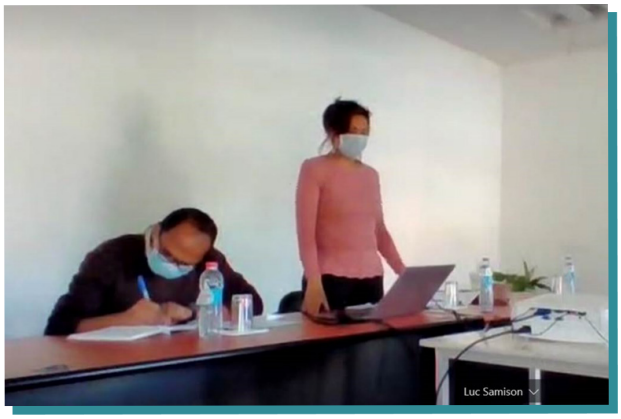
- Evaluation of viral shedding in different biological materials in patients with COVID-19
- Acute neurological manifestations associated with SARS-CoV2
- Detection of SARS-CoV2 in salivary glands and oral cavity
- Covid-19 in pregnant and postpartum women

Cassia Mendes Correa, Tropical Medicine Institute, São Paulo University, Brazil

Understanding and preventing nosocomial transmission of COVID-19 in LMICs: the NOSOCOR study

The NOSO-COR study is an international multicenter, prospective, observational, hospital-based study in adults and children. It will provide a reliable description of the cases of nosocomial COVID-19 infection and the potential chains of transmission, taking into account the infection prevention and control practices and policies in the hospital.

The principal aim of this study is to estimate the prevalence and incidence of suspected or confirmed cases of SARS-CoV-2 infection



among healthcare personnel and patients. The different activities carried out in the study are the description of community and hospital-acquired SARS-CoV-2 infections and their clinical spectrum and the documentation of infection prevention and control (IPC) practices implemented during the occurrence of hospital cases of SARS-CoV-2 in order to correlate these practices to the attack rates of nosocomial SARS-CoV-2 infection.

The Mérieux Foundation is conducting the study in partnership with the Lyon Civil Hospitals and partner institutions in the Ivory Coast (Institut National d'Hygiène Publique and Treichville University Hospital in Abidjan), Guinea (Institut national de Santé Publique and University Hospital in Conakry), Madagascar (Charles Mérieux Center for Infectious Disease of the University Ankatso in Antananarivo and the Befelatanana and Anosiala Hospitals in Antananarivo), Mali (Charles Mérieux Center for Infectious Disease of Bamako and Point G University Hospital), Bangladesh (iccdr,b Dhaka Hospital) Lebanon (Rodolphe Merieux Laboratory in Beirut and Saint Joseph Hospital) and Brazil (Hospital das clinicas) in Sao Paulo.

Valentina Sanchez Picot, Marie Moroso, Cindy Grasso, Florence Komurian Pradel, Mérieux Foundation

The strengthening for the SARS-CoV2 diagnostic

As of September 1, 2020, 24 shipments have been sent by the Mérieux Foundation (plus 19 shipments in collaboration with EVAg from Marseille) to 13 countries to provide diagnostic support to the Mérieux Foundation's partners. This corresponds overall to:

- 60 extraction kits (i.e. 15,000 sample extractions)
- 133 RT-PCR kits (for performing 10,000 tests) and primers and probes for the equivalent of 17,000 tests.

In addition:

EVAg has sent 19 positive controls to 12 countries.

As part of its donation program, bioMérieux is planning to send 94 Argene kits to our partners in Mali, Lebanon, Bangladesh, Cambodia, Madagascar, and Brazil.

COVID-19 diagnostics and Research Activities at ideSHi

In this moment of crisis during the global pandemic of COVID-19, ideSHi has shifted its research focus from basic research on immunology and molecular biology/genetics of infectious diseases to COVID-19-related works, including diagnosis and research.

IdeSHi is among the first of 10 organizations selected by the Bangladesh Government for COVID-19 detection. Until now, ideSHi has tested more than 20,000 samples for COVID-19. Diagnostic COVID-19 detection is carried out using the kit-based RT-PCR approach. In addition to the analysis of samples provided by the Government of Bangladesh for COVID-19 detection, ideSHi also analyzes those from a COVID-19 Testing and Triage booth run by a tripartite collaboration between ideSHi, Digital Healthcare Solutions, and Mugda Medical and Hospital in Dhaka.

In addition, ideSHi has conducted studies on the COVID-19 IgG immune responses to understand whether anti-COVID IgG responses can render protection to human hosts. For this, ideSHi was a partner in a seroprevalence study in collaboration with the Institute of Epidemiology, Disease Control and Research (IEDCR) and icddr,b in Dhaka, and Harvard University. To describe the role of IgG responses to COVID-19 infections, two manuscripts have been submitted for publication.

In another study, ideSHi has worked as a CRO in carrying out a clinical trial to investigate "Safety and Efficacy of Favipiravir (Favipira) for COVID-19 Treatment: A Double-Blind

Randomized Controlled Study." Furthermore, as a CRO, ideSHi has been involved in a validation study to investigate performance evaluation of a locally manufactured RT-PCR kit for COVID-19 detection.

IdeSHi has also performed MinION-based sequencing of the COVID-19 genome to understand source tracing, viral strains, and clinical manifestations.

Firdausi Qadri and Kaiissar Mannor, ideSHi, Bangladesh

The GABRIEL network receives support from bioMérieux and Bioaster.